Effect of Electrotherapy on Pain, Functional Activity, and Health-related Quality of Life of Nigerian Individuals with Knee Osteoarthritis

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Abstract

Osteoarthritis (OA) of the knee is a chronic degenerative articular disease that causes pain, limits joint mobility and physical function and reduces quality of life. Electrotherapeutic modalities such as interferential current (IFC) and therapeutic ultrasound (US) are used in the management of chronic pain and reduced physical activity in individuals with knee OA. It is not clear whether simultaneous application of these physical agents as a combination therapy (CT) would improve pain, physical activity and health-related quality of life (HRQoL) of individuals with knee OA.

Objective: This study aimed to determine the effects of CT, IFC, and US on pain, functional activity and HRQoL of individuals with knee osteoarthritis in Nigeria.

Participants: Participants diagnosed with knee osteoarthritis according to the American College of Rheumatology, attending the Physiotherapy Outpatient Units of Rasheed Shekoni Specialist Hospital (RSSH), the Federal Medical Centre (FMC), and Dutse General Hospital were recruited for the study. A total of 133 participants, with ages ranging between 58 and 82 years (mean = 66.19 ± 8.50 years) and out of which 53 (40%) were male and 80 (60%) were female (median = 56 years), participated in the study.

Methods: This is a multi-center randomized controlled study. The participants were randomly assigned to 4 groups*:* US (n = 34), IFC (n=34), CT (n=33), and control (n=32). Each group had 3 treatment sessions per week for 12 weeks. Participants in the control group received heat therapy using infrared radiation (IRR). The visual analogue scale (VAS), Western Ontario and McMaster Universities Osteoarthritis (WOMAC) Index, Short Form-36 Health Survey (SF-36) questionnaire, and goniometer were used to assess pain severity, functional activity, HRQoL and knee range of motion (ROM) respectively. All measurements were taken and recorded at baseline and post-treatment.

Main outcome measures: The primary outcome measures were pain, functional activity, and health-related quality of life, with active and passive knee range of motion being secondary outcomes. The variables were analyzed using one-way ANOVA, and independent and dependent sample *t*-test using the Statistical Package for the Social Sciences.

Results: At baseline, there were no significant differences ($p<0.05$) between all the groups on the primary (pain, physical function and HRQoL), and secondary (ROM) outcomes. One-way between-subjects ANOVA was conducted to compare the post-intervention effects of the electrotherapy combination (US & IFC) therapy with the control group on pain, functional

activity, and HRQoL. There were significant differences in the pain severity, physical function, and HRQoL scores ($p<0.05$) of participant in the electrotherapy (US, IFC & CT) groups compared to the control group. Post-hoc comparisons using the Tukey HSD test indicated that the mean scores of the electrotherapy groups differed significantly from the control group. However, comparisons were made between the intervention (US, IFC & CT) groups post-treatment. There was no significant difference ($p>0.05$) between each of the intervention groups (US, IFC &CT) on pain, functional activity and HRQoL post-treatment. In terms of effects, no interventional group was superior to another among the experimental groups.

Between-group comparison at follow-up (each group compared with the control group) showed significant improvement in measures of pain severity, improved physical activity and quality of life in each group. Changes in secondary outcomes, over time, were statistically significant ($p<0.05$) in the experimental groups (US, IFC, & CT). There were increases in knee range of motion, both active and passive. No differences were observed in knee range of motion, both active and passive, in the control group ($P >0.05$).

Conclusion: The use of electrotherapy modalities – CT (US & IFC), US and IFC – was beneficial as they elicited improvement in pain severity, functional activity and HRQoL in individuals with knee osteoarthritis, but none of the modalities proved to be more effective than the others.

DECLARATION 1 - PLAGIARISM

I, **Zubair Usman**, declare that:

1. This thesis was composed solely by me and that it has not been submitted, in whole or part, for another degree, and is my original research work.
2. This thesis does not contain other persons' data, pictures, graphs or other information, unless specifically acknowledged as being sourced from other persons.
3. This thesis does not contain other persons' writing, unless specifically cited as being sourced from other researchers. Where other written sources have been quoted, then:
    a. Their words have been re-written but the general information attributed to them has been referenced;
    b. Their exact words have been used, and then their writing has been placed in italics and inside quotation marks, and referenced.

DECLARATION 2 - PUBLICATIONS AND PRESENTATION/CONFERENCES

Conferences

1. Usman Z & Maharaj SS. The Influence of Combined Therapy and Therapeutic Ultrasound on the Quality of Life of Patients with Chronic Knee Osteoarthritis: A Randomized Controlled Pilot Study**.** Oral presentation at the 56th Annual Conference of the Nigeria Society of Physiotherapy. Held from 23rd to 29th of October 2016 in Kaduna State, Nigeria.
2. Usman Z & Maharaj SS. Effect of Interferential Current Therapy on Functional Activities and Health-related Quality of Life in Patient with Knee Osteoarthritis. Oral presentation at the Disability Conference organized by Department of Physiotherapy, Bayero University, Kano, Nigeria; 23rd to 25th August, 2016.DC-2016-PP-030.
3. Usman Z & Maharaj SS. Efficacy of Interferential Current and Infrared Therapy on Functional Activities in the Rehabilitation of Patients with Knee Osteoarthritis: a Randomized Control Trial Study. Oral presentation at the Annual Research Symposium organized by the College of Health Sciences, University of Kwazulu-Natal, Durban, South Africa, from 9th to 11th September 2016.

Publications

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DEDICATION

This thesis is dedicated to my parents, Usman Sidi and Rabi Usman who have always loved and supported me unconditionally, and whose good example and teachings have taught me to work hard for the things that I aspire to achieve in my life. They inculcated in me discipline and the value of learning.

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LIST OF ABBREVIATIONS AND ACRONYMS

ACR	American College of Rheumatology
ANOVA	Analysis of Variance
AAOS	American Academy of Orthopedic Surgeons
BMI	Body Mass Index
BP	Bodily Pain
BREC	Biomedical Research Ethics Committee
Ca+	Calcium Ion
COSMIN	Consensus-Based Standard for the Selection of Health Measurement Instruments
COX –II	Cyclooxygenase- II
CT	Combination Therapy
DC	Direct Current
EULAR	European League against Rheumatism
FMC	Federal Medical Centre
GDP	Gross Domestic Product
GH	General Health
HRQoL	Health-related Quality of Life
Hz	Hertz
IFC	Interferential Current therapy
IRR	Infrared Radiation
LLLT	Low Level Laser Therapy

MCS	Mental Component Summary
MH	Mental Health
Na+	Sodium Ion
NICE	National Institute for Health and Care Excellence
NSAIDs	Non-steroidal Anti-inflammatory Drugs
OA	Osteoarthritis
OARSI	Osteoarthritis Research Society International
PCS	Physical Component Summary
PF	Physical Functioning
Qol	Quality of life
RCT	Randomized Controlled Trial
RE	Role Limitation – Emotional
RF	Role Limitation – Physical
ROM	Range of Motion
RSSH	Rasheed Shekoni Specialist Hospital
SF	Social Functioning
SF-36	Short Form-36 Health Survey
SWD	Short Wave Diathermy
TENS	Transcutaneous Electrical Nerve Stimulation
UKZN	University of KwaZulu-Natal
US	Therapeutic Ultrasound
USA	United States of America
VAS	Visual Analogue Scale

VT	Vitality
WOMAC	Western Ontario and McMaster Universities Osteoarthritis Index

CHAPTER ONE

1.1 Introduction

Osteoarthritis (OA) is a chronic, painful and disabling joint disease (Mahir et al., 2016), which damages the articular surfaces of the bone, cartilage, and synovial membrane, causing swelling of the joint with newly formed bones and inflammation (Dieppe and Lohmander, 2005). It mostly affects elderly people; approximately 11% of adults aged 65 and above (Peat et al., 2001). Osteoarthritis is a common chronic disease and costly public health problem (Bennell et al., 2011). The disease is not limited to any ethnic group or geographical location. It is the most common long-term cause of disability, particularly in the elderly. Globally, it is estimated that 10% of people over the age of 50 years have OA, and 80% of people with the condition have movement limitations, with 25% not being able to perform major activities of daily living (Zhang et al., 2007a).

The incidence of OA increases with age and is greater in women than men (Reginster, 2002). Though the etiology of OA is unknown, it is generally a multifactorial disorder that involves genetic and environmental factors (Berenbaum, 2012). Factors affecting the progression of the disease include age, obesity, joint injury, genetic predisposition, gender, muscle weakness, race, inflammatory joint diseases and metabolic/endocrine disorders (Leslie, 2000). The knee is one of the joints most frequently affected by osteoarthritis with quite serious repercussion due to its weight-bearing nature.

The American College of Rheumatology (ACR) recommends the combination of pharmacological and non-pharmacological treatment for osteoarthritis (Hochberg et al., 2012). The goal of the treatment is to alleviate pain, improve and maintain joint mobility, reduce disability, improve health-related quality of life and limit the progression of the joint damage. Treatment also involves educating patients about the nature of the disease and its management (Zhang et al., 2007b). Treatment approaches should be individualized to suit each patient. Safer and conventional treatments should be the first option. Surgery should only be considered if pain control has not been achieved with conservative managements (Hunter et al., 2009, White et al., 2007). Pharmacological treatment includes the use of acetaminophen and glucosamine with or without chondroitin (White et al., 2007), Non-steroidal anti-inflammatory drugs (NSAIDs) are also effective for the treatment of osteoarthritis pain (Bjordal et al., 2004).

The use of non-pharmacologic treatment as part of the management of OA has become routine in outpatient physiotherapy units, with electrotherapy treatment modalities playing a

significant role. Currently, the electrotherapy modalities which have found wide application in the management of knee OA include low level laser therapy (LLLT), interferential current therapy (IFC), short wave diathermy (SWD), therapeutic ultrasound (US) and transcutaneous electrical nerve stimulation (TENS). These have been employed as adjunct therapies to enhance the relief of both acute and chronic pain and joint inflammation, increase functional ability through enhancing blood flow, inhibit nociceptive impulses, achieve pain gate control, blockade pain transmission through afferent nerves, sympathetic blockade, and release of endogenous opiate substances (Samuel and Maiya, 2015, Goats, 1990, Kitchen et al., 2002), and alleviate local muscle spasm (Yang et al., 2011). In a comparative study conducted to investigate the efficacy of TENS, IFC and SWD in patients with knee OA, Atamaz et al. (2012) concluded that electrotherapy modalities, exercise and education produced the best outcome in terms of pain relief, increase in range of motion (ROM) and decrease in disability.

Therapeutic ultrasound (US) is an electrotherapy modality commonly used by physiotherapists for the treatment of painful musculoskeletal conditions (Huang et al., 2005). It has demonstrated significant benefits in the treatment of knee OA, in reducing joint edema, improving joint range of motion (ROM), and accelerating healing (Huang et al., 2005). Research has shown that about 79% of orthopedic physiotherapy specialists in the USA administer ultrasound therapy at least once a week in their clinical practice (Sauers, 2005).

Melzack and Wall (1965) explained TENS and IFC as analgesic electrotherapy modalities that work based on the “pain gate theory”. According to the theory, cutaneous stimulation of afferent (large diameter) sensory fibers activates inhibitory neurons in the dorsal horn of the spinal cord and thus blocks the nociceptive signals which are carried through the smaller diameter fibers (A and C fibers). IFC produces stimulation deeper in the tissues through medium frequency modulated current, to overcome skin impedance (Watson, 2010). The currents produced are conveyed through high speed myelinated afferent fibers to higher centers (Samuel et al., 2015). Interferential current therapy is also clinically used in electro-analgesia to reduce edema, elicit muscle contraction and modify the autonomic nervous system (Goats, 1990).

The current management trend for knee OA is control of pain, improvement of functional status and enhancing quality of life (QoL) (Ondrésik et al., 2016, Salaffi et al., 2005). Several researchers have found that the lowest QoL was usually reported for chronic musculoskeletal diseases, and the highest results were found for hip and knee OA, osteoporosis, rheumatoid arthritis and fibromyalgia (Picavet and Hoeymans, 2004). The clinical presentation of knee

OA has a direct and negative impact on patient's social interactions, sleep, and physical and mental functioning (Muraki et al., 2010). Therefore, assessment of QoL is an important outcome in quantifying the disease impact and evaluating the effects of an intervention. The Medical Outcomes Study Short Form-36 Health Survey (SF-36) has been used for arthritis, rheumatoid arthritis, spinal problems and other musculoskeletal disorders. Thus, the SF-36 health survey questionnaire is an outcome measure that has been extensively treated and shown to be reliable and valid in different populations (Jenkinson et al., 1994).

1.2 Background to the problem

It is estimated that 10% of people older than 55 years have symptoms of OA, either radiologic, clinical, or both and a quarter are severely disabled. The incidence of OA is expected to increase by 40% by the year 2050, largely due to increase of the aging population and the obesity epidemic (Woolf and Pfleger, 2003). As a medical disorder, OA is now also identified in younger adults (Sowers et al., 2000), thus, if a simple effective conservative and/or non-invasive intervention is not developed, joint replacement surgery may become the treatment option in younger adults, to maintain mobility and quality of life. In the elderly population with knee OA, reduced quadriceps muscles strength and increased postural sway have been identified as causes of frequent falling. Falling in the elderly population is a significant health issue in today's society (Hausdorff et al., 1997). However, the prevalence of the disease has been identified as a burden not only on the health care system of a country but also on the economy. Governments at all levels are currently facing problems regarding the rational management of health care resources. The economic burden consists of direct and indirect costs. Directs costs are associated with drugs, medical services, maintenance or running of health facilities such as hospitals, research, and personnel costs. Indirect costs consist of premature mortality, and short and long-term morbidity resulting in loss of working hours. As the most widespread form of a musculoskeletal disease, OA is estimated to cost 1-1.5% of the gross domestic product (GDP) of developing countries (Reginster, 2002).

The pharmacologic treatment of OA is mostly the symptomatic approach; to relieve the pain using analgesic drugs such as NSAIDs (Cox-I and Cox-II inhibitors). The disadvantages of NSAIDs include poor safety profile, gastropathy, renal and cardiovascular complications (Chan et al., 2008), allergic reactions, and drugs interactions (Conaghan, 2012). Thus, prostaglandin analogue drugs (misoprostol) have been combined with NSAIDs to reduce the risk of gastropathy (Committee and Britain, 2012). The combination did not yield any fruitful result (White et al., 2007). Selective cyclooxygenase-II (Cox-II) inhibitors were found to

have a significant role in vascular disorders such as myocardial infarctions and stroke (Hippisley-Cox et al., 2005). Practitioners are, therefore hesitant to prescribe the medications due to reasonable adverse effects and risk of taking NSAIDs, especially in elderly patients who are most likely to have chronic knee OA (Bjarnason et al., 1993).

Studies show that high increases in physical and psychological stress associated with individuals with knee OA worsen clinical symptoms, consequently reducing QoL (Kawano et al., 2015). It has been stated that amplitude modulated frequency (AMF) is the main electro-analgesic component of IFC (Noble et al., 2000a), which achieves its pain modulation by stimulating afferent large-diameter nerve fibers. There is strong evidence that IFC is an effective therapeutic physical modality in the treatment of painful musculoskeletal problems such as sports injuries, bruising and swelling, low back pain, osteoarthritis, rheumatoid arthritis, and muscular pain (Jarit et al., 2003, Eftekharsadat et al., 2015, Lara-Palomo et al., 2013, Wong et al., 2007). Therapeutic ultrasound is one of the most frequently applied electrotherapeutic modalities in orthopedic physiotherapy (Wong et al., 2007). It produces thermal effects which increase tissue metabolism, collagen elasticity, and capillary blood flow, and reduces skeletal muscle spasm (Kapidzic, 2011). Therapeutic ultrasound is often used in the management of knee osteoarthritis and is believed to be effective in enhancing inflammatory response and tissue repair, and is absorbed especially in tissues (Atamaz et al., 2012)

Besides the individual therapeutic effects of ultrasound and interferential current therapy, their combination (combination therapy [CT]) is more effective than each of them applied separately in eliciting localized analgesia in previously detected painful areas (Jones et al., 2014). CT was shown to be effective in relieving pain and improving quality of sleep following a treatment of patients with fibromyalgia (Almeida et al., 2003).Furthermore, in spite of advances in technology and the availability of state-of-the-art electrotherapy equipment, there has not been adequate evidence-based research exploring the effect of the use of combination therapy on functional activity and QoL as part of treatment for individuals with OA. This study therefore aimed to investigate the effect of the use of electrotherapy combination (CT: US + IFC) on pain, physical activity and quality of life of Nigerian rural dwellers suffering from knee OA.

1.3 Research Questions

Osteoarthritis (OA), a chronic and progressive disease of the joint cartilage and bone, is the most frequent degenerative joint disease (Litwic et al., 2013b) associated with enormous socioeconomic burden, in addition to physical and psychological consequences. Essentially, the burden of suffering imposed on individuals with this condition is of major concern. This burden can be significant with far-reaching adverse consequences. Pain or discomfort, with restriction or loss of functions are the basic domains of this burden, and collectively, often significantly lead to increased dependency in activities of daily living, with the consequent substantial decrease in quality of life (QoL) (van Dijk et al., 2008; Elliott et al., 2007).

The use of non-pharmacologic approaches such as electrotherapy in the management of chronic musculoskeletal conditions such as OA could reduce dependence on the administration of drugs which are associated with adverse effects. Consequently, the following research questions might be used to guide this study:

1. What are the therapeutic effects of combination therapy (CT: US+IFC), IFC, and US on pain, functional activity and HRQoL of Nigerian individuals with knee OA?
2. Are there any differences in the therapeutic effects of combination therapy (US+IFC), IFC and US on pain, functional activity and HRQoL of Nigerian individuals with knee OA?

1.4 Objectives of the study

The objectives of this study were to determine:

1. The effect of combination therapy, IFC and US on pain, functional activity, and HRQoL of Nigerian individuals with knee OA.
2. The differences between the effects of combination therapy of US+ IFC, IFC and US on pain, functional activity, and HRQoL of Nigerian individuals with knee OA.

1.5 Significance of the study

Osteoarthritis of the knee is a painful chronic degenerative joint disease that reduces functional status and quality of life, and therefore has a major impact on activities of daily living. The findings of this study will provide evidence-based information that would be used in the rehabilitation of patients with chronic knee osteoarthritis. Also, it would reduce patients' dependency on the use of drugs. Thus, it is hoped to significantly reduce the adverse effects associated with drug therapy such as gastrointestinal bleeding, myocardial infarction, polypharmacy, drug interactions and so on. This area is not well investigated. A large volume

of information would thus be provided by this study on the effects of the use of US, IFC & simultaneous application of IFC and US on HRQoL and physical function in the rehabilitation of patients with knee osteoarthritis. Published documents in this area are inadequate and most of the information is anecdotal or based on the experiences of those who use the modality frequently (Watson, 2010).

Therefore, this study was designed, using randomized controlled intervention, to determine the effects of US, IFC and the simultaneous application of US & IFC on pain, physical function and QoL in the management of individuals with knee osteoarthritis.

The outcome of the study is expected to be:

1. An important additional strategy that could be used in the rehabilitation of osteoarthritis patients to improve physical function and quality of life. Also, it would make available new data, which would add to existing literature on the use of IFC, US and combination therapy in the rehabilitation of patients with impaired physical function and quality of life.
2. A source of literature that future researchers can use for reference or as a guide to obtain useful information about electrotherapy combination therapy in the rehabilitation of patients with chronic musculoskeletal conditions. The findings of this study could serve as an impetus that would stimulate more interest in research on US, IFC and combination therapy for individuals with knee osteoarthritis and other musculoskeletal disorders. In addition, clinical evidence with empirical and accepted explanations of the therapeutic effects of combination therapy would be provided. Physiotherapists may use these findings as a source of evidence-based management to enhance functional activity and quality of life of patients with knee osteoarthritis.
3. Evidence in clinical decision-making in the rehabilitation of patients with knee OA. Thus, it is expected to reduce the overdependence on pharmacological therapy which is associated with adverse effects such as gastropathy, cardiovascular complications, polypharmacy, and drug interactions. Furthermore, it could reduce the burden of the cost of pharmacological treatments as well as improve the quality of life of Nigerian patients with knee OA.

1.6 Hypotheses of the study

The following are the major null and alternative hypotheses for the study:

1. **H_I**: Pain, functional activity measures and HRQoL will be different between the experimental (US, IFC & CT) groups and the control group in patients with knee OA.
2. **H_0**: There will be no differences in pain, functional activity measures and HRQoL between the experimental (US, IFC & CT) groups and the control group in patients with knee OA.
3. **H_I**: Pain, functional activity measures and HRQoL will be different in the combination therapy group (CT: US & IFC) compared to the control group in patients with knee OA.
4. **H_0**: There will be no differences in pain, functional activity measures and HRQoL between the combination therapy group (CT: US & IFC) and the control group in patients with knee OA.
5. **H_I**: Pain, functional activity measures and HRQoL will be different in the IFC group compared to the control group in patients with knee OA.
6. **H_0**: There will be no differences in pain, functional activity measures and HRQoL between the IFC group and the control group in patients with knee OA.
7. **H_1**: Pain, functional activity measures and HRQoL will be different in the US group compared to the control group in patients with knee OA.
8. H_0: There will be no differences in pain, functional activity measures, and HRQoL between the US group and the control group in patients with knee OA.

1.7 Summary

Osteoarthritis of the knee is a degenerative articular disease associated with joint instability, pain on weight bearing and/or at rest, reduced range of motion, reduced functional ability and a compromise in quality of life of the patients. Treatments include pharmacological and non-pharmacological approaches. Non-pharmacological methods include various electrotherapy modalities with US and IFC being widely used by physiotherapists in the management of OA and other chronic musculoskeletal disorders.

Despite the established evidence on the therapeutic efficacy of electrotherapy in the management of musculoskeletal disorders, the combined therapeutic effects of US with the electro-analgesic effect of IFC in the management of patients with knee osteoarthritis and on health-related quality of life have not been elucidated. Also, there is little or no published work on the effects of US and IFC on HRQoL of Nigerian individuals with knee OA. Most of

the information is anecdotal and based on the experiences of those who use the modalities frequently. Thus, there is a paucity of research on the effect of US, IFC and combination therapy (US and IFC) in the management of knee OA with respect to change in QoL, functional activity, and pain in Nigerian patients with knee OA.

Therefore, the aim of the study was to evaluate the effect of US, IFC and combination therapy (US & IFC) on pain, physical activity and HRQoL of Nigerian individuals with knee osteoarthritis compared to a control group.

CHAPTER 2

Review of the Literature

2.0 Overview

Osteoarthritis is the most common degenerative joint disease that causes pain and disability. Pain is the important symptom of knee osteoarthritis and the most frequent reason individuals with osteoarthritis see a health care provider (Coriolano et al., 2016). The degenerative changes ensuing from osteoarthritis not only cause pain, but also stiffness and swelling that result in chronic disease and disability. In people with advanced age, it seriously alters quality of life (QoL). This literature review includes the epidemiology of osteoarthritis, pathophysiology and risk factors, diagnosis and treatments, the role of electrotherapy in its management, the efficacy of therapeutic ultrasound (US) on knee OA, the efficacy of interferential current therapy (IFC) and the effects of combination therapy on musculoskeletal disorders.

2.1 Epidemiology of Knee Osteoarthritis

Osteoarthritis is the most common degenerative joint disease (Felson and Zhang, 1998) and a major public health problem throughout the world (Millennium, 2003, Arden and Nevitt, 2006). The disease is characterized radiographically by marginal osteophytes formation, destruction of joint cartilage, cyst formation and subchondral bone changes (Andrianakos et al., 2006, Arden and Nevitt, 2006). Clinical symptomatology includes joint pain, loss of function, and limitation of range of motion (Murphy et al., 2016). It is a primary cause of chronic disability in people over the age of 50 (Zhang and Jordan, 2010, Michael et al., 2010). The prevalence of knee osteoarthritis has been increasing with the increase in the aging population and the obesity epidemic; by 2050, the prevalence of the disease is expected to increase by 40% (Woolf and Pfleger, 2003). Studies have shown that knee OA in men aged 60 to 64 affected the right knee more (23%) than the left knee (16.3%), while in women, the distribution was evenly balanced with 24.2% presenting with the right knee and 24.7% with the left (Andrianakos et al., 2006, D'Ambrosia, 2005).

According to World Health Organization (WHO) reports on the global burden of diseases, knee OA is likely to become the fourth most important cause of disability in women and the eighth in men. According to the 2010 global study estimate of burden of disease, hip and knee OA were ranked as the 11th highest contributor to global disability and the 38th highest

in years of life lived with disability. Knee OA is one of the leading causes of global disability (Cross et al., 2014). Also, osteoarthritis is accountable for approximately 2% of all public health expenses (Le Pen et al., 2005). Currently, there is no cure for the disease as the mechanism by which it arises and progresses remains unclear (Michael et al., 2010). Thus, the goal of treatment is to relieve pain, increase/restore joint functions, slow the disease progression and improve the patient's quality of life. The American College of Rheumatology (Gamble et al., 2000) and the Osteoarthritis Research Society International (Zhang et al., 2010) recommend a combination of pharmacological and non-pharmacological management. Physiotherapy is a non-pharmacological approach that is widely used in the rehabilitation of both acute and chronic musculoskeletal disorders. Electrotherapy modalities such as IFC, US, and TENS are found to be effective (Adedoyin et al., 2005, Gundog et al., 2012, Ulus et al., 2012). Pain and other clinical symptoms negatively affect quality of life, both physical functions and psychological aspects.

2.2 Definition of Osteoarthritis

Though there are different definitions of OA, both symptomatic and radiographic definitions are widely combined clinically. The most commonly used radiographic grading system for knee OA is the "Kellgren-Lawrence" (K-L) grading system which determines the severity of radiographic OA on the basis of the presence and degree of osteophytes, joint space narrowing, sclerosis of the subchondral bone and deformity affecting the tibiofibular joint, irrespective of clinical symptoms (Fig. 2.1). Radiographic OA of the knee usually is defined by a K-L grading of 2 or higher. K-L grading is also used for the hip, hand and other joints (Suri et al., 2012). The standard for increasing severity of osteoarthritis according to the K-L system is shown in table 2.1 and characterized with sequential features of osteophytes, joint space loss, sclerosis and cyst. The K-L 2-3 grade could be classified as minimal to moderate OA, characterized with definite osteophytes, unimpaired joint space to moderate diminution of joint spaces. Clinically, this may translate to ambulant knee OA patients. Fig 2.2 indicates an estimate of radiographic OA prevalence among men and women (Arden and Nevitt, 2006).

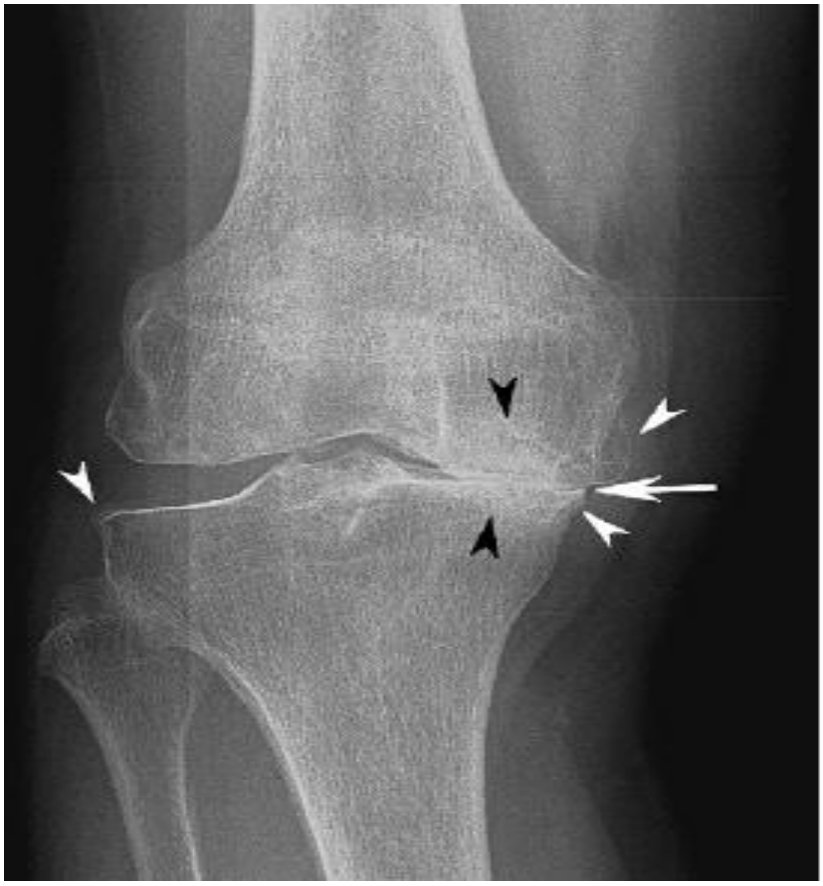

Figure 2. 1 A weight-bearing plain radiograph of the knee depicting the characteristic features seen in OA: medial tibiofemoral joint space narrowing (white arrow), marginal femoral and tibial osteophytes (white arrowheads), and medial tibia and femoral subchondral sclerosis (black arrowheads). Adopted from Hunter, (2009).

Table 2.1 The Kellgren-Lawrence grading system of osteoarthritis

Radiological features on which grades were based		
Formation of osteophytes on the joint margins or, in the case of the knee joint, on the tibial spines		
Periarticular ossicles; these are found chiefly in relation to the distal and proximal interphalangeal joints		
Narrowing of joint cartilage associated with sclerosis of subchondral bone		
Small pseudocystic areas with sclerotic walls situated usually in the subchondral bone		
Altered shape of the bone ends, particular in the head of the femur		
Radiographic criteria for assessment of OA		
Grade 0	None	No features of OA
Grade 1	Doubtful	Minute osteophyte, doubtful significance
Grade 2	Minimal	Definite osteophyte, unimpaired joint space
Grade 3	Moderate	Moderate diminution of joint space
Grade 4	Severe	Joint space greatly impaired with sclerosis of subchondral bone

Reproduced from Spector and Cooper (1993. *Osteoarthritis and Cartilage* 1:203–206) with permission.

Adopted from: Arden, N. & Nevitt, M.C. (2006). Osteoarthritis: epidemiology. *Best practice & research Clinical rheumatology*, *20*(1), 3-25.

Symptomatically, OA is defined as the presence of radiographic OA in combination with symptoms which include pain, stiffness, damage to articular cartilage, abnormal remodeling of sub-articular bone, marginal osteophytes (Arden and Nevitt, 2006).

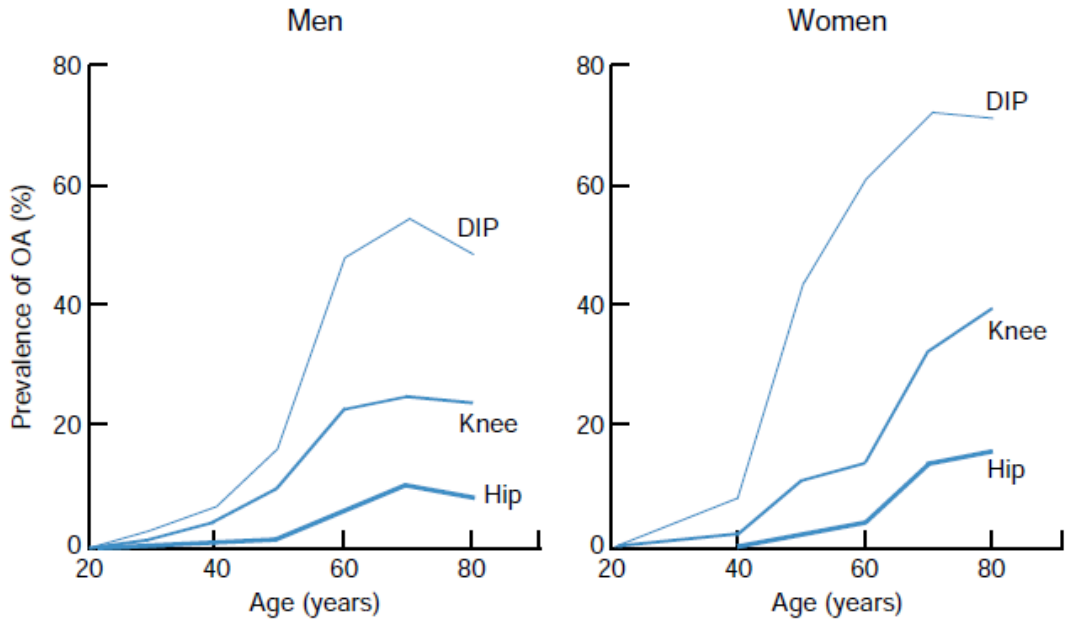

Figure 2. 2 Estimates of the prevalence of radiographic osteoarthritis (OA) affecting the distal interphalangeal (DIP) joint, knee and hip in a large Dutch population sample. By Arden, N. and Nevitt, M.C., 2006. Osteoarthritis: epidemiology. Best Practice & Research Clinical Rheumatology, 20*(1), pp.3-25.*

2.3 Pathogenesis of Osteoarthritis

OA develops as a result of multiple interactions between systemic and local factors (Muraki et al., 2013). The degenerative processes lead to joint pain, swelling, reduced joint range of motion resulting in limited functional activity and disability (Zhang and Jordan, 2010). As a result of this combination of risk factors, which include advancing age, trauma, knee misalignment (varus or valgus deformity), increased biomechanical loading secondary to obesity and overweight, reduced bone density and physiological imbalances (Yusuf, 2012, Eaton, 2004).

Normally, healthy cartilage produces positive joint loading and increases regional thickness, however, in disease or injury state, the cartilage degenerates and decreases in regional thickness (Vincent et al., 2012, Andriacchi et al., 2009). The quality of this matrix is critical for maintaining the functional properties of the cartilage (Dieppe and Lohmander, 2005). Cartilage is uniquely adapted to withstand mechanical stress because of the presence of an elaborate extracellular matrix made up of proteoglycans, aggrecan and type 2 collagen (Martel-Pelletier, 2004). Chondrocytes, which are the only cells in cartilage, are responsible

for maintaining the slightly altered matrix components by the chondrocytes (Aigner et al., 2006).

According to Pelletier (2001), the disease process is generally divided into 3 stages. Stage I is the proteolytic degradation of cartilage matrix. Stage II is the stage at which cartilage fibrillation and erosion take place; this results in the release of broken-down products into the synovial fluid. Stage III, the presence of broken parts of the cartilage in the synovial fluid, leads to synovial inflammation. This triggers the process of phagocytosis by the synovial cells and produces proteases and inflammatory cytokines. These events at molecular level result in early morphological changes in cartilage surface fibrillation, cleft formation and later, loss of cartilage volume (Dieppe and Lohmander, 2005). Within the joint, there is also thickening or sclerosis of the subchondral bone and episode synovitis (Tonia & Wall, 2010), development of osteophytes at the margin through ossification of cartilage outgrowths, and major changes in the vascularity and turnover of the subchondral bone (Dieppe et al., 1993). Subchondral bone changes could be an important part of the pathogenesis of progressive joint diseases (Mazzuca et al., 2004), partly because the bone has greater ability to repair, adopt and change the shape of the joint than cartilage, and there might be an association between progression and osteoporosis (Dieppe and Lohmander, 2005).

2.4 Diagnostic Criteria

The most widely used OA diagnostic criteria were developed by the American College of Rheumatology (Sarzi-Puttini et al., 2005). These criteria identify subjects with clinical OA using joint pain for most days of prior months as the major inclusive criteria (Poitras et al., 2007). This contrasts with the use of radiographic changes alone, wherein many subjects do not report joint pain. The algorithms for classification were developed by comparing patients with site-specific joint pain due to other arthritic or musculoskeletal diseases (Arden and Nevitt, 2006). According to the ACR, a diagnosis of knee OA is confirmed if the following radiographic and clinical symptoms are present (Altman et al., 1991): (1) clinically when there is knee pain for most days of the prior month, (2) crepitus on active joint motion, (3) morning stiffness of <30 minutes duration (4) age >38 years, (5) bony enlargement of the knee on examination (Sarzi-Puttini et al., 2005). Table 2.2 shows the ACR criteria of osteoarthritis diagnosis.

Table 2. 2 American College of Rheumatology Criteria for OA of the hand, hip and knee

. American College of Rheumatology (ACR) criteria for OA of the hand, hip and knee.

Hand	Clinical	OA is present if the items present are
	1. Hand pain, aching or stiffness for most days or prior month 2. Hard tissue enlargement of two or more of ten selected hand joints[a] 3. MCP swelling in two or more joints 4. Hard tissue enlargement of two or more DIP joints 5. Deformity of one or more of ten selected hand joints	1, 2, 3, 4 or 1, 2, 3, 5
Hip	Clinical and radiographic	
	1. Hip pain for most days of the prior month 2. ESR ≤20 mm/h (laboratory) 3. Radiograph femoral and/or acetabular osteophytes 4. Radiograph hip joint-space narrowing	1, 2, 3 or 1, 2, 4 or 1, 3, 4
Knee	Clinical	
	1. Knee pain for most days of prior month 2. Crepitus on active joint motion 3. Morning stiffness ≤30 minutes in duration 4. Age ≥38 years 5. Bony enlargement of the knee on examination	1, 2, 3, 4 or 1, 2, 5 or 1, 4 5
	Clinical and radiographic	
	1. Knee pain for most days of prior month 2. Osteophytes at joint margins (radiograph) 3. Synovial fluid typical of OA (laboratory) 4. Age ≥40 years 5. Morning stiffness ≤30 minutes 6. Crepitus on active joint motion	1, 2 or 1, 3, 5, 6 or 1, 4, 5, 6

MCP, metacarpal joint; DIP, distal interphalangeal joint; ESR, erythrocyte sedimentation rate; PIP, proximal interphalangeal joint; CMC, carpometacarpal joint.

[a] Ten selected joints include bilateral second and third PIP joints, second and third PIP joints, and first CMC joints.

Reproduced from Arden and Nevitt (2006).

2.5 Risk Factor of Osteoarthritis

The risk factors for developing OA are determined by systemic/genetic and biomechanical factors. Several systemic factors have been identified (Andriacchi et al., 2015) and include obesity and metabolic disease, age, gender, race, genetics, nutrition, smoking, bone density and muscle function (Litwic et al., 2013a, Felson et al., 1997, Garstang and Stitik, 2006), as shown below in figure 2.3. Studies have shown there are specific factors linked to progression in individuals with previous OA diagnosis such as knee misalignment, low vitamin D and C levels and obesity (Felson, 2013, Glover et al., 2012).

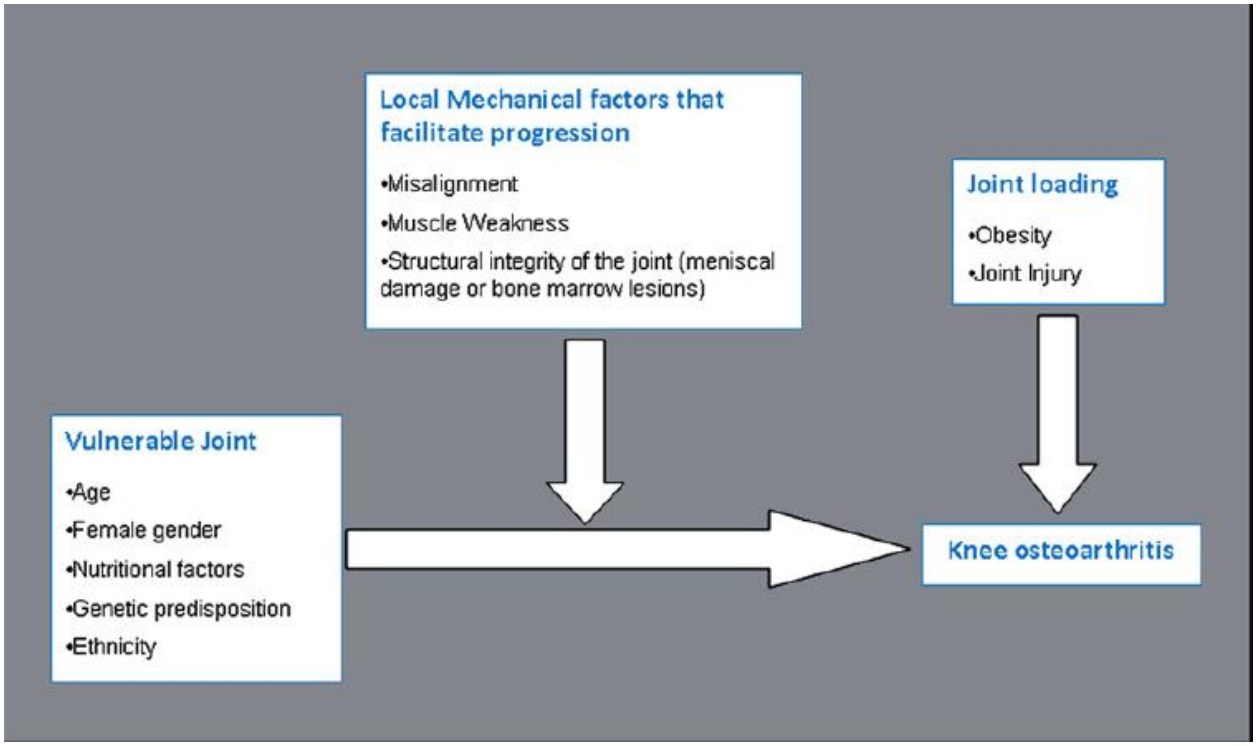

Figure 2. 3 Schemata demonstrating the risk factors for OA onset and progression. Adopted from (Hunter, 2009).

2.5.1 Aging and osteoarthritis

Age is critical to the widespread incidence of knee OA. The relationship between age and OA has been described as a "wear and tear", where gradual and progressive articular stress over a period of time causes cartilage to break down and lose it functions (Felson et al., 1987). Radiographic and symptomatic OA have shown a considerable positive correlation with age increase (Felson, 1990). Studies have shown the involvement of numerous factors that enhance the process; these include oxidative damage, thinning of cartilage, muscle weakening, and a reduction in proprioception (Hunter, 2009). Furthermore, basic cellular mechanisms that maintain tissue homeostasis decline with aging, leading to an inadequate

response to stress or joint injury and resultant joint tissue destruction and loss (Litwic et al., 2013a).

A study (Zhang and Jordan, 2010) has shown that about 13% of women and 10% of men aged 60 and above present with symptomatic knee OA; the number of affected individuals with symptomatic OA is likely to increase due to the increase in the aging population and obesity. Close to 10% of individuals aged over 55 have painful disabling knee OA, one quarter of whom are severely disabled (Peat et al., 2001).

2.5.2. Gender as risk factor

Studies have shown a higher prevalence of OA in women than men (Felson, 2004, O'Connor, 2006), and in women it increases drastically at the time of menopause (Srikanth et al., 2005). In a study by Keefe et al. (2000), the reported prevalence of OA is as high as 68% in women compared to 58% in men aged 65 and older. Also, women have a greater level of pain perception and functional impairment than men (Cicuttini and Spector, 1995).In a community based study conducted in Nigeria, Ojoawo et al. (2016) reported that the prevalence of knee OA is higher in female than male.

Srikanth et al. (2005) conducted a meta-analysis study based on population and found that men had a lower risk of prevalent radiographic knee OA (risk ratio 0.63, 95% confidence interval [95% CI] 0.53 – 75) and incident radiographic knee OA (incidence rate ratio 0.55, 95% CI 0.32 – 0.94), (incidence rate ratio 0.64, 95% CI 0.48 – 0.86), and prevalent radiographic hand OA (risk ratio 0.81, 95% CI 0.73 – 090).

In a longitudinal study conducted by Nishimura et al. (2011), aimed to investigate risk factors for the incidence and progression of radiographic knee osteoarthritis among Japanese individuals, it was reported that female gender (odds ratio [OR] 2.849, 95% confidence interval [CI] 1.170-6.944) was significantly associated with the incidence of knee OA. The rates of incidence and progression of knee OA among 360 participants (241 women, 119 men) who fulfilled the study criteria were 4.0 and 6.0% per year respectively.

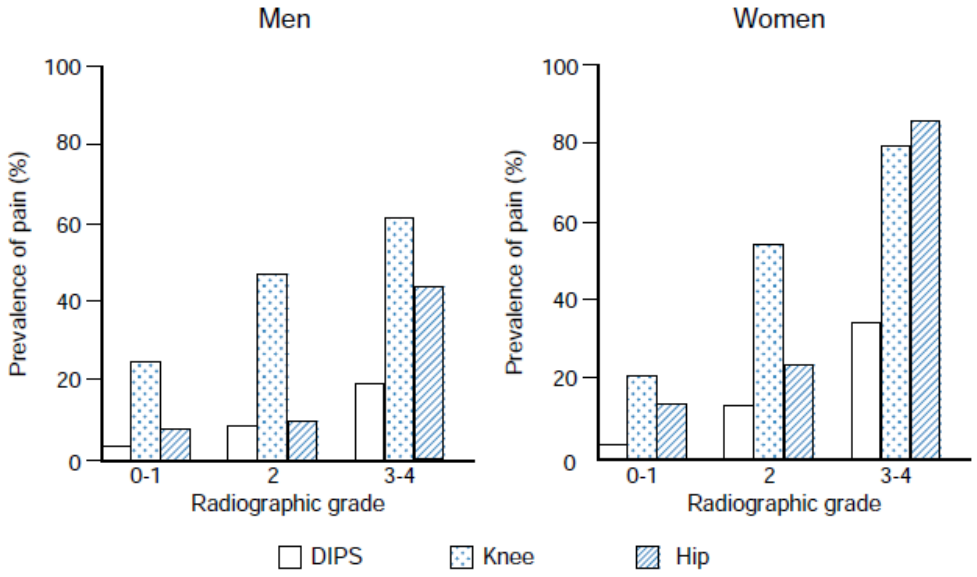

Figure 2. 4 Joint symptoms and radiographic features of osteoarthritis (OA). Data from Lawrence (1977. Rheumatism in Populations. London: Heinemann). ***Adopted from:*** *Arden, N., & Nevitt, M. C. (2006). Osteoarthritis: epidemiology. Best Practice & Research Clinical Rheumatology, 20(1), 3-25.*

2.5.3 Ethnicity and race

The prevalence and characteristics of OA vary among different racial and ethnic groups. There is clear evidence that a significant number of black Americans have a similar overall incidence rate of knee and hip OA as compared to white Americans (Arden and Nevitt, 2006, Tepper and Hochberg, 1993), with a slightly higher prevalence of knee OA in black women than in white women. Zhang and Jordan (2010) conducted a comparative study between Chinese and white Americans and reported equal prevalence in knee OA in men, and a greater prevalence of knee OA in Chinese women than white American women.

2.5.4 Genetic influences to OA

A study has shown positive correlation between development of knee OA and genetic component. Valdes et al. (2007) reported that heritability estimates for the influence of genetic factors in radiographic OA knee, hip and hand are 30%, 60% and 59% respectively, with a similar range of estimates for cartilage volume change and progressive knee OA.

All types of OA have strong positive correlations with genetic factors, which accounts for at least 60% of hip and hand and up to 40% of knee OA (Spector and MacGregor, 2004). Many studies indicated that different genes have been identified, including the gene for vitamin D receptor insulin-like growth factor (Felson et al., 2000), and type 2 collagen and growth differentiation factor 5 (GDF5) (Palotie et al., 1989), and play a significant role in OA pathophysiologic processes and thus contribute to OA risk. These genes may thus serve as a target for the pharmacological approach to treatment of OA. However, many of these study

findings are yet to be confirmed in all ethnicities and populations possibly due to phenotype evaluation of control on social differences (Johnson and Hunter, 2014).

2.4.7 Obesity

Obesity increases the risk of OA having both systemic and mechanical effects. An obese or overweight person has nearly 3 times the risk of incidence of knee OA compared with those who are of normal weight (Felson et al., 1997, Neogi and Zhang, 2013, Silverwood et al., 2015). It was discovered that changes in BMI by $\geq$ 2 units had the significant effect of reducing the risk of developing knee OA in women who had undergone the Framingham study (Felson et al., 1997). Similarly, the Johnson country study found a 30% reduction of the risk of developing symptomatic knee OA for a person with a BMI 18-25, 47% risk reduction for a person with a BMI of 25 – 30, and 61% risk reduction for a person with a BMI > 30 (Nelson et al., 2010).

2.4.8 Sarcopenia

Muscle weakness may be an important risk factor for knee OA (Scott et al., 2012). Men and women with pre-existing radiographic evidence of knee OA have been identified as having weaker knee flexor muscle groups than those without OA, particularly when the joints are symptomatic (Puenpatom and Victor, 2009).

There is evidence indicating that a patient with OA is more likely to develop sarcopenia as this was linked to inflammatory activities in the condition (Haseeb and Haqqi, 2013, Loeser, 2010). Inflammatory cytokines such as interleukin-1b (IL-1b) and tumor necrosis factor (TNF-a) are shown to play a significant role in protein catabolism (Roubenoff et al., 1997). This explains the reduction in muscle mass in patients with this condition due to reduced physical activity as a result of arthritic pain (Scott et al., 2012).

It has also been shown that muscle weakness occurs around the knee in the absence of pain or any muscle wastage. This may be due to arthrogenous inhibition of muscle contraction. Quadriceps weakness has strong correlation with prevalence of knee OA and evidence suggests that thigh muscle strength may protect against knee-joint damage and progression of existing OA (Litwic et al., 2013a).

Recent data show that greater muscle mass was positively associated with medical tibial cartilage volume, and lower limb muscle strength at baseline was positively associated with total cartilage volume change (Sharma et al., 2003). Quadriceps muscle weakness could potentially contribute to increasing loading of the knee joint (Amin et al., 2009). However,

there is considerable evidence that lower limb strengthening exercises improve this symptom (Sharma et al., 2003).

2.4.9 Mechanical Risk Factors

Acute and chronic injuries to the articular structures, such as meniscal or cruciate tears, can predispose an individual to high risk of knee OA. Also, strong blunt and direct crush injuries, including fracture and dislocation of the articular surfaces can directly increase the risk of development of OA (Hunter, 2009).

2.4.10 Excessive Repetitive Joint Loading

Joints are highly specialized organs that allow repetitive pair force and largely frictionless movements. This function occurs particularly because of articular cartilage and notably, its ECM, which plays an essential role in load transfer across the joint (Egger et al., 1995). However, repetitive loading of normal joints can exceed the tolerance of a joint and cause degeneration (Aigner et al., 2006). Occupational overuse of the knee joint in obese subjects or in jobs that require repeated kneeling, squatting, or bending, as well as lifting of heavy loads is a risk factor for knee OA, and it has increased the incidence of knee OA in men by 15 – 30% (Dieppe and Lohmander, 2005). It was shown that participation in sports that repetitively expose joints to high levels of impact also increase the risk of joint degeneration.

2.5 Management of Knee Osteoarthritis

Currently, knee osteoarthritis has no cure. The objectives of the management of the disease are to relieve pain, improve and maintain function, decrease disability, slow the disease or prevent progression and improve quality of life. Several clinical practice guidelines (CPGs) exist in rheumatology, which are intended to facilitate knowledge translation from research to evidence-based practice and clinical decision-making in the management of osteoarthritis (Brosseau et al., 2014). However, there are some management approaches which are only used sub-optimally, and which need further clinical studies to educate both clinicians and patients about their significance in improving health outcomes (Porcheret et al., 2007). For clinicians to make the best and precise clinical decisions, health professionals should be equipped with high quality CPGs. Several systematic reviews have reported that the management of OA should be considered from both the pharmacological and non-pharmacological approaches (Misso et al., 2008, April et al., 2013, Brand et al., 2013, Brosseau et al., 2014).

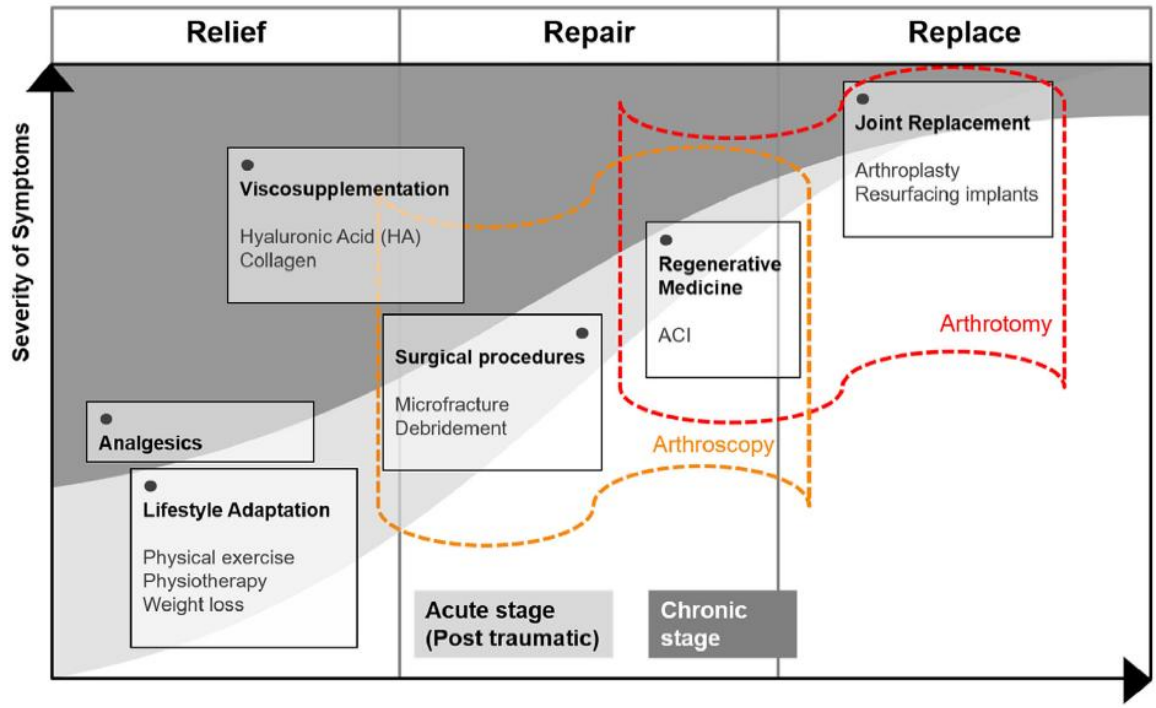

Figure 2. 5 Schematic representation of the current approaches for osteoarthritis management, depending on the severity of symptoms. Analgesics and lifestyle adaptation are the first options to postpone osteoarthritis development and provide pain relief. Viscosupplementation displays a more invasive approach, and is usually applied when there is an increasing pain experience caused by damage to the cartilage. Viscosupplementation is applied to restore the rheological properties of the synovial fluid and to ease the pain. Surgical procedures such as micro fracture and debridement are applied to slow down cartilage erosion, while autologous chondrocyte implantation (ACI) aims to regenerate the degenerated cartilage surfaces. In cases where the above mentioned applications are insufficient, the only solution left is replacement of the joint. Arthroplasty and surface replacements are the most invasive approaches at present, and only applied in established osteoarthritis. Adopted from (Ondrésik et al., 2016).

2.5.1 Pharmacological Approaches to Knee OA

Consensus guidelines and recommendations of various experts have been developed to concisely update patient-focused pharmacological management of knee osteoarthritis. These guidelines are intended to inform all stakeholders in the management of knee OA, viz. patients, physicians, and other health care professionals.

In a systematic review study, Mahendira and Towheed (2009) reported that the European League Against Rheumatism (EULAR), the American College of Rheumatology (ACR), and the National Institute for Health and Care Excellence (NICE) have recommended the use of pharmacological approaches in the management of knee OA. The bodies recommended, if the need arises, the use of local pharmacological therapies such as topical NSAIDs and capsaicin for systemic therapies. However, non-selective oral NSAIDs at the lowest effective doses were recommended due to their efficacy. Both short and long-acting and partial agonist opioids have been shown to improve pain in OA (Goodman, 1996). However, long-term use

of these drugs leads to severe side effects. It was also recommended that, treatment shall be individualized and localized (McAlindon et al., 2014).

2.5.2 Non-Pharmacological Approaches to Knee OA

Typically, the objective of non-pharmacological treatment is to reduce or eliminate clinical symptoms such as pain, joint stiffness, physical dysfunction and disability that are associated with knee OA, and to improve QoL of the patient. Different professional societies have published recommendations for the management of knee and hip osteoarthritis. These include the American College of Rheumatology (ACR), the Osteoarthritis Research Society International (OARSI) (McAlindon et al., 2014), the European League Against Rheumatism (EULAR) (Fernandes et al., 2013), and the American Academy of Orthopedic Surgeons (AOOS) (Nelson et al., 2014).

According to the above professional societies' guidelines for the management of knee OA, non-pharmacological treatment of knee OA involves the use of exercises (land and water-based), self-management and education, strength training, weight reduction management and physical therapy. These evidence-based recommendations can only be used as guidance, based on clinical experts' and panel input to patients and practitioners on treatment of all patients with knee OA.

2.6.0 Physiotherapy Management of Knee Osteoarthritis

Physiotherapy approaches have been shown to be beneficial in relieving pain, improving functional activity, increasing joint range of motion, and improving the quality of life of individuals with knee OA. Such modalities include transcutaneous electrical nerve stimulator (TENS), shortwave diathermy, therapeutic ultrasound, interferential current therapy and many forms of manual therapies.

2.6.1 Therapeutic ultrasound: production

Therapeutic ultrasound (US) refers to mechanical vibrations that are converted to acoustic energy through mechanical deformation. This deformation is possible with the transducer (treatment head) that holds a piezoelectric crystal (Johns, 2002a). This crystal contracts and produces a polarity under the transducer which is described as a direct piezoelectric effect. It then expands and reverses polarity which is an indirect piezoelectric effect, and in turn, produces the US. When these acoustic waves are absorbed by the body tissue, it results in oscillatory movements (Watson, 2008). The oscillatory movements occur when the acoustic or sound waves bring about a mechanical change. Mechanical changes occur with thermal as well as non-thermal US depending on the parameter setting (continuous or pulse).

2.6.2 Therapeutic effects of therapeutic ultrasound

Therapeutic US can simply be defined as sound waves or pressure waves with a frequency between 16-20 kHz which is above the limit of human hearing (DYSON and Pond, 1973). The sound energy is transformed into mechanical energy in the tissues depending on the frequency. The energy is absorbed, propagated, or reflected into the tissues to exert physiological effects. The machine generates two types of US modes, namely continuous and pulsed modes. The continuous US generates thermal effects that stimulate increased capillary blood flow, tissue metabolism, collagen elasticity, and subsequently brings about muscle relaxation and decreases muscle spasms (Rand et al., 2007). The pulsed mode exerts its therapeutic effects mainly by producing non-thermal physiological effects that stimulate increased tissue metabolism, increase fibrous tissue extensibility, improve the inflammatory process and relieve pain (Johns, 2002b, Baker et al., 2001).

Several studies, including experimental, animal, and human research, have reported that the use of US can stimulate an array of systematic bio-effects that may be used in the management of various musculoskeletal disorders (Doan et al., 1999, Dromi et al., 2007, Zhang et al., 2016).

In an experimental study, Doan et al. (1999) investigated the vitro effects of ultrasound that could revert or prevent the hypoxia, hypo-vascularity and hypo-cellularity observed in osteoradionecrosis. The authors concluded that therapeutic US in vitro can stimulate cellular proliferation, collagen/non-collagenous protein (NCP) production, bone formation and angiogenesis. Several clinical trial studies have proven the therapeutic effect of US in managing musculoskeletal pain (Ebadi et al., 2014), and improving joint range of motion (Morishita et al., 2014) and functional activity (Zhang et al., 2016).

2.6.3. Efficacy of therapeutic ultrasound on knee osteoarthritis

Zhang et al. (2016) conducted a meta-analysis aimed at investigating the effects of therapeutic ultrasound on pain, physical function and safety outcomes in patients with knee osteoarthritis. The authors chose only randomized controlled trials that compared the effect of therapeutic ultrasound with sham ultrasound or no intervention on pain and physical function in patients with knee osteoarthritis. A total of 2493 articles were searched, out of which only 10 trials with a total study population of 645 patients were considered for the study. It was concluded that US is beneficial for relieving knee pain and improving physical function in patients with knee osteoarthritis and could be a safe treatment modality.

Similarly, Zeng et al. (2014) investigated the efficacy of continuous and pulsed ultrasound (US) in the management of knee osteoarthritis (OA). They identified 1796 articles and

assessed them for eligibility; only 12 studies met the study inclusion criteria. The authors reported that pulsed therapeutic ultrasound was more effective in both improving pain and physical function when compared with the control group. However, they added that the use of continuous therapeutic ultrasound could only be considered as a pain relief treatment in the management of knee OA. The study also assured that none of the modes is dangerous.
In a meta-analysis conducted by Welch et al. (2003), an attempt was made to review the effectiveness of ultrasound therapy for the treatment of patellofemoral knee pain syndrome. The authors selected all randomized controlled trials (RCTs), controlled clinical trials (CCTs), case control and cohort studies, comparing therapeutic ultrasound against placebo or other active interventions in people with patellofemoral pain syndrome according to an a priori protocol. They critically assessed the normal methodological quality of the RCTs and CCTs using a validated scale. Out of 85 articles searched, only 8 articles were potentially relevant (fulfilled the study criteria). In addition, only one RCT, with 53 participants with patellofemoral pain syndrome, identified for the review, met the study criteria. The authors concluded that ultrasound therapy was not shown to be clinically important. Their conclusions were limited by the poor reporting of the therapeutic application of the ultrasound and low methodological quality of the one trial that met the inclusive study criteria.

Similarly, Welch et al. (2001) conducted a systematic study to investigate the effect of US in the treatment of patellofemoral pain syndrome. They concluded that therapeutic ultrasound was not shown to relieve pain for patients with knee osteoarthritis. They attributed this to insufficient qualities and quantities from the studies reviewed.

Rutjes et al. (2010) carried out a meta-analysis study comparing the therapeutic effects of US with sham or usual care on pain intensity and functional activity in patients with knee and hip OA. Four articles met the inclusion criteria with a total of 341 patients with OA. They concluded that US may be beneficial for pain relief and improvement of functional status of patients with knee OA. This finding is consistent with that of Özgönenel et al. (2009) which stated that US significantly improved pain relief and function in patients with knee OA.

Theoretical, biological and clinical rationales for the use of US in the management of non-surgical knee OA have been reported. Therapeutic acoustic radiation is transmitted into the target tissues via US as high-frequency pressure waves generated by the piezoelectric crystal in the sound head (transducer) of the US machine. These pressure waves produce mechanical

effects and/or thermal effects aimed at heating the deeper tissues to increase blood flow, local metabolism, tissue regeneration and collagen elasticity, and decrease inflammatory response and/or enhance soft tissue heading (Bailey et al., 2003). The non-thermal mechanical effects are achieved through the application of pulsed, low-intensity US (Johns, 2002a).

The above indicate inconclusive review results on the effectiveness of US in the management of knee OA. These controversies may be due to the low quantity and quality of the research conducted, particularly on the methodology, study population, and outcome measures. Further research on the efficacy of US in the management of knee OA with better research designs of sound quality and quantity need to be carried out.

2.6.4 Interferential current therapy (IFC): Definition

Interferential current therapy (IFC) is a form of electrical stimulation that is produced by superimposing two medium frequency currents (i.e. carrier current) so that they produce an amplitude modulated at low-frequency (0–250 Hz). These currents are set up so that their paths cross, and in simple terms, they interfere with each other. This interference gives rise to *an interference or beat frequency,* which has the characteristics of low-frequency stimulation.

2.6.5 Principle of interferential therapy

According to the study conducted by Nemec (1959), IFC production is based on 2 fundamental aspects, namely (1) using medium frequency, skin impedance is reduced, (2) application of two medium frequency currents simultaneously produces a low-frequency current which is termed "beat" frequency with "beating" effects.

Basically, the principle of interferential current therapy (IFC) utilizes the application of current modulation that is integrated by constructive and destructive interference from the two circuits (Goats, 1990). Normally, for low-frequency electrical stimulation to exert its effects, at sufficient intensity and tissue depth, the patient experiences unpleasant sensations and discomfort in the tissue (skin). This discomfort is due to the skin impedance (resistance) which is inversely proportional to the frequency of the stimulation. In other words, the lower the stimulation frequency, the greater the impedance, which means more discomfort is experienced as the current is passed into body tissue. The skin impedance at 50Hz is approximately 3200 whilst at 4000Hz it is reduced to approximately 40. However, stimulation of body tissues with higher frequency will pass more easily through the skin, needing less electrical stimulation to reach the deeper tissues with mild discomfort and unpleasant sensations.

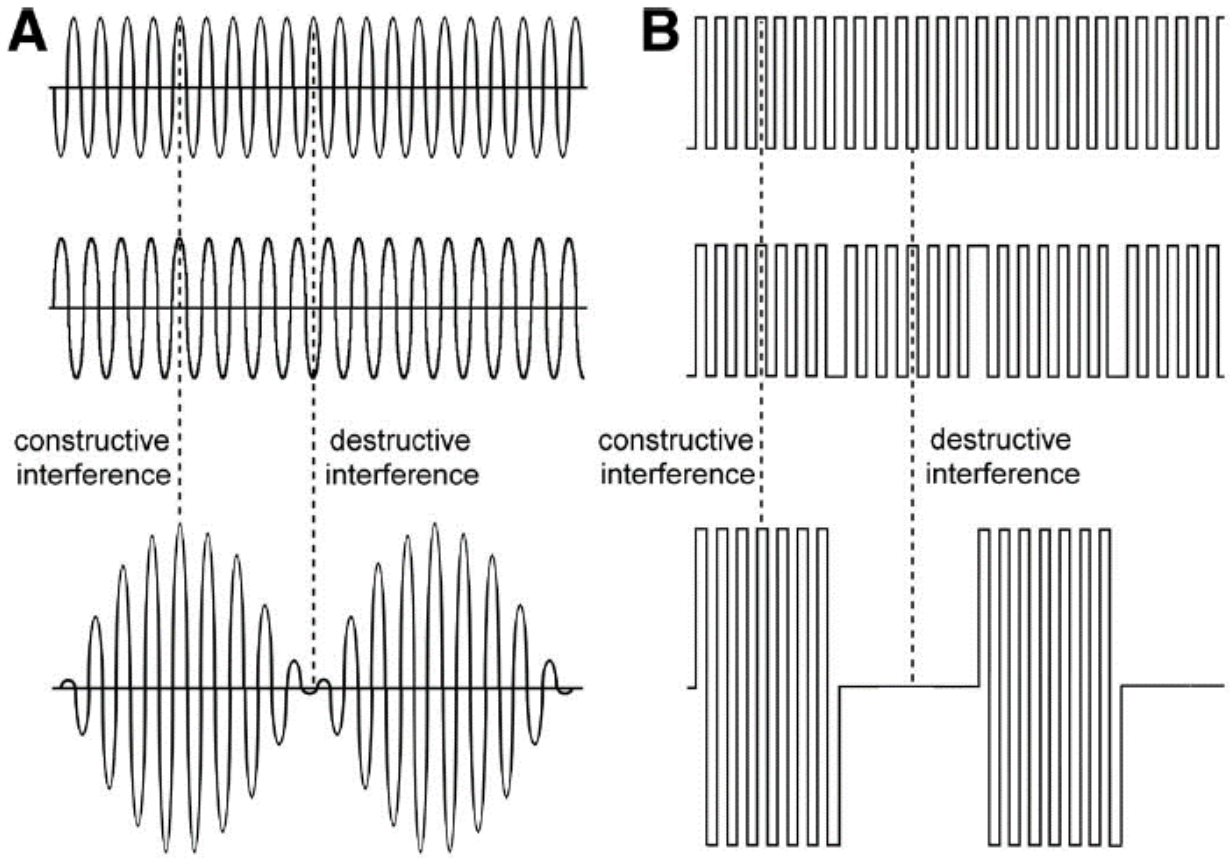

Figure 2. 6 The resultant current produced by (A) interference of 2 sinusoidal currents of different frequencies and (B) interference of 2 rectangular pulsed currents shifted in and out of phase. Adopted from "A Comparison of True and Premodulated Interferential Currents" Source: Ozcan et al., 2004.

A combination of different waveforms is used to produce sinusoidal waveform. This is achieved as the current drifts smoothly in and out of phases (Fig.2.6A). A rectangular waveform is produced as a result of sudden movement change of the current in and out of the phase (Fig. 2.6B).

The machine can either be bipolar or quadra-polar. The 2-pole electrodes can be successfully achieved by electrically manipulating the machine parameters to generate amplitude modulated current within the machine system (Fig. 2.7), and the output is termed pre-modulated IFC (also known as bipolar or exogenous IFC). In quadra-polar arrangements, 4 electrodes are placed subcutaneously with constant amplitude modulated frequency current via 2 different circuits and the currents cross and interfere within the body tissues (Fig. 2.7) (Ozcan et al., 2004).

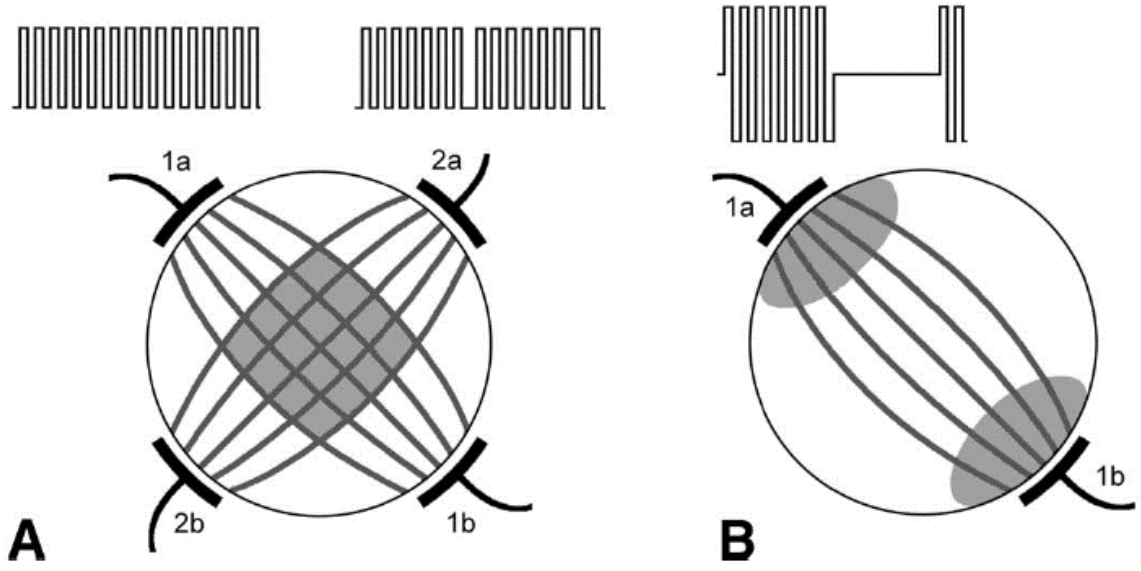

Figure 2. 7 Regions of maximum stimulation (shaded), which are predicted with application of (A) true and (B) premodulated IFCs. Adopted from "A Comparison of True and Premodulated Interferential Currents" by Ozcan, J., Ward, A. R., & Robertson, V. J. 2004, Archives of physical medicine and rehabilitation, 85*(3), 409-415.*

2.7.0 Therapeutic Effects of IFC

2.7.1 Interferential current therapy and pain management

Several studies have shown that IFC is widely used in clinical practice in the management of both acute and chronic musculoskeletal pain of various conditions and different patient populations.

Fuentes et al. (2016) conducted a systematic review and meta-analysis study attempting to evaluate the available literature on the therapeutic efficacy of IFC in the management of musculoskeletal pain. They concluded that the use of IFC as a supplement to another intervention seems to be more effective in reducing pain when compared with a placebo in the management of musculoskeletal pains.

In a randomized and single-blind study, (Gundog et al., 2012) reported the superiority of IFC with some gain on pain and disability outcomes when compared with sham IFC for the management of knee osteoarthritis. Studies have shown that IFC achieves electro-analgesic effects as explained through the "Pain Gate Theory" postulated by Melzack and Wall (1967). The theory explains that activation of afferent smaller nerve fibers causes pain, and that stimulating the larger diameter nerve fibers leads to inhibition of nociceptive impulses from the smaller diameter nerve fibers where the pain is reduced. This explains a physiological "gating mechanism" at the dorsal horn of the spinal cord. The 'gate' opens and closes to

allow or inhibit transmission of nociceptive impulses to the higher center of the brain where it will be processed.

However, since studies have demonstrated that interferential therapy is an effective electro-therapeutic modality in producing a consistent hypo-analgesia in both clinical and experimentally-induced pain, physiotherapists may have increased confidence in its clinical application.

2.7.2 Muscle stimulation

Studies have shown that it is possible to influence a range of physiological activities of different nerve fibers, by manipulating the frequency at the interference zone. This can be achieved by alternating the activation of primary nerve fibers; the machine produces a modified physiological as well as therapeutic outcome (Samuel and Maiya, 2015). However, different frequencies can be used primarily to stimulate motor nerve fibers resulting in muscle stimulation ranging from low frequency muscle twitches (<15Hz) to tetanic and sustained muscular contractions (Kroeling et al., 2009).

2.7.3 Increased blood flow

Clinical studies have demonstrated that the use of IFC increases cutaneous blood flow (Johnson and Tabasam, 2003). Lamb and Mani (1994) reported that the use of IFC significantly increases arterial blood flow. Similarly, Noble et al. (2000b) described that the use of beat frequency current of 10-20Hz can significantly increase cutaneous blood flow. However, these results indicate that low frequency current has a significant effect on cutaneous blood flow, thus, could be used in clinical management of peripheral vascular diseases (Noble et al., 2000b). It was postulated that IFC achieves this vascular change due to its inhibition of sympathetic nerve activities in the smooth muscular wall of blood vessels causing peripheral vasodilation (Goats, 1990).

2.7.4 Efficacy of Interferential Current Therapy on Knee Osteoarthritis

Zeng et al. (2014) conducted a systematic review and meta-analysis study to investigate the effect of different electrical stimulation therapies on pain relief in patients with knee osteoarthritis. The authors used RCTs, comparing electrical stimulation therapies with control intervention (sham or blank) or with each other. They concluded that IFC seems to be the most promising pain relief treatment for the management of knee OA. Gundog et al. (2012) reported that IFC is an electro modality that can be used to reduce pain and disability in the management of patients with knee osteoarthritis. In a similar study, Eftekharsadat et al. (2015) evaluated the therapeutic effects of APS and IFT on patients with knee OA. The authors concluded that short-term treatment with action potential stimulation and

interferential current therapy could significantly reduce pain and improve physical function in patients with knee OA. The therapeutic effects of IFC in relieving pain and improving functional disability have been reported in some other disease conditions; and have shown important significant clinical improvement (Lara-Palomo et al., 2013, Fuentes et al., 2016).

2.8.0 Combination Therapy (Interferential Current Therapy +Therapeutic Ultrasound)

Combination therapy (CT) involves simultaneous application of therapeutic ultrasound and electrical stimulation. In Europe, diadynamic current is frequently utilized, but in the UK and USA, it is most often combined with bipolar interferential therapy current (Watson, 2000). Almeida et al. (2003) defined combination therapy as combining the therapeutic effects of pulsed US and bipolar electrotherapeutic current in a modality of physiotherapy.

In the present context, combination therapy can be defined as the use of a physical modality that combines the therapeutic effects of continuous mode of therapeutic ultrasound and bipolar IFC in the rehabilitation of knee OA to reduce pain, improve physical activity, and quality of life of the patient with knee OA. Continuous US was chosen to be part of the CT because of its benefits in subacute and chronic conditions with no active inflammation, since osteoarthritis is considered to be a chronic degenerative condition. Normally, continuous US is used for its thermal effect that is capable of enhancing healing at the cellular level. It is used when thermal effect is needed but non-thermal effects will also occur. There is evidence that continuous US interacts with all phases of tissue repair. By stimulating phagocytic activities in inflammatory cells such as macrophages, US promotes release of a chemical mediator from inflammatory cells which attracts and activates fibroblasts to the site of injury, and stimulates and optimizes collagen production and functional strength of scar tissues.

It has been suggested that by combining IFC and US, the advantages/effects of each modality can be realized (Watson, 2000), but lower intensities are used to achieve the effects. Furthermore, the accommodation effects of IFC can be eliminated or reduced (Watson, 2000). It also provides the added advantage of localizing the area of lesion, especially chronic painful areas by a process called “electrodiagnosis” (Almeida et al., 2003).

The mechanisms by which CT provides pain relief are not clearly known (Almeida et al., 2003). There is evidence that IFC inhibits nociceptive inputs (Moretti et al., 2012). This may be as a result of stimulation of the afferent fibers (large diameter fibers) that inhibit the entrance of nociceptive impulse into the posterior horn of the spinal cord through the smaller diameter afferent fibers. IFC promotes analgesia by blocking pain potentials in the dorsal

horn of the spinal cord (Goats, 1990). This is in line with the "pain gate theory", as postulated by Melzack and Wall (1967), that action potentials in the form of impulses travelling along large diameter fibers compete for access into the central ascending sensory tracts in the dorsal horn of the spinal cord with nociceptive impulses travelling along smaller diameter nociceptive fibers. The former fibers conduct faster, therefore, their action potentials gain precedence over the nociceptive impulse, closing the gates against nociceptive action potentials which therefore fail to reach conscious level (Adedoyin et al., 2002).

2.8.1 Therapeutic Effects of Combination Therapy

The simultaneous application of US and IFC is widely used in the management of musculoskeletal pain. For instance, Almeida et al. (2003) conducted a study to investigate the effects of combination therapy with pulsed ultrasound and interferential current therapy on pain and sleep in FM. The authors concluded that combination therapy can be an effective electrotherapeutic approach for improving pain and sleep disturbance as presents in fibromyalgia. Similarly, (Çıtak-Karakaya et al., 2006) conducted a study to assess short and long-term therapeutic effects of simultaneous application of US therapy (US and high-voltage pulsed galvanic stimulation) and connective tissue manipulation on pain, sleep and functional activity in patients with fibromyalgia. They reported that combination therapy seemed to improve pain, restoration of sleep, and improved functional activity in patients with fibromyalgia.

S˘ varcova et al. (1988) conducted a study to compare the analgesic effects of combination therapy (US therapy and galvanic currents) and shortwave diathermy on pain intensity in patients with knee osteoarthritis. They reported that combination therapy is an effective physical therapy modality to improve pain in individuals with knee osteoarthritis.

The likely advantages of combination therapy are that the beneficial therapeutic effects of both modalities might be exerted simultaneously, making the treatment more efficient and with less duration of treatment. Robertson et al. (2006) stated that there is no evidence of possibilities of better therapeutic effects between the two modalities.

2.9.0 Outcome Measures

The assessment of the effectiveness of treatments for OA are generally considered on the patient's subjective rating of 4 main domains: pain, functional impairment, joint impairment (range of motion) and quality of life assessment. The clinical assessments of perceived pain, functional activity and QoL are of clinical importance to clinicians, and should be used as the primary outcome measures of treatment effects in clinical trials. A key factor that may affect

the evaluation of pain and quality of life is the subjective nature of self-reported assessments. For instance, there could be external variables in a patient's life that may influence the response to a subjective question even though they are not related to the questions asked. The outcomes of subjective questionnaires should be supported with more objective and valid measures of function such as the six-minute walk test, joint active ROM, and muscle strength.

2.9.1 Ontario McMaster Universities Osteoarthritis Index (WOMAC)

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), a standardized and specific outcome measure with high psychometric values focused on issues with a specific health diagnosis or disease is used to evaluate the severity of symptoms and the efficacy of an intervention. WOMAC is used for evaluating and monitoring functional outcomes in individuals with knee OA.

Description: A multidimensional, self-administered health status instrument for patients with knee and hip OA (Bellamy et al., 1988). The WOMAC index was developed to examine and quantify the level of pain perception, joint stiffness and disability related to osteoarthritis of the knee and hip (Bellamy et al., 2011). It has also been used for patients that have undergone knee and hip arthroplasty (joint replacement surgery) (Hashimoto et al., 2003). It is a self-administered questionnaire consisting of 24 questions divided into 3 subscales, 5 related to pain, 2 to stiffness and 17 to physical function. It can be used to monitor the course of the disease or to determine the effectiveness of a variety of interventions (pharmacologic, surgical, physiotherapy, etc.) (Walsh and Hurley, 2009, Herrero-Beaumont et al., 2007, Jones et al., 2005). In 1994, a consensus meeting recommended the use of WOMAC as a primary measure of efficacy in osteoarthritis trials (Bellamy et al., 1988). The WOMAC takes approximately 12 minutes to administer and can be taken on paper, over the telephone or on computer. Both the electronic versions: computer and mobile, ~~versions~~ of the WOMAC have been found to be comparable to the paper version, with no significant difference (Theiler et al., 2002).

Gandek (2015) conducted a systematic review of the measurement properties of WOMAC to evaluate the quality of WOMAC measurements using COSMIN (Consensus-Based Standard for the Selection of Health Measurement Instruments). The author reported that WOMAC scales have higher psychometric values with good (≥ 0.71) internal consistency reliability for the pain and stiffness scales and excellent (≥ 0.90-0.95) internal consistency reliability for the function scale.

Stucki et al. (1998) evaluated the psychometric properties of the WOMAC in German in patients with hip and knee OA. The authors reported that the Cronbach's alpha value of WOMAC was 0.81-0.96. In a similar study, Symonds et al. (2015) conducted a study to establish the reliability, validity and sensitivity to change of the WOMAC among Chinese individuals with knee OA. They reported a good test-retest reliability with strong internal consistency; the Cronbach's alpha for the 3 subscales of WOMAC was 0.84, 0.86, and 0.96, respectively. It was concluded that WOMAC is valid, reliable, and sensitive to change for patients with OA of the knee.

2.9.2 Health-related Quality of Life (HRQoL)

In recent years, much attention has been focused on exploring the impact of physical and mental illnesses on the overall quality of life. The psychosocial biomedical measures have been shown to play an important role in ensuring positive patient outcome from both the clinician's and the patient's perspectives, and is an important outcome measure when evaluating treatment (Skevington, 1999).

However, investigations have indicated that for an effective explanation to be derived, it is essential to view quality of life as a concept consisting of a number of social, environmental, psychological and physical values (Theofilou, 2013). The concept of quality of life (QoL) broadly encompasses how individuals measure the "goodness" of multiple aspects of their lives. These evaluations include one's emotional reactions to life occurrences, disposition, sense of life fulfilment and satisfaction with work and personal relationship (Diener et al., 1999).

HRQoL is concerned specifically with health while also counting for general QoL components. It has been understood in several ways and so has been measured using a variety of instruments (Theofilou, 2013).

Even the concept of HRQoL is problematic since it needs to be interpreted in various ways when applied to specific stages of a disease (Poradzisz and Florczak, 2013). According to Taylor et al. (2008), the definition of HRQoL for young people with chronic diseases is

> *"Subjective, multidimensional, and dynamic. It is unique to each individual young person and includes aspects of physical, psychological and social functions. It is dependent upon not only the stage of development but also the illness trajectory. This involves the achievement of goals and aspirations and constraints imposed through ill-health and treatment".*

2.9.3 Short Form-36 Questionnaire (SF-36)

The Short Form 36-Item Health Survey (SF-36) is one of the most widely-used generic outcome measures used to assess HRQoL with good psychometric values, and has considerable information on its clinical applications and research settings. The tool contains 36 items with 8 scales which are: Physical Functioning (PF), Role Limitation-Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role Limitation-Emotional (RE), and Mental Health (MH). Total scores range from 0-100, with a mean of 50 and standard deviation of 10 being norm-based for the general population (Maruish, 2011). Scores from the eight domains can be computed into two measures which are the physical component summary (PCS) and mental component summary (MCS) which provide greater accuracy and remove the floor and ceiling effects marked in many of the domains (Salaffi et al., 2003). Higher scores indicate improved health status and a better QoL. Evidence has shown that the SF-36 is a standardized and validated outcome measure that has been widely used to evaluate patients' health status (Mbada et al., 2015, Sloan et al., 2015) among apparently healthy individuals, and for other conditions (Watt et al., 2014) and in patients with knee osteoarthritis (Kwan et al., 2016).

2.10 Summary

Osteoarthritis is the most common articular disorder in the world, and its prevalence is rising due to progressive increases in aging and obese populations. Generally, it causes pain, loss of physical function, disability and reduces quality of life in adults. The diagnosis of knee osteoarthritis is based on the recommendations of the American College of Rheumatology (ACR). The risk factor for developing OA is determined by systemic/genetic and biomechanical factors. Treatment of osteoarthritis involves alleviating pain, improving physical function, attempting to rectify mechanical misalignment, and identifying and addressing manifestations of joint instability and improving quality of life. However, the treatment of OA includes pharmacological and non-pharmacological approaches. Pharmacologically, the management involves the use of NSAIDS, opioids, capsaicin to systemic therapies. The use of non-pharmacological approaches include physiotherapeutic management, education, weight management, nutrition, etc. The physiotherapy approach includes electrotherapy such as IFC, US, and combination therapy to relieve pain, improve physical function, strengthen muscles and enhance the quality of life of individuals with knee OA.

Different outcome measures are used to evaluate the effects of clinical intervention on individuals with knee OA. WOMAC is an OA-specific outcome measure used to monitor the course of the disease or determine the effectiveness of a variety of interventions, whereas, SF-36 is a generic outcome measure that assesses both physical and mental components of quality of life of patients with knee OA.

CHAPTER 3: METHODOLOGY

3.1 Introduction

This chapter presents information concerning the methodology of the present study. The chapter begins with a discussion of the setting, research design and the population from which study participants were drawn. Sampling procedure and criteria for inclusion and exclusion are also described. The data collection methods used in this study are presented, including the psychometric properties and corresponding validity and reliability of outcome measures used for the study. Finally, the chapter ends with a presentation of the statistical analyses that were conducted and ethical considerations.

3.2 Research Design

This is a multicenter randomized controlled, single-blind study conducted using between-subjects design. It assessed the effects of therapeutic ultrasound (US), interferential current therapy (IFC) and combination therapy (CT) on the quality of life of Nigerian individuals with knee osteoarthritis. Prior to the main intervention, a protocol for electrotherapy, particularly for the simultaneous application of IFC and US (including its feasibility and safety among persons with knee OA) was developed. The extent to which the electrotherapy modalities impacted on pain, functional activity and quality of life in individuals with knee OA was also evaluated.

3.3 Setting

Individuals with knee osteoarthritis attending physiotherapy outpatient clinics were recruited from the Rasheed Shekoni Specialist Hospital (RSSH), the Federal Medical Centre (FMC), Birnin Kudu, and Dutse General Hospital, Dutse, all in Jigawa State, Northwestern Nigeria. The RSSH and the FMC were established in 1975 and 2000 respectively. These are the major referral hospitals serving patients from both the metropolitan and rural areas of the state as well as some neighboring states and some nearby foreign countries such as Niger and Cameroon. The facilities also serve as referral centers for both public and private hospitals within and outside the state. The RSSH is a 300-bed capacity tertiary facility while the FMC is a 200-bed capacity health institution that receives patients from within Jigawa State as well as from neighboring states. Similarly, Dutse General Hospital is a 200-bed capacity secondary health care facility that receives referrals from within the state and from neighboring states. These hospitals provide outpatient consultations and inpatient specialist services to patients presenting from other levels of care or on self-referral.

3.4 Ethical Clearance

The study was scrutinized and approved by the University of KwaZulu-Natal Biomedical Research Ethics Committee (approval number: BFC 374/14; Appendix G), the Ethics Committee of the Jigawa State Ministry of Health (approval number: MOH/SEC/3/5/495/1/47; Appendix E), and the Ethics Committee of the Federal Medical Centre, Birnin Kudu (FMC/HREC/APP/CLN/001/1/9; Appendix F***)*** in conformity with the principles of ethical research involving human subjects as stated in the Declaration of Helsinki. All participants were duly informed about the procedures, risks, and discomforts that may occur with the interventions and provided written informed consent (Appendix B).

Data were coded without any direct reference to the identity of the participants and kept and protected using a password. The hard copies such as interview notes, prints of photographs, or video or audio tapes were kept securely locked away in a locked filing cabinet that can only be accessed by agreed members of the research team. Similarly, the study has been registered with the Pan African Clinical Trial; the unique identification number for the registry is PACTR201709002536342 (Appendix J).

3.4.1 Consent procedures

The recruited volunteers were briefed on the concept and full details of the procedures involved in the study and had the electrotherapy intervention, and exercise class explained. It was also reiterated by the PI that volunteers would only be included in the study if they were interested in participating.

Following an affirmative answer, participants were served with the consent form (Appendix B) which was read to the volunteer, and written consent obtained. The form contains the title of the study and the PI's name and signature as well as the participant's names and all the research protocols; a copy of the signed form was issued to each participant. Participants in all phases of the study were informed that they could refuse to answer any specific questions, participate in any testing, or terminate their involvement at any time and that their arthritis care would not be affected whether or not they participated in the study.

Potential risks. Risks to the individuals participating in this study were minimal and associated with the interferential current therapy, therapeutic ultrasound and the use of infrared radiation. With IFC, participants experience a tingling, 'pins and needles' sensation that is followed by involuntary muscle contraction (Nelson et al., 2014). This sensation and the following muscle contraction can be uncomfortable. Indeed, the general practice of ultrasound therapy is regarded as safe and effective, but there have been some minor cases of physical pain due to "cavitation" described as a burning feeling. Cavitation is caused by the

heating of the gas contained in the body tissue. Also, burns can occur from the use of thermal-based therapies. With the infrared lamp treatment, the only hazard in most cases is that prolonged exposure to a very high level of infra-red radiation could result in a burn, just like exposure to a hot stove or any other heat source. This was taken care of with calculation of ideal distance and treatment exposure time.

Results from the pilot study showed that after the initial use of the electrical stimulator (IFC), the sensation became more familiar and less uncomfortable. Also, it showed no associated risk or harm to the participants when treated with US, IRR and combination therapy. Potentially, skin redness might occur due to skin sensitivity to the electrode adhesive (Nelson, Hayes, & Currier, 1999). Participants were told to discontinue use of the electrical muscle stimulator if this occurred and to call the attention of the investigative team.

Risk/Benefit. The risk/benefit ratio indicated that the benefits outweighed the risks. The risks were minimal for individual participants. All participants attended the pre-treatment briefing. This was designed to increase their knowledge of arthritis and their personal capabilities in the daily management of arthritis and to inform them of the activities that diminish pain and improve functional ability.

3.5 Sampling Size and Power Calculation

The sample for the study comprised 136 male and female patients (aged 58 to 82 years) diagnosed with knee osteoarthritis and selected by convenience sampling according to the stated study criteria from the three hospitals. Individuals who met the inclusion criteria were identified by the researcher during clinical assessment and screening processes at the outpatient units of the 3 hospitals (RSSH, FMC B/Kudu and Dutse General Hospital).

The sample size (N) was determined using Cohen's table [Cohen 1988] at $\alpha = 0.05$ degree of freedom (μ) = k- 1, where K is the number of groups (k = 4), with effect size (f) = 0.35 (from the pilot study) and power (w) 80%, sample size (n) = 20. Sample size (N) was 140 and 16 extra participants were added to make room for attrition. Therefore, N was 136 and each group had n = 34.

3.6 Randomization and Blinding

Randomization was conducted following the capture of relevant baseline data. Participants were blinded to the group assignment. However, they were fully informed of the randomization process to avoid any disappointment or disagreement with group assignment. Research assistants were blinded to group allocation at the level of outcome assessments, data entry and data analysis. Participants were assigned randomly to therapeutic ultrasound (n =

35), interferential current therapy (n = 35), combination therapy (n=35) and control (n=35) by means of a computer-generated 1:1 randomization (Uitenbroek, 1997).

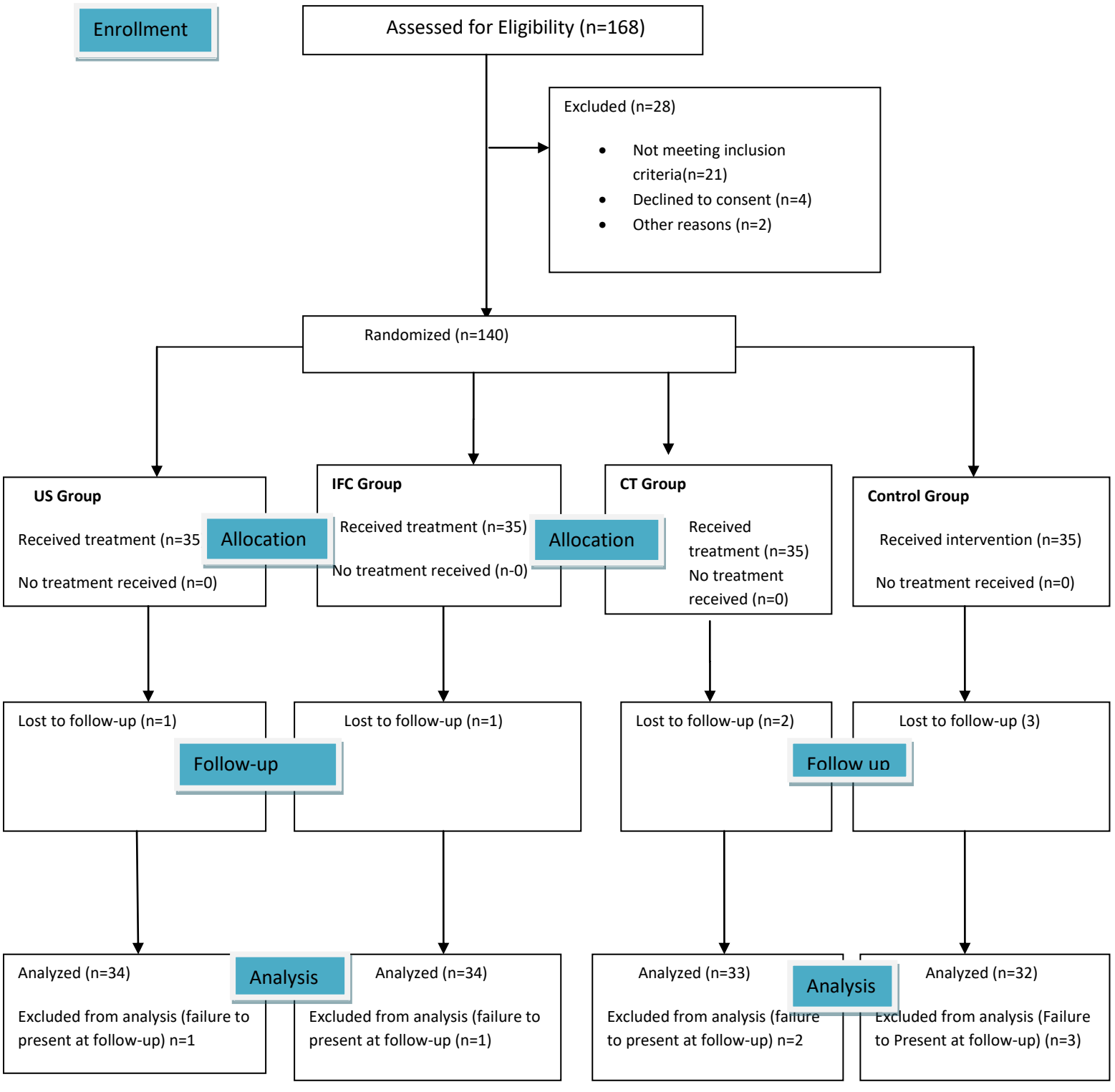

Figure 3. ***1 CONSORT diagram depicting the participants from Enrolment to analysis***

3.7.0 Description of Population

The population of the study comprised all male and female individuals with chronic knee OA (as defined in the study inclusion criteria) attending the outpatient physiotherapy clinics at Rasheed Shekoni Specialist Hospital (RSSH), Dutse; the Federal Medical Centre, Birnin Kudu (FMC); and Dutse General Hospital, Dutse, out of which 140 patients were selected using purposive sampling.

3.7.1 Assessment for Eligibility

Patients willing to participate responded to the invitation for recruitment through their referring rheumatologists from the three recruitment centers. Eligible patients were then scheduled to be evaluated by rheumatologists at the recruitment centres (FMC, RSSH and Dutse General Hospital). Each evaluation consisted of a review of clinical history, physical examination, systems review, and diagnosis based on American College of Rheumatology criteria and a radiologic grade of 2 or 3 on the Kellgren-Lawrence scale for severity of OA, OA of the knee of at least 6 months duration and other study criteria as earlier mentioned. Also, at the physiotherapy outpatient clinics, participants were screened for any contraindications or otherwise to the treatment with electrotherapeutic modalities. Majorly, these contraindications included impaired skin sensation, cardiac pacemaker, vascular insufficiency, malignant tumor, etc.

Consenting participants then completed baseline measurements of the outcome measures. Baseline testing lasted approximately one hour, during which participants signed informed consent, filled the 36-Item Short Form Health Survey (SF-36) questionnaire, the WOMAC questionnaire, the visual analogue scale (VAS), and the demographic data form. Height and weight measurements were also taken and range of motion assessed. All baseline testing and data collection were conducted by trained research assistants and the principal investigator. Following baseline evaluations of the outcome measurements, a research assistant randomized the participants, using a computer application, into one of the four treatment groups: US, (Group I), IFC (Group II), CT (Group III), and control (Group IV).

The standard care for a patient with knee osteoarthritis in Nigeria basically goes in line with the American College of Rheumatology treatment guidelines, which includes pharmacological and non-pharmacological modalities. A few modifications were made based on up-to-date clinical practice to suit the standard health care service delivery in Nigeria.

All participants were covered by the National Health Insurance Scheme (NHIS) provided by the Federal Government of Nigeria.

3.7.2 Inclusion criteria

Patients were included if they met the following criteria:

- Aged ≥55 years
- Diagnosed with knee OA according to the American College of Rheumatology criteria
- Symptoms of at least three months duration and grade II and III OA confirmed by radiography according to the Kellgren-Lawrence grading (Kellgren and Lawrence, 1957).
- Self-ambulatory
- Attending the physiotherapy outpatient units of RSSH, FMC or Dutse General Hospital

3.7.3 Exclusion criteria

Patients were excluded if they had any of the following:

- Kellgren-Lawrence grade IV and V radiographic changes.
- Knee joint diseases other than osteoarthritis.
- Involvement of the foot joints.
- Serious concomitant systemic diseases such as heart diseases, chronic obstructive pulmonary disease, cancer, severe hypertension, opened and infected ulcers.
- Intra-articular joint fluid effusion.
- Injection of corticosteroid or hyaluronic acid during the last one month, or chondroprotective agent.
- History and clinical signs and symptoms of any contraindications to electrotherapy, such as pregnancy, and cardiac pacemakers, active bleeding, metal implant, impaired skin sensation and skin infections.
- Undergone knee surgery such as joint replacement or arthroscopy within the 6-months prior to the study.
- Poor general health status that interferes with the functional assessments during the study

3.8 Data Collection Instruments

A purpose-designed form (Appendix J) made up of two parts was used to record data at baseline and at the end of the 12-week intervention period as outcome measures. The instrument was designed by the researcher to assess the demographic data and knee range of motion of the participants. The first section of the form covered information on participants'

demographic characteristics (age, gender, and body mass index), while the second part was for recording knee range of motion, both active and passive, and other variables of clinical importance.

Table 3. 1 Instruments and corresponding variables assessed in the study

S/No	Materials	Test/Activity
1	Sonicator Plus 920® (Mettler Electronics Corp., Anaheim, CA, USA)	Electrotherapeutic modalities (combines therapeutic ultrasound interferential therapy)
2	Goniometer (Baseline Digital Absolute Goniometer; EW12/027	Assessment of joint range of motion
3	Stadiometre (Model 217, Seca ® Company, Berlin, Germany	Height measurement
4	Tape measure	Waist, knee circumferences
5	SF-36 Survey Questionnaire	HRQoL
6	Visual Analogue Scale (VAS)	Assessment of level of pain perception
7	WOMAC	Functional limitation
8	Informed Consent Form	To seek for the patient's approval to participate in study

Sonicator Plus

The Sonicator Plus 920® is a two-channel combination unit with both a membrane panel and a touch-sensitive screen. It allows clinicians to set up quickly for treatments and the choice between two different wave forms. Using either wave form, both channels can be used simultaneously with different amplitude modulation options including surge, reciprocation,

and vector sweep. The machine offers 1 and 3 MHz ultrasound using a dual frequency 5.5cm^2 applicator.

Table 3. 1 Technical specifications of Sonicator® Machine

Input	100-240V ~ 50/60 Hz, 95 Va
Frequency	1.0 & 3.0 MHz
Modes	Continuous, Pulsed- 5, 10, 20, 30, 40, 50% duty cycle
Output Power	11W (100%) with 5.5cm^2 Applicator, 1 MHz
Electrical Stimulation Waveforms	Interferential, Premodulated, EMS, Russian, High Volt, TENS, Microcurrent, and Direct Current
Current	500 ohm
Max Treatment Time	60 minutes- electrical stimulation & 30 minutes- ultrasound or combination therapy
Dimensions	4.9"H x 13.6"W x 10.5"D
Weight	11 lbs

3.9 Pilot Study

This comprised a three-stage small-scale study to investigate the effects of electrotherapy (US, IFC & CT) on the HRQoL of Nigerian individuals with knee OA. The study was conducted for 4 weeks, prior to the commencement of the main intervention. Twenty patients were recruited from the physiotherapy outpatient clinics of RSSH, FMC Birnin Kudu, and Dutse General Hospital. The aim of the feasibility study was to translate and pre-test the SF-36 health survey, develop the electrotherapy treatment protocols as well as find out the feasibility and safety of the electrotherapy combination treatment model. It was also an opportunity for members of the research team to become more conversant with the operational procedures of the equipment involved and other logistic issues, thus ensuring quality in the measurements taken by research assistants.

The study results were made available to the participants during an interactive session. Participants were also given opportunities to ask questions and also had post-trial access.

3.10 Phase 1: Questionnaire translation and pre-testing

Short Form-36 (SF-36) questionnaire (Appendix A) was used to assess the quality of life of the participants. The questionnaire was translated into the target language (i.e. Hausa), which is the predominantly spoken language in Northern Nigeria. The purpose of the questionnaire

translation was to have semantic equivalence across the two languages, conceptual equivalence across cultures, and normative equivalence to the source survey (Harkness et al., 2004) The forward-backward-forward technique was used (Koller and West, 2005), i.e. English to Hausa then back to English again, for conceptual retention. Two separate forward translations were conducted by two independent academic translators from a local university who are native speakers of Hausa language. The Hausa translated version was compared with the original English version to ensure accurate translation of the content (content validity). The source questionnaire (English version) was then reconciled with the target questionnaire (Hausa version), and the two separate backward translations were compared. Below is a figure that depicts the processes that led to the development of the Hausa translated version of the SF-36 for use in the study (Figure 3.1).

The participants were given full explanation of the importance of pre-testing the SF-36 questionnaire. The survey was verbally administered, and data were collected from all the twenty participants with knee osteoarthritis. At the end of the survey, a meeting was held with the participants to discuss issues and problems regarding overall comprehension, clarity of the questions and to share any concerns related to perceived difficulties encountered while responding to the questions. Based on the outcomes of the survey, some minor modifications were made with expert opinion and support to improve understanding of some of the questions. The finalized forward translation was then produced in readiness for use in the main study.

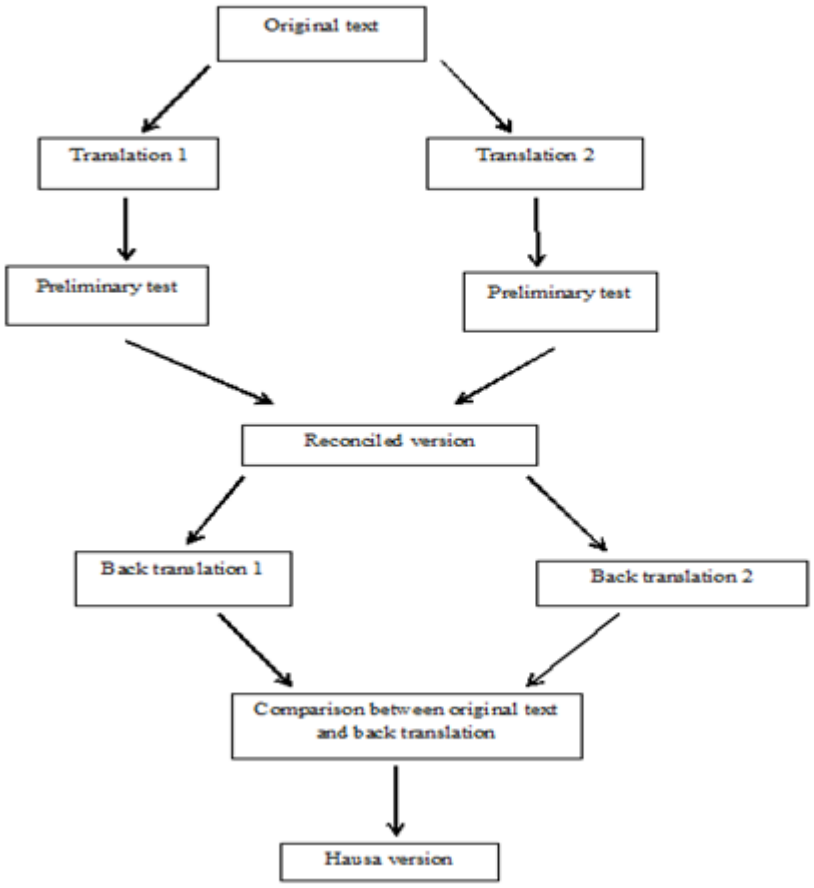

Figure 3. 2 Process of translation and back translation of the SF-36 health survey: adopted from Nuhu, 2015.

3.11 Phase 2: Development of the Electrotherapy Treatment Protocols

The Sonicator Plus 920® (Mettler Electronics Corp., Anaheim, CA, USA) was used to generate the US, IFC, and the combination therapy. It is a two-channel combination unit for therapeutic ultrasound and muscle stimulation. The machine has a microprocessor that provides interferential (4-pole), pre-modulated (2-pole interferential), medium frequency (Russian), EMS, high volt, TENS, micro-current and direct current (DC) waveforms. In addition, it offers 1 and 3 MHz ultrasound using a dual frequency 5.5 cm² applicator. An optional 0.9 cm² applicator at 1 and 3 MHz is also available. The two-channel Sonicator Plus 920® provides up to two different waveforms using two channels simultaneously. Several different amplitude modulation options such as the surge, reciprocation and vector sweep can be chosen. The interferential and premodulated modes offer frequency modulation as well as a static frequency option.

US treatment dosage calculation

Knee OA is a chronic degenerative articular disease, eliciting deep hyperalgesia resulting from damaged articular tissues. The following are calculated dosage parameters for US treatment.

Treatment frequency: Considering the anatomy of the lesion, 1 MHz frequency was chosen because it absorbs less rapidly with progression through the tissues and penetrates within 2.5-5 cm; it is therefore more effective at greater depth. ***According (Watson, 2008),*** it can be shown in this equation:

$$\mathbf{E}\text{nergy}_{\text{final}} = \mathbf{E}\text{nergy initial} - (\mathbf{E}\text{reflected} - \mathbf{E}\text{absorbed})$$

Where:

Energy final = total energy produced by machine

Energy initial = total energy produced /cm^2 that gets to the skin

Energy reflected = amount of ultrasonic energy that is scattered/lost when it hits tissue surface

Energy absorbed = amount of ultrasonic energy that is absorbed and causes tissue effects

Pulse ratio: The pulse ratio defines the concentration of the energy on a time basis. The machine was calibrated to 100% duty ratio (1:1) i.e. “Continuous mode”. The selection of continuous mode was based on the knowledge that knee OA is a chronic joint disease in nature.

Treatment intensity: The treatment intensity depends on the state of the tissue injury (acute or chronic) and its depth. The more acute the lesion, the less strong the ultrasound needs to be in order to achieve/maintain the tissue excitement. The more chronic the tissue state, the less sensitive, and hence the greater the intensity required at the lesion in order to instigate a physiological response.

According to (Watson, 2000), the therapeutic US treatment dose for chronic osteoarthritis can be calculated as follows:

On examination, the primary focus of the lesion is determined to be at the deep intra-articular capsule of the joint, the following clinical decisions were made:

The lesion is deep seated (not superficial), hence 1HMz would be most appropriate.

The lesion is chronic, thus the intensity of 0.5watt/cm^2 was sufficient to treat the lesion.

Considering the need to **increase the surface dose** to allow for loss of ultrasound at depth, it was estimated that the required surface dose would need to be 0.75 W/cm^2 (though of course, this will depend on the size of the patient. It is not a universal formula)

The lesion is **chronic**; therefore a pulse ratio of 1:1 will be most appropriate.

Working on the principle of 1 minute worth of ultrasound per treatment head area, the total time taken to treat the lesion will be:

$$Tt = 1\text{min} \times TH \times PR$$

Where:

Tt = total treatment time (min):

TH = number of areas the treatment head fits over the lesion (cm^2): 5.5cm^2

PR = pulse rate (in ratio): 1:1

Thus, $Tt = 1\text{min} \times (5.5\text{cm2}) \times (1) = 5.5\text{min}$

The final treatment dose is 1 MHz; 0.8Watt/cm^2; pulse ratio 1:1 for all the patients.

Treatment Parameters for IFC

The Sonicator Plus 920® was calibrated for IFC use with the following therapeutic parameters ***as reported by Eftekharsadat et al. (2015):***

Treatment polarity: Quadra-polar electrodes/ two channels

Treatment Frequency: 4000 Hz
Base: 90Hz
Sweep: 40Hz
AMF / Beat Frequency: 90-130 Hz
Duration of the treatment: 10 minutes

Treatment parameters for Combination Therapy

Combination therapy is the simultaneous application of US and IFC to achieve the maximum therapeutic benefits of the two modalities with minimal intensity. The machine was calibrated for CT use with the following treatment parameters in Moretti et al. (2012):

- US treatment dose
  Frequency: 1MHz
  Intensity: 0.8watt/cm^2
  Mode: continuous mode
  Duration: 10 minutes

- IFC treatment dose
  Frequency: 4,000Hz
  Base frequency: 90Hz
  Sweep frequency: 40Hz
  Polarity: Bipolar (2 electrodes)

3.12 Phase 3: Measurements and treatment

The eligible participants were screened for any contraindication to electrotherapy. They were randomized into four groups, using a computer-based application. It was important for the participants to be fully informed of the randomization process to avoid any disappointment or disagreement with the group assignment. The research assistants who took the pre and post-treatment measurements were blinded to the treatment groups. This single blinding process was necessary to prevent or reduce performance and ascertainment bias and avoid any reaction or responses after randomization. This happened at the level of outcome assessments and data entry. Participants were assigned randomly into one of the four study groups: therapeutic ultrasound (n = 34), interferential therapy (n= 34), combination therapy (n =33) and control (n=32), by means of a computer-generated 1:1 randomization (available at http://www.quantitativeskills.com/sisa/calculations/randmiz.htm).

Information on participants, such as medical history and other relevant data were kept confidential and presented in group form, instead of individual form. Participants were not identified by name in any reports, publications or presentations regarding findings in this

project. All completed documents were coded and marked only with an ID number and kept locked in a file cabinet that was only available to the principal investigator of this project.

Following measurement of participants' baseline demographic characteristics (weight, height, body mass index, age, and sex), clinical symptoms such as pain, joint stiffness, and level of functional activity were recorded using WOMAC and VAS respectively, while HRQoL was measured and recorded using the SF-36 health survey questionnaire.

Participants were treated according to their respective random allocated groups. All the treatment sessions were conducted by the research assistants using accurate treatment calibrations of the equipment as calculated and described (in phase 2 of this pilot study). It was necessary to deliver the prescribed doses of all the treatments to the patients for the purpose of this study as well as for safety and effectiveness.

Participants were comfortably positioned for treatment supine on a couch with a pillow supporting the head. The knee undergoing treatment was slightly flexed and supported with a pillow. The area to be treated was cleaned with alcohol to improve skin conductivity and to remove any oil. All treatment were conducted 3 times a week for 4 weeks.

US group (Group I): Participants were informed about the treatment procedure and what they were expected to feel and to do during the treatment session. A transmission medium (coupling gel was applied to the cleaned and dried knee for treatment. Treatment parameters were set as described (in phase 2). The transducer was moved in a circular pattern and the intensity was turned to the required level. Treatment areas were limited to 2 times the size of the transducer for effective treatment. The transducer movement was slow and deliberate to achieve approximately 4cm/ second coverage. The transducer was in contact with skin and in motion throughout the treatment session to avoid overheating and crystal damage. Treatment was given 3 times a week for 4 weeks.

Interferential current therapy group (Group II).

All treatments were conducted by the research physiotherapists. The treatment was given 3 times a week for 4 weeks (pilot study) using quadra-polar self-adhesive and disposable electrodes, measuring 8 × 6 cm using two channel outlets. The four electrodes were placed in diagonal (posterior-anterior and mediolateral) arrangements to the affected knee so that the two channels cross each other for effective treatment. Participants were informed that for effective treatment the intensity had to be maintained at a strong but comfortable level throughout the treatment session. Also, they were told that during the treatment session they would feel a tingling or 'pins and needles' sensation at the contact area of the electrode and around the area being treated. This sensation may continue for a brief period following the

treatment. The intensity should be increased within patients comfort level, and stronger intensity usually has more beneficial effects but should not be increased so high as to cause skin discomfort. The treatment parameters were already explained in the first phase of this pilot study.

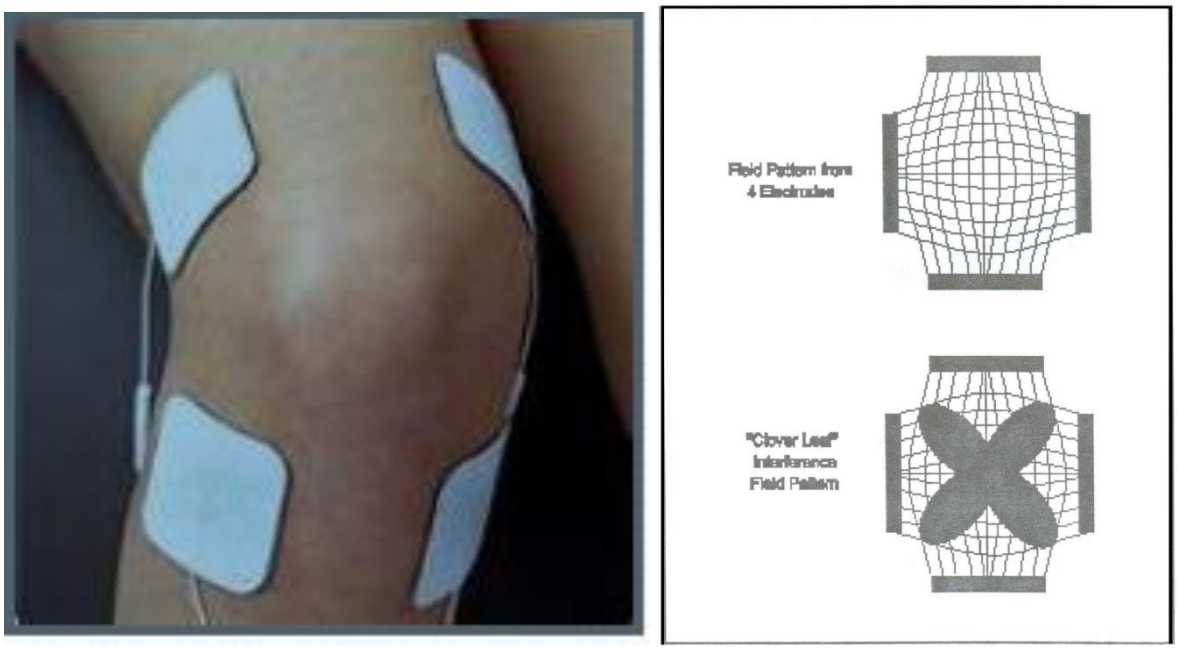

Figure 3. 3 A diagonal electrode arrangement or quadra-polar techniques

3. 13 Combination therapy group (Group III)

Combination therapy (CT) is the simultaneous application of IFC and US to maximize their therapeutic benefits with lower intensity (Watson, 2000). The CT has the advantage of localization of lesions (particularly chronic), i.e. electrodiagnosis. The patient's preparation was the same as explained above in Groups I & II. Machine calibration and dosage calculations were also explained in phase II of this pilot study. Participants were told that they were expected to feel mild 'tingling' sensation or mild 'pins and needles' sensation. Treatment was conducted 3 times a week for 4 weeks.

Control Group (Group IV)

This is the fourth group of the study whose members received luminous infra-red radiation therapy (IRR) to affect the knee. Luminous IRR (Philips IRR, Infraphil ® 150W) was applied from a distance of 60 cm from the lamp to the patient's skin.

Participants were positioned comfortably in supine lying with affected knee semi flexed at 60^0-80^0, supported underneath with a pillow. The area to be treated was exposed and cleaned. Participants were instructed that they were expected to feel a mild comfortable warmth but if

the heat was getting too hot they should inform the physiotherapist in-charge by pressing a bell. Also, they were instructed not to look directly at the infra-red light as it could cause damage to the eyes.

The IRR lamp was placed 60 cm from the participant's skin at 90^0 for maximum and effective irradiation of the affected area. The treatment time was 15 minutes exposure.

3.14 Intervention Programs

This section describes the details of the main intervention procedures of the study. The section includes patient's assessment for eligibility, randomization, and grouping, to baseline measurement, treatment procedures and post-treatment measurements. The study was conducted from January to December 2015. The main intervention procedures were the same as for the pilot study, with little modifications as described below.

3.15.1 Demographic data form

A self-designed demographic information form was developed by the principal investigator to collect all participants' demographic data such as age, gender, weight, height and BMI (Appendix A). This information was collected before the study commenced and was processed and kept in the participants' database for future study references. All data collected belong to the PI and were kept confidentially.

3.15.2 Anthropometric measures

The participants' anthropometric measurements, including weight, height, and body mass index (BMI), were taken by trained research assistants using standard protocols.

Each participant's height was measured using a stadiometre (Seca *217,* Seca GmbH & Co. KG., Hamburg, Germany). The standiometre is lightweight and portable and allows measurement accuracy of height to the nearest 1mm. The range is from 0 – 2.07m, in 1mm graduations. It comes in the form of a plastic rod, in four sections which slot together. There are unique codes at each end of each rod (i.e. star shape, square, circle, etc.) which line up with each other to ensure that the sections are slotted together properly. It has a base plate for the individual to stand on, two stabilizing side arms that make contact with the wall and a head plate with arrows indicating the point at which the measurement should be read. Each rod is marked in metric (centimetres and millimetres) and imperial (feet and inches) units. The height of each participant was taken by two trained research assistants, one holding the participant's head in the correct position and the other reading the value. The procedures were fully explained to the participants and were asked to stand erect and straight as possible. The participant assumed an erect posture (standing barefoot on both feet) with heels, buttocks, and occiput in contact with the straight rod of the stadiometre. Both arms were held

loosely by the side of the body with eyes directed straight ahead. It was ensured that the head was in the "Frankfort plane". This position is an imaginary line from the center of the ear hole to the lower border of the eye socket. This is a midline position. The reading of the height was taken from the eye level to the nearest 1 mm. The measurements were taken three times and the mean was calculated by adding the 3 values together and dividing by 3.

Similarly, the participant's body weight was taken with the participant standing erect, still and without footwear in the middle of the scale platform with feet slightly apart and eyes directed straight ahead. Body weight was distributed equally on both feet with the arms hanging down loosely at the sides of the body in a relaxed manner (Stewart et al., 2011). The measurement was taken to the nearest 0.1 kg. Body mass index (BMI) in kg/m^2 was calculated by dividing weight (kg) by the square of height (m^2).

3.15.3 Measurement of pain intensity

Clinical assessment of knee pain was conducted using the visual analogue scale (VAS) at baseline and after the 12 weeks of treatment (Appendix C). VAS is a single-item numerical scale normally in a straight horizontal or vertical line of fixed length, usually 10cm (i.e. 100mm) (Hawker et al., 2011). The ends are defined as the extreme limits of the parameter to be measured with anchor points 0 (no pain) and 10 (maximum pain). The visual analogue scale is a highly reliable instrument for measuring pain (Bijur et al., 2001), with high psychometric values (Todd et al., 1996, Gallagher et al., 2001, Phan et al., 2012, Pedersen et al., 2016). Each participant was instructed to point to the number corresponding to his or her level of pain intensity and it was recorded. Pain assessments were conducted in full weight bearing and participants were instructed not to under- or overestimate their pain. The assessments were carried out at baseline and at the end of 12 weeks of the treatment session.

3.15.4 Clinical assessments

Clinical symptoms of the disease such as pain, joint stiffness, and physical functioning were assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) (Appendix D). It is a tri-dimensional disease-specific outcome measure, purposely built with high performance for evaluating research in osteoarthritis clinical trials (Bellamy et al., 1988). The WOMAC, which is self-administered, covers three subscales: pain (5 items), stiffness (2 items), and physical functions (17 items). This study used the Likert scale version (LK3.1) of the outcome measure, which has the following response options: 0 = none; 1 = mild; 2 = moderate; 3 = severe; and 4 = extreme (Bellamy et al., 2011). Evidence has shown that WOMAC is reliable, valid and sensitive to change in the

health status of a patient with hip and knee OA. The purpose of administering the questionnaire was fully explained to the participants. They were given the translated Hausa version of the tool during interview sessions and were asked to be as honest as possible in answering questions describing what they were experiencing related to their knee condition for accurate capture of WOMAC data. Participants were carefully briefed about the questions and given adequate instructions on how to answer the questions. To ensure consistency, the Hausa version of the survey was administered by research assistants trained for the data capture using face-to-face interview, irrespective of the participant's literacy level.

3.15.5 Assessment of Quality of Life (QoL)

Participants' HRQoL was assessed at baseline and after 12 weeks of intervention using the Short Form-36 (SF-36) health survey questionnaire (Appendix E). The questionnaire has 36 items with 8-scales: Physical Functioning (PF), Role Limitation-Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role Limitation-Emotional (RE), and Mental Health (MH). Total scores range from 0-100, with a mean of 50 and standard deviation of 10 being norm-based for the general population (Maruish, 2011). Scores from the eight domains can be computed into two measures: the physical component summary (PCS) and mental component summary (MCS). These provide greater accuracy and remove the floor and ceiling effects marked in many of the domains (Salaffi et al., 2003). Higher scores indicate improved health status and a better QoL. Evidence has shown that the SF-36 is a standardized and validated outcome measure that has been widely used to evaluate patient's health status (Mbada et al., 2015, Sloan et al., 2015) among apparently healthy individuals (Watt et al., 2014) and in patients with knee osteoarthritis (Kwan et al., 2016).

The Hausa version of the survey was administered during interview sessions, where the purpose of administering the questionnaire was explained. Participants were requested to be as honest as possible in describing what they were experiencing in relation to their condition for accurate capture of QoL data. To ensure consistency, the Hausa translated version of the survey was administered by research assistants trained for the purpose using face-to-face interview (Bito and Fukuhara, 1998), irrespective of the participant's literacy level. Prior to questionnaire administration, questions were carefully explained and adequate instructions were given on how to answer them.

3.15.6 Knee Goniometry

The participant was comfortably positioned in supine lying on an examining table with the head of the table elevated to about 25 to 30 degrees. The leg to be measured was extended, with a pillow as support under the ankle. It was high enough for the participant's knee to be raised slightly off the table (provides space for a participant to fully extend their knee actively). The participant was asked to tighten their quadriceps muscles to actively extend their knee (push their knee into the table) three times. The axis of the goniometer was placed at the intersection of the thigh and shank at the knee joint centre of rotation, i.e., the lateral femoral condyle. The stationary arm was placed along the lateral aspect of the thigh, following the line from the knee joint to the greater trochanter at the hip. The moveable arm was placed along the lateral aspect of the fibula (from knee centre of rotation to the lateral malleolus at the ankle). Active and passive knee extensions were measured using the goniometer and recorded in degrees.

After the knee extension measurement, the pillow support was removed and the participant was asked to place their foot as close as possible to their buttocks (foot on the table) for knee flexion measurement. The research assistant measured the angle in degrees using the goniometer, being careful to use angles that are referenced as follows: the fully extended knee will be considered the zero position, and the degrees of maximum flexion. Maximum extension and extension deficit of the presentation were recorded. A deficit in ROM score for extension indicates that the participant was unable to carry out the extension, and maximum extension was described as the excursion range and recorded.

3.16 Therapeutic Ultrasound (Group I)

This group received continuous mode of therapeutic ultrasound treatment. Participants and the machine were prepared for the treatment as described below.

Patient preparation: The participants were fully informed about the procedures involved, and told that they were not expected to feel warmth during the treatment. Also, they were informed to report to the treating therapist if the treatment head (transducer) feels hot on the skin surface. The participant was asked to dress in minimum clothing in such a way to allow treatment to the affected knee. The participant was comfortably positioned in supine lying with a pillow under the affected knee. The area to be treated was cleaned with mentholated spirit and dried.

Machine preparation: The Sonicator Plus 920® (Mettler Electronics Corp., Anaheim, CA, USA) was used to generate the treatment parameters for the therapeutic ultrasound (as explained in the pilot study section). Below are the treatment parameters used in the US group (Group I).

Frequency: 1 MHZ

Treatment intensity: 0.8watt/cm^2

Mode: Continuous.

Time: 10 minute

Session of the treatment: 3 sessions per week for 12 weeks

Application Procedure:

US treatment application procedures are described below, from patient preparation, to machine operation to termination of treatment

Step 1: A substantial amount of coupling medium was applied to participant's cleaned and dried skin

Step 2: The transducer was moved in a circular or stroking pattern

Step 3: The intensity was turned up to treatment level

Step 4: Each circle/stroke overlapped the previous by ½

Step 5: Treatment area was limited to 2 times the size of the transducer (i.e. 10-11cm)

Step 6: The transducer was slowly and deliberately moved (approximately 4 cm per second)

Step 7: The transducer was in contact and motion to avoid overheating and damage to the crystal.

Termination of treatment

After the treatment, the ultrasound head was wiped with a clean and dry cleaning material and returned to its bracket. The participant's skin was cleaned to remove the coupling medium. The intensity level was turned back to zero, so the intensity is not on when the machine is turned on for the next treatment. The participant was asked if he/she felt any sensations during or after the treatment and the response was documented in the participant's case file.

Table 3. 2 Contraindications, precautions, and risks of continuous mode of ultrasound therapy

Contraindications	Precautions	Risks
• Acute injury or inflammation • Hemorrhagic conditions • Impaired circulation or sensations • Impaired cognition or communication • Eyes, anterior neck, carotid sinus, reproductive organs • DVT or thrombophlebitis (local) • Infection or tuberculosis (local) • Malignancy (local) • Recently radiated tissue (local) • Pregnancy (local) • Skin disease (local) e.g. psoriasis, eczema, etc. • Electronic device (local) • Plastic or cement implants (local)	• Active epiphysis • Chronic wound • Damaged or at-risk skin Regenerating nerves	• Burn • Pain • Surge

Adopted from: http://www.physio-pedia.com/Therapeutic_Modalities.

3.17 Interferential Current Therapy IFC (Group II)

This is the second group of the study that received interferential current therapy (IFC) treatment. The IFC treatment procedures are described below, from patient preparation to machine calibration, to treatment procedure and completion of treatment.

3.17.1 Patient instructions

The participant was informed fully of the procedure involved, and what they were expected to experience during and after the treatment session. During treatment, the participant was expected to feel a tingling or ‘pins and needles' sensation at the contact area of the electrodes and could also feel the tingling sensation throughout the area being treated. This sensation could also continue for a brief period following treatment as well. The intensity should be increased to a level that is comfortable for the participant. Stronger intensities usually have more beneficial effect but the intensity should not be turned up so high as to cause it to be uncomfortable.

3.17.2 Machine preparation

All the machines were calibrated prior to use in the study. The Sonicator Plus 920® (Mettler Electronics Corp., Anaheim, CA, USA) was used to generate the treatment parameters for interferential current therapy (group II). Below are the treatment parameters as indicated in the pilot study section:

Frequency: 4000Hz

Base frequency: 90Hz

Sweep frequency: 40Hz

AMF/Beat frequency: 90-130Hz

Polarity: 4 electrodes

Duration of the treatment: 10 minutes

3.17.3 Application procedure

IFC treatment procedures are described below from step 1 to 5.

Step 1- Four self-adhesive electrodes were applied in a diagonal pattern to the affected knee (anterior-posterior and mediolateral).

Step 2- Treatment parameters were set on the machine as stated above to the recommended values.

Step 3- Instructions to the participant were reiterated as regards what he/she would experience.

Step 4- The treatment intensity was gradually increased to the participant's comfort level.

Step 5- The participant was also re-informed that a stronger IFC current would usually have a more beneficial effect but the intensity should not be turned up so high as to cause pain. Also, the participant was told to inform the therapist-in-charge if the intensity of the treatment was low due so the intensity could be increased.

3.17.4 Termination of treatment

At the end of the treatment session, all the machine knobs were turned back to zero in preparation for the next session of treatment. Electrodes were removed and treated area was inspected for any skin reaction or irritation following the application of the electrodes. Participants were told to report immediately to the therapist-in-charge should any allergy occur.

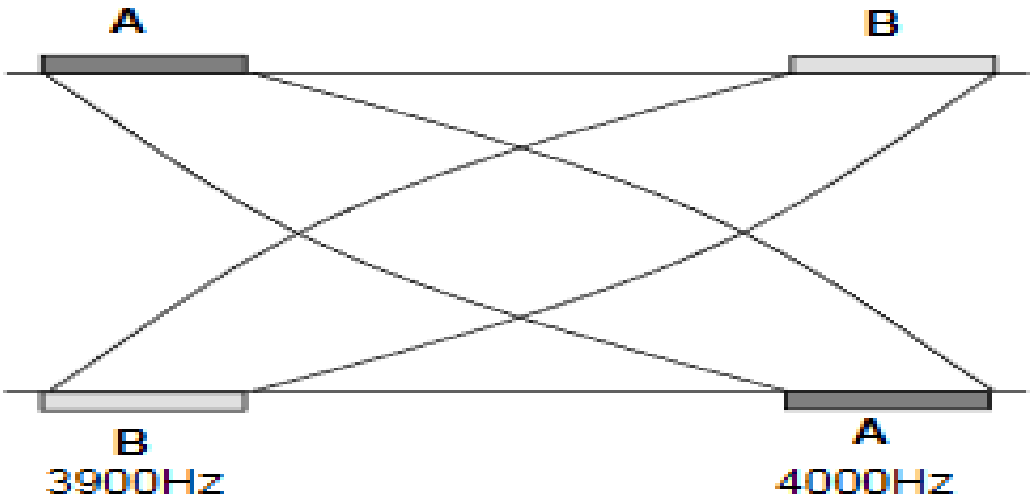

Figure 3. 4 In current A-A is at 4000 Hz and incurrent B-B is at 3900 Hz then the interference will have a 'beat frequency' of 100Hz. Adopted from https://electrostimulateurs-manuels.fr/fichiers/publications/Interferential-Therapy/interferential-therapy.pdf.

Table 3.4. Contradictions, Precautions, and Risks of IFC

Contraindications	Precautions	Risks
• DVT or thrombophlebitis • Hemorrhagic conditions • Pregnancy • Eyes, anterior neck, carotid sinus, head, reproductive organs • Impaired cognition or communication • Regenerating nerves • Cardiac failure (local) • Damaged or at-risk skin (local) • Infection or tuberculosis (local) • Malignancy (local) • Recently radiated tissue (local) • Electronic device (local) Impaired sensation (local)	• Active epiphysis • Skin disease • Impaired circulation • Chest, heart	• Pain • Skin irritation • Surge

Adopted from, http://www.physio-pedia.com/Therapeutic_Modalities.

3.18 Combination Therapy (Group III)

This is the third group of the study. Participants in this group received a simultaneous application of therapeutic ultrasound and interferential current therapy. The procedure for the combination treatment are described below:

Patient preparation: The participant was fully informed about the treatment procedure and what was expected of him/her. The participant was comfortably positioned in supine lying

with knee supported with a pillow. The area to be treated was cleaned with menthylated spirit and dried.

Machine preparation: A Sonicator Plus 920® (Mettler Electronics Corp., Anaheim, CA, USA) was used to generate the treatment parameters for simultaneous application of interferential current therapy and therapeutic ultrasound (treatment parameters are as discussed in the study section). Prior to the main treatment in this group, the participants had electro-diagnosis of the most painful spot on the affected knee. This procedure is one of the advantages of combination therapy over the individual modalities. A "Continuous" mode with intensity of 1MHz; 0.5Watt/cm^2 , and IFC: AMF-100Hz; intensity in the tactile sensation threshold were used by Almeida et al. (2003). Following the process of electro-diagnosis of the most painful spot on the affected knee, treatment parameters were set on the machine as discussed in the pilot study section. They are as follows:

- *US treatment dose:*

  Frequency: 1MHZ

  Intensity: 0.8watt/cm^2

  Mode: Continuous mode

  Duration: 10 minutes

- *IFC treatment dose:*
  Frequency: 4,000Hz
  Base frequency: 90Hz
  Sweep frequency: 40Hz
  Polarity: Bipolar (2 electrodes).

3.18.0 Application procedure

The application procedure of combination therapy are described below:

Step 1**:** IFC electrodes were placed with an indifferent electrode applied to the most painful spot on the knee

Step 2: A substantial amount of coupling medium was applied to the participant's cleaned and dried skin

Step 3: Treatment parameters were set as recommended above, with US parameters set first then IFC parameters

Step 4: Gradually the IFC intensity was increased until the normal 'tingling sensation' was experienced by the participant

Step 5**:** The transducer was moved in a circular or stroking pattern

Step 6: The intensity of IFC required to achieve the usual effect was lower than normal.

3.18.2 Termination of treatment

At the end of the treatment session, all the machine parameters were turned off in preparation for next treatment session. Electrodes were removed and treated and the remaining contact gel was cleaned off the skin and the area inspected for any skin response. In the case of any adverse reaction, participants were asked to report to the therapist-in-charge. The treatment procedure was safe and effective.

3.19 Control /Infrared radiation (Group IV)

Participants in this category were the control group for the study, and they received infrared radiation. The treatment procedure is as described below:

3.19.1 Patient preparation

The participant was positioned comfortably in supine lying with the affected knee semi-flexed at 60^0-80^0 and supported underneath with a pillow. The area to be treated was exposed and cleaned. The participant was instructed that he/she was expected to feel a mild

comfortable warmth, but if the heat became too hot, the participant should inform the physiotherapist in-charge by pressing a bell. Also, the participant was instructed not to look directly at the infra-red lamp as it could cause damage to the eyes.

The IRR lamp was placed 60 cm away from the participants' skin at 90^0 for maximum and effective irradiation of the affected area. The treatment time was 15 minutes exposure.

3.19.2 Infrared radiation treatment parameters

Duration of the treatment: 15 minutes

Frequency: 3 times / week for 12 weeks

Dosage: Distance (60 cm) + Time (10mins).

3.19.3 Application procedure

Step 1**:** The participant was instructed on what he/she was expected to experience during and after the treatment session.

Step 2**:** Distance from the source of the radiation to the participant's skin was determined.

Step 3**:** The lamp was put on together with the timer.

3.19.4 Termination of treatment

Treatment was terminated once the stipulated treatment time was reached. The lamp was moved away from the participant. The treated area was inspected for excessive erythema or blisters and the participant was asked to watch out for any skin reaction or blister.

3.20 Statistical Analysis

Data were analyzed descriptively and inferentially using the IBM SPSS (Version 21.0, SPSS Inc., and Chicago IL, USA). Outcomes were found to be normally distributed; the variance in the samples being compared were homogenous, and all the data were measured in either ratio or interval scales. Thus, parametric statistics were used to compare the means among the study groups. One-way analysis of variance (ANOVA) was used to determine whether there were any statistically significant differences between the means of the four independent (unrelated) study groups. To determine which specific groups differed from each other, a post-hoc test analysis was conducted. Our study met the assumption of homogeneity of variances, thus, we used Tukey's honestly (Tukey's HSD) post hoc analysis. An independent sample t-test was used to compare the results of each treatment modality with those of the control group, whereas, the paired sample t-test was used to compare within each group. All statistical analyses were two-tailed with an alpha level of 0.05 or less indicating statistical significance

3.21 Summary

This chapter describes the methodology of the study protocols and how it was designed, data collection procedures from baseline to the end of the 12 weeks intervention study period and the statistical analysis used in the study. Standardized and valid outcome measures were described and used to collect the data (participants' joint ROM, pain perception, clinical symptoms and health-related quality of life) that changed with the intervention procedures.

CHAPTER 4: RESULTS

4.0 Introduction

This chapter reports the major findings following analysis of the data collected, examining the effects of electrotherapy treatment on pain intensity, functional activity, and health-related quality of life in patients with knee osteoarthritis. The baseline characteristics of the study participants are first examined and a summary of the descriptive and inferential analyses of all relevant continuous and categorical outcome data are presented. This is followed by hypothesis testing in relation to the variables measured with the interpretation of the results. Results are generally interpreted both in descriptive and inferential terms with summaries presented using tables. The final section of the chapter provides a summary of the findings.

4.1 Findings of the Study

4.2 Characteristics of the Study Participants

A total of 133 individuals with knee OA, comprising 53 (40%) males and 80 (60%) females, participated in the study. All participants were from the Hausa-Fulani ethnic group of Northwestern Nigeria. The combination therapy group had a female to male ratio of 4:1, while the US and control groups had ratios of 1.5:1 each and the IFC group was 0.6:1. The ages of the participants were between 58 and 82 years (mean = 66.19 ± 8.50 years, median = 56 years). The average total BMI mean was 25.58 (±4.27). Participants' demographic characteristics are shown in Table 4.1.

There were no significant differences among the groups with respect to participants' age (p= 0.153), weight (p= 0.985), height (p=0.780) and BMI (p= 0.621) **(**Table 4.1**)**. Similarly, no significant difference was found for baseline values on any of the outcome variables among the four study groups (Table 4.1). The groups were, therefore, adjudged comparable, at least with regard to these criteria.

Table 4.1 Participants' demographic characteristics

Variables	All Participants N=133 M(±SD)	US Group n=34 M(±SD)	IFC Group n=34 M(±SD)	CT Group n=33 M(±SD)	Control Group n=32 M(±SD)	p value
Age(years)	66.19(±8.50)	66.40(± 7.68)	65.76(± 8.51)	65.8(± 9.21)	66.8(±8.61)	0.153
Weight (Kg)	69.96(±10.47)	70.25(±11.77)	70.26(± 9.64)	69.29(±10.88)	70.04(±9.66)	0.985
Height (M)	1.67(±0.25)	1.67(± 0.10)	1.69(± 0.07)	1.66(± 0.08)	1.67(±0.76)	0.780
BMI(Kg/M^2)	25.58(±4.27)	24.85 (±4.91)	26.50(1±5.13)	25.43(±3.8)	25.54(± 3.20)	0.621
Gender M/F (%)	40/60%	40/60%	60/40%	20/80%	40/60%	ND
Gender Ratio		1.5:1	0.6:1	4:1	1.5:1	ND

BMI, Body Mass Index; M, Male; F, Female; M, Mean; SD, Standard Deviation. * p>0.05; ND, no data .P values are for parametric test (ANOVA) for comparison among the four groups *indicates statistical significance. *P* values are from the results of ANOVA comparing the means of the four groups.

4.2.1 Primary Outcomes at Baseline

4.2.2 Pain Intensity

The baseline VAS scores of the participants in the four groups indicated their pain status before treatment. A comparison of the mean scores of the four groups was made using the one-way ANOVA (Table 4.2). No significant difference was found (F = 0.692; df = 3; p = 0.559), indicating homogeneity of the groups at recruitment (P=0.612).

Table 4.2 Participants' Baseline VAS and WOMAC Scores

Variables (%)	All Participants (N=133) M (±SD)	US Group (n=34) M (±SD)	IFC Group (n=34) M (±SD)	CT Group (n=33) M (±SD)	Control Group (n=32) M (±SD)	P value
VAS	7.02(±1.58)	7.05(±1.61)	7.32(±1.58)	7.07(±1.74)	7.00(±1.33)	0 .612
WOMAC						
Pain	18.80(±2.60)	18.87(±3.09)	18.80(±2.17)	18.77(±2.78)	18.80(±2.38)	0 .995
Stiff.	5.86(±1.18)	5.90(±1.27)	5.73(±1.05)	5.77(±1.00)	5.93(±1.41)	0 .921
PF	56.28(±6.84)	56.07(±7.12)	56.33(±8.49)	56.10(±7.35)	56.60(±5.73)	0 .990

WOMAC, Western Ontario and McMaster Universities Arthritis Index; CI, confidence interval**;** M, Mean; SD, Standard Deviation; * Denotes significance p<0.0; **VAS**, Visual Analogue Scale; **n** = number of participants; **N** = total number of participants; **M,** mean; **SD,** standard deviation. *P* values are from the results of ANOVA comparing the means of the four groups.

4.2.3 Physical Function

One-way ANOVA was used to compare the baseline scores WOMAC index (Table 4.2). There were no statistically significant differences in WOMAC index scores between the groups at baseline, i.e. pain subscale (F = 0.008; df = 3; p = 0.995); stiffness (F= 0.163; df =3; p=0.921); and physical function (F= 0.380; df =3; p= 0.990)

The baseline scores for physical function, joint stiffness, and pain subscales of WOMAC did not significantly differ between the four groups (Table 4.2, P>0.05). The mean values of PF in the US, IFC, CT and the control groups are 56.07(±7.12), 56.33(±8.49), 56.10(±7.35) and, 56.60(±5.73) respectively, which shows homogeneity of the groups at baseline.

Table 4.3 Participants' Health-related Quality of Life at Baseline for all the groups

Variables (%)	All Participants (N=133) M(±SD)	US Group (n=34) M(±SD)	IFC Group (n=34) M(±SD)	CT Group (n=33) M(±SD)	Control Group (n=32) M(±SD)	P value
PF	54.64(±5.88)	54.56(±4.76)	55.67(±7.60)	55.62(±5.60)	52.70(±4.88)	.171
RLPH	51.90(±7.62)	52.38(±5.62)	51.22(±7.62)	51.57(±10.90)	52.42(±7.35)	.909
RLEP	66.67(±7.52)	67.09(±10.11)	65.87(±7.8)	66.94(±6.11)	52.42(±7.35)	.925
E/F	61.54(±6.52)	60.90(±7.64)	60.57(±4.83)	61.97(±6.72)	62.64(±6.70)	.605
EWB	66.05(±6.53)	65.67(±10.93)	66.20(±4.83)	66.80(±4.43)	65.55(±4.43)	.910
SF	57.20(±7.70)	57.65(±8.57)	66.20(±6.09)	66.80(±4.42)	65.55(±7.32)	.861
Pain	50.86(±7.67)	51.53(±7.67)	51.00(±5.72)	49.97(±8.56)	50.92(±5.49)	.855
GH	51.53(±6.22)	50.82(±7.67)	51.00(±5.73)	49.98(±8.57)	51.57(±5.49)	.730
PCS	52.37(±5.15)	52.37(±1.67)	52.52(±1.68)	50.52(±9.69)	51.62(±2.56)	.425
MCS	63.10(±2.45)	63.10(±2.42)	62.75(±1.68)	63.26(±2.42)	63.30(±1.62)	.820

PCS, Physical Component Summary; **MCS**, Mental Component Summary; **PF**, physical function; **RLPH**, role of limitation due to physical health; **RLEP**, role of limitation due to emotional problems; **EF**, energy/fatigue; **EWB**, emotional well-being; **SF**, social functioning ;**GH**, general health. *Denotes significance p<0.05. *P* values are from the results of ANOVA comparing the means of the four groups.

4.2.4 Health-related Quality of Life

The pre-treatment mean scores for QoL of all the participants from the four different groups were compared using one-way ANOVA (Table 4.3). No significant difference was found (P>0.05). The participants from the four groups did not differ significantly before the treatments. The mean scores of all domains of SF-36 did not significantly differ in all the groups before the interventions, thus the groups were considered comparable pre-treatment.

4.2. Knee Goniometry

Table 4.4 shows baseline mean scores of the participants' knee ROM, both active and passive flexion and extension, for the four study groups. There were no statistically significant differences ($p<0.05$) in the mean ROM scores of all the groups at baseline. This indicates homogeneity of the variables in the participants from all the groups, with the active and passive flexion of the combination group having the least ROM, whereas, active extension in the control group had the highest ROM.

Table 4.4 Participants' Baseline active flexion, passive flexion, active extension and passive extension scores for the four groups

Variables ROM	US Group (n=34)	IFC Group (n=34)	CT Group (n=33)	Control Group (n=32)	P value
	M (±SD)	M (±SD)	M (±SD)	M (±SD)	
PreActFlx	124.46± (7.76)	124.22(±4.85)	123.57(±6.16)	124.20(±5.12)	0.950
PrePassFlx	120.87±13.62)	118.76(±5.90)	118.59(±4.67)	118.69(±3.10)	0.635
PreActExt	127.58(±8.09)	128.54(±5.57)	128.19(±6.13)	128.59(±4.30)	0.916
PrePassExt	124.92(±8.27)	123.97(±6.02)	124.19(±5.42)	124.31(±1.64)	0.932

PreActFlx: pre-active flexion; **PrePassFlx:** pre-passive flexion; **PreActExt: pre**-active extension; **PrePassExt: pre**-passive extension. M, Mean; SD, Standard Deviation. * p>0.05 .P values are for parametric test (ANOVA) for comparison among the four groups *indicates statistical significance

4.3.0 CT vs Control

4.3.1 Pain Severity

An independent sample *t*-test was calculated to compare the mean VAS scores between the CT group and the control group before the treatment. No significant difference was found ($t(65) = 0.85$, $p= 0.612$) (Table 4.5). The mean score of the CT group was 7.07(±1.74) while the control group was 7.00 (±1.33).

Table 4.5 ***VAS and WOMAC Baseline scores for the combination and control groups***

Variables	Combination Therapy Group (n=34) M ±(SD)	Control Group (n=32) M±(SD)	p-value
VAS	7.07(±1.74)	7.00(±1.33)	0 .612
WOMAC			
Pain	18.77(±2.78)	18.800(±2.38)	0.995
Stiff	5.77(±1.00)	5.93(±1.41)	0.921
PF	56.10(±7.35)	56.60(±5.73)	0.990

WOMAC, Western Ontario and McMaster Universities Arthritis Index; CI, confidence interval**;** M, Mean; SD, Standard Deviation; *Denotes significance p<0.05. P values are for parametric test Independent sample *t*-test*)* for comparison groups *indicates statistical significance.

4.3.2Functional Activity

Table 4.5 shows baseline WOMAC index scores for the CT and the control groups. An independent sample *t*-test was conducted to compare functional activity of participants in the two groups. There were no statistically significant differences in WOMAC scores at baseline between the groups, i.e. pain subscale (t (65) = -14.74; *p* = 0.995; stiffness (t (65) =-9.40; p=0.921); and physical function (t (65) = 0.22; p= 0.990).The pain mean scores for the CT group (M=18.77; SD±2.78) were not significantly greater than those for the control group (M=18.800,DS±2.38) in all the WOMAC subscales (Table 4.5).

4.3.3 Health-related Quality of Life

Table 4.6 shows the pre-treatment mean scores for quality of life (QoL) of the participants in both the combination therapy and the control groups. An independent sample t-test was used to compare the pre-treatment mean scores for QoL between the groups. There were no significant differences (p>0.05) in the group scores for all domains of SF-36. The groups were the same in QoL before the intervention.

Table 4.6 Participants' Baseline Health-related Quality of Life (HRQoL) scores among the two groups

Variables (%)	Combination Therapy Group (n=34)	Control Group(n=32)	P-value
	M± (SD	M± (SD)	
PF	54.57(±4.76)	52.70(±4.88)	0.139
RLPH	52.38(±5.62)	52.42(±7.35)	0.984
RLEP	67.09(±10.11)	66.76(±5.57)	0.876
EF	60.98(±7.64)	62.64(±6.70)	0.378
EWB	65.67(±10.93)	65.55(±6.52)	0.960
SF	57.65(8.57)	57.95(±5.71)	0.875
Pain	51.54(±7.67)	50.92(± 5.49)	0.720
GH	50.82(±6.94)	51.57(±4.17)	0.614
PCS	52.37(±1.66)	51.62(±2.56)	0.185
MCS	63.10(±2.42)	63.29(±1.62)	0.720

***PCS**, Physical Component Summary; **MCS**, Mental Component Summary; **PF**, physical function; **RLPH**, role of limitation due to physical health; **RLEP**, role of limitation due to emotional problems; **EF**, energy/fatigue; **EWB**, emotional well-being; **SF,** social functioning **;GH**, general health; M, Mean; SD, Standard Deviation; *Denotes significance p<0.05.* P values are for parametric test Independent sample *t*-test*)* for comparison groups *indicates statistical significance.

4.4.0 IFC vs Control

4.4.1 Pain Severity

An independent *t*-test was conducted comparing the VAS mean scores of the participants with at baseline in the IFC group and the control group (Table 4.7). No significant difference was found (t (65) = 0.895, p=0.128). The mean VAS score of the IFC group (M= 7.32; SD ±32) was not significantly different from that of the control group (M= 6.67; SD±1.33). The two groups had the same level of pain severity before the treatment.

4.4.2 Functional Activity

Table 4.7 shows comparison of pre-treatment scores for the WOMAC subscales for the IFC and control groups. There were no statistically significant differences in WOMAC scores at baseline between the groups; pain subscale (t (65) = -14.74; *p>0.05*); stiffness (t (65) =-9.40; p=0.545); and physical function (t (65) = 0.22; p= 0.87). The mean score for the IFC group (M=18.80, SD= ±2.17) was not significantly greater than that of the control group (M=18.80,

SD=±2.38) in all the subscales of WOMAC. Thus, the two groups had the same level of physical activity before the treatment.

Table 4. 7 VAS and WOMAC Baseline scores for the IFC and control groups

Variables	IFC Group (n=30) M ±(SD)	Control Group (n=29) M±(SD)	p-value
VAS	7.32(±32)	6.67(±1.33)	0.128
WOMAC			
Pain	18.80(±2.17)	18.80(±2.38)	1.000
Stiff.	5.73(±1.05)	5.93(±1.46)	0.545
PF	56.33(±7.32)	56.60(±5.73)	0.87

WOMAC, Western Ontario and McMaster Universities Arthritis Index; CI, confidence interval**;** M, Mean; SD, Standard Deviation; *Denotes significance p<0.05. P values are for parametric test Independent sample *t*-test*)* for comparison groups *indicates statistical significance.

4.4.3 Health-related Quality of Life

Table 4.8 compares the pre-treatment scores for QoL between the IFC group and the control group. Participants did not show significantly different (p>0.05) mean scores in any of the domains of the SF-36 survey at baseline. Therefore, the two groups had similar QoL scores before the intervention.

Table 4. 8 Participants' Baseline Health-related Quality of Life (HRQoL) scores among the two groups

Variables (%)	IFC Group M± (SD	Control Group M± (SD)	P-value
PF	64.83(±15.51)	60.23(±19.52)	0.316
RLPH	43.33(±19.52)	57.61(±23.92)	0.660
RLEP	65.53(±39.62)	59.26(±32.17)	0.503
EF	64.08(±22.78)	64.65(±14.98)	0.910
EWB	74.27(±17.49)	67.87(±17.28)	0.159
SF	75.92(±13.19)	69.53(±19.06)	0.242
Pain	67.17(±13.19)	68.67(±14.78)	0.242
GH	66.67(±24.36)	57.93(±13.29)	0.680
PCS	59.27(±13.67)	58.39(±9.93)	0.900

MCS	65.86(±16.62)	64.23(±11.38	0.66**0**

***PCS**, Physical Component Summary; **MCS**, Mental Component Summary; **PF**, physical function; **RLPH**, role of limitation due to physical health; **RLEP**, role of limitation due to emotional problems; **EF**, energy/fatigue; **EWB**, emotional well-being; **SF,** social functioning **;GH**, general health; M, Mean; SD, Standard Deviation; *Denotes significance p<0.05.* P values are for parametric test Independent sample *t*-test*)* for comparison groups *indicates statistical significance.

4.5.0 US vs Control

4.5.1 Pain Severity

An independent sample t-test was conducted to compare the pre-treatment mean VAS scores between the therapeutic ultrasound group and the control group of participants with knee OA. The mean score for the US group (M= 7.05; SD±1.61) did not significantly differ from that of the control group (6.733(±1.34) before the treatment. Therefore, there was no significant difference in the scores between the two groups at baseline (t (65) =-0.78, P = 0.411.) Thus, the two groups had the same level of pain severity before the treatment.

Table 4. 9 VAS and WOMAC Baseline Scores for the US and Control Groups

Variables	US Group (n=34) M ±(SD)	Control Group (n=32) M±(SD)	p-value
VAS	7.05(±1.61)	6.733(±1.34)	0.411
WOMAC			
Pain	18.87(±3.09)	18.80(±1.27)	0.926
Stiff.	5.90(±5.90)	5.90(±1.46)	0.25
PF	56.07(±7.18)	56.60(±5.73)	0.752

WOMAC, Western Ontario and McMaster Universities Arthritis Index; M, Mean; SD, Standard Deviation; * Denotes significance p<0.05. P values are for parametric test Independent sample *t*-test*)* for comparison groups *indicates statistical significance.

4.5.2 Functional Activity

An independent sample *t* test was conducted to compare the level of functional activity between the US and the control groups. The mean score of PF in the US group (M= 56.07, SD±7.18) did not significantly differ from the control group (M=56.60, SD±5.73). There was no statistically significant difference (P=0.752) in physical function scores at baseline between the groups (t (65) = 0.32; p=0.752) (Table 4.9). The mean scores in the US group

were not significantly greater than those of the control group in all the subscales of WOMAC. Therefore, the groups had the same level of physical function before the treatment.

4.5.3 Health-related Quality of Life

Table 4.10 shows pre-treatment QoL scores of the therapeutic ultrasound (US) and control groups. An independent t-test was used to compare the pre-treatment mean scores for all the domains of SF-36 of the two groups. There were no significant differences ($p>0.05$) between the scores of the groups, i.e. no significant difference in the QoL scores of the groups pre-treatment.

Table 4. 10 Participants' Baseline Health-related Quality of Life (HRQoL) scores of the two groups

Variables (%)	US Group (n=34) M± (SD)	Control Group (n=32) M± (SD)	P-value
PF	54.57(±4.76)	52.70(±4.88)	0.139
RLPH	52.38(±5.62)	52.42(±7.35)	0.984
RLEP	67.09(±10.11)	66.76(±5.57)	0.876
E/F	60.99(±7.64)	62.64(±6.70)	0.378
EWB	65.67(10.93)	65.55(±6.52)	0.960
SF	57.65(±8.57)	57.95(±5.71)	0.875
Pain	51.54(±7.67)	50.92(±5.49)	0.720
GH	50.82(±6.94)	51.57(±4.17)	0.614
PCS	52.34(±1.66)	51.62(±2.56)	0.185
MCS	63.10(±2.42)	63.30(±1.62)	0.720

***PCS**, Physical Component Summary; **MCS**, Mental Component Summary; **PF**, physical function; **RLPH**, role of limitation due to physical health; **RLEP**, role of limitation due to emotional problems; **EF**, energy/fatigue; **EWB**, emotional well-being; **SF,** social functioning **;GH**, general health; M, Mean; SD, Standard Deviation; **US,** therapeutic ultrasound *Denotes significance $p<0.05$.* P values are for parametric test Independent sample *t*-test*)* for comparison groups *indicates statistical significance.

4.6.0 Primary Outcomes at Follow-up and Tests of Hypotheses

4.6.1 Null-hypothesis One

Pain, functional activity measures and HRQoL will not be different between the experimental (US, IFC & CT) groups and the control group in patients with knee OA.

4.6.2 Change in Pain Intensity

Post-treatment comparison of the mean scores of pain intensity between the four groups was made using one-way ANOVA. There was significant difference between the groups (F =17.515; df=3; p = 0.001). A Tukey post-hoc test was used to determine the nature of the difference between the groups. This analysis revealed that the pain score was significantly lower in the IFC (2.23±1.00, p = .001), US and CT (2.60±1.10, p = .001) groups compared to the control group (6.24 ± 1.10). Therefore, there was significant difference between the US, IFC, CT (experimental), and the control groups. Participants in the experimental groups thus had significant pain relief compared to the control group (p <0.05). The first research question has been answered, as use of electrotherapy (US, IFC & combination therapy) was shown to effect changes in pain severity by reducing VAS scores post-treatment in patients with knee osteoarthritis. Hypothesis one sought to test whether pain severity will be different between the experimental (US, IFC &CT) groups and the control group in patients with knee OA. The null hypothesis stated that there will be no difference in pain severity between the experimental groups and the control group. Using one-way ANOVA to test this hypothesis, pain severity improved significantly following electrotherapy (US, IFC & CT) intervention in patients with knee OA. Since the observed p-values was less than 0.05, the null hypothesis was therefore, rejected.

Table 4. 11 Baseline to post-intervention changes in VAS and WOMAC scores following 12 weeks of intervention between the groups

Variable	Pre-intervention					Post-intervention				
	US (n=34)	IFC (n=34)	CT (n=33)	Control (n=32)	P-value	US (n=34)	IFC (n=34)	CT (n=33)	Control (n=33)	P-value
VAS	7.05(±1.61)	7.32(±1.58)	7.07(±1.74)	7.00(±1.33)	0.612	2.45(±1.74)	2.23(±1.00)	2.60(±1.10)	6.24 (±3.12)	0.001*
WOMAC										
Pain	18.87(±3.09)	18.80(±2.17)	18.77(±2.78)	18.800(±2.38)	0.995	15.57(±3.44)	10.17(±2.19)	09.96(±3.88)	14.17(±13.38)	0.003*
Stiffness	5.90(±1.27)	5.73(±1.05)	5.77(±1.00)	5.93(±1.41)	0.921	2.87(±1.25)	2.23(±1.38)	1.133(±2.06)	4.33(±0.80)	0.040*
PF	56.07(±7.12)	56.33(±8.49)	56.10(±7.35)	56.60(±5.73)	0.990	49.40(±7.12)	51.03(±7.66)	45.77(±9.1)	49.09(±16.22)	0.020*

P values are from the results of One-way ANOVA test for comparison of baseline and post-intervention data in each of the four groups. * indicates statistical significance. ($p<0.05$).

4.6.2 Functional Activity

One-way ANOVA was used to compare the WOMAC index scores post-treatment between the four study groups. There were statistically significant differences in the WOMAC scores, i.e. pain ($F=203.87$; df =3; $p=0.003$), stiffness ($F= 50.55$; df =3; $p= 0.040$) and physical function ($F=8.50$;df =3; $p=0.020$) subscale scores. The Tukey's HSD post-hoc analysis was conducted to determine the nature of the differences. There were significant differences in the pain ($p<0.05$), joint stiffness ($p<0.05$), and physical function ($p<0.05$) subscales of WOMAC in the experimental (US, IFC, & CT) groups compared to the control group. The participants in the US, IFC and CT groups had significant improvement in pain, physical function and joint stiffness compared to the participants in the control group. None of the experimental treatment modalities was superior to the others (Table 4.11). The use of electrotherapy (US, IFC and combination therapy) was shown to improve functional activity as the participants' PF subscale scores on the WOMAC index increased. The null hypothesis stated that there will be no difference in functional activity between the experimental groups and the control group in patients with knee OA. Using one-way ANOVA to test the null hypothesis, functional activity significantly improved following electrotherapy (US, IFC & CT) treatments. This indicated significant improvement in functional activity, pain measures in

the experimental groups compared with the control group. The observed p-value is less than 0.05, the hypothesis was, therefore, rejected.

4.6.3 Health-related Quality of Life

One-way ANOVA was used to compare the post-treatment mean scores for HRQoL between the 3 experimental groups (US, IFC & CT) and the control group. There were statistically significant differences in physical function (F =57.76; df=3; p<0.001); role limitation due to physical health (F=13.58; df=3; p<0.001), role limitation due to emotional problems (F= 4.001; df =3; p = 0.009), social function (F= 30.78;df= 3; p<0.001), pain (F= 32.80; df =3; p=0.006), general health (F =11.83; df= 3; p=0.025), physical component summary (F= 51.67; df=; p=0.007) and mental component summary (F= 10.58; df=3; p<0.001) of the SF-36 domains. No significant difference was found in energy/fatigue (F =1.18; df =3; p=0.332) and emotional well-being (F=2.46; df= 3; p=0.066). There were significant improvements in all the domains of SF-36 except energy/fatigue and emotional well-being between the groups post-treatment. A Tukey HSD post hoc was conducted to determine the nature of the differences. There was significant difference between all the experimental groups (US, IFC & CT) on PSC and MCS of HRQoL compared with the control group.

The domains of the SF-36 health survey improved significantly from baseline to post-treatment (P<0.05), with the exception of energy/fatigue. The highest increase was in the RLPH domain (from a median of 51.22 to 84.35%) (Table 4.14). In the control group, the scores on the domains either had little improvement (EWB, SF, pain, E/F and RLEP) or did not change (MCS) from baseline to post-treatment. Between-group comparison at follow-up indicated significant differences in all the domains with the exception of emotional well-being and energy/fatigue (Table 4.14). This answers the first research question as increasing values for the domains of the SF-36 health survey show that the use of electrotherapy (US, IFC & CT) influenced QoL in patients with knee osteoarthritis. Hypothesis one sought to test whether QoL will be different between the experimental (US, IFC &CT) groups and the control group in patients with knee OA. The null hypothesis stated that there would be no difference in HRQoL between the experimental groups and the control group in patients with knee OA. Using one-way ANOVA test, QoL generally improved significantly for all domains except energy/fatigue following electrotherapy (US, IFC & CT) intervention in patients with knee OA. The null hypothesis was, therefore, rejected at the 5% level of significance.

4.7.0 Null Hypothesis 2

There will be no difference in pain, functional activity and HRQoL measures between the combination therapy group and the control group in patients with knee OA.

4.7.1 Pain Severity

Independent t-test was used to compare the post-treatment changes in VAS scores between the two groups. The mean VAS scores for the combination therapy was significantly lower (2.60±1.10) compared to the control group (6.24±3.12) (Table 4.12). Thus, there was a significant difference (p= 0.001) in the post-treatment VAS scores between the two groups. Participants treated with combination therapy had lower post-treatment pain scores compared to the control group. The null hypothesis was, therefore, rejected at the 5% level of significance. This implies that combination therapy improves pain in patients with knee OA compared with the control group. This answers the second research question, as the treatment was shown to influence pain by decreasing VAS scores.

Table 4. 12 Baseline to post-intervention changes in VAS and WOMAC scores following 12 weeks of intervention in the CT and Control groups

Variables	Combination Therapy Group			Control Group		
	Pre-treatment M±(SD) (n=33)	Post-treatment M±(SD) (n=33)	P-Values	Pre-treatment M±(SD) (n=32)	Post-treatment M±(SD) (n=32)	P-Values
VAS	7.07(±1.74)	2.60(±1.10)	<0.05	7.00(±1.33)	6.24±3.12	0.001
WOMAC						
Pain	18.77(±2.78)	09.96(±3.88)	<0.05	18.800(±2.38)	14.17(±13.38)	0.001
Stiffness	5.77(±1.00)	1.13(±2.06)	<0.05	5.93(±1.41)	4.33(±0.80)	0.033
PF	56.10(±7.35)	45.77(±9.10	0.023	56.60(±5.73)	49.09(±16.22)	0.023

WOMAC, Western Ontario and McMaster Universities Arthritis Index; M, Mean; SD, Standard Deviation; * Denotes significance p<0.05. P values are for parametric test; Independent sample *t*-test*)* for comparison groups *indicates statistical significance.

4.7.2 Functional Activity

An independent sample *t*-test was conducted to compare functional activity between the CT group and the control group. It was found that there were significant differences (p<0.05) in the WOMAC scores of the combination group compared to the control group. The mean scores of the combination group, i.e. pain (09.96±3.38), stiffness (1.13±2.06) and physical function (45.77±9.10) were significantly lower than those of the control group, i.e. pain

(p=0.001), 14.17±13.38; stiffness (p=0.033), 4.33±0.83; and PF (p=0.023), 49.09±16.22. Between-group comparison at follow-up showed significant differences between the two groups (Table 4.13). This answered the third research question. The increase in the physical function subscale scores of WOMAC indicate that use of combination therapy impacts functional activity in patients with knee OA. The null hypothesis stated that there will be no difference in functional activity between the combination therapy group and the control group in patients with knee OA. This hypothesis was tested using the independent sample *t*-test. Significant lower values of physical function of WOMAC subscale scores were found following the use of combination therapy. This implies that patients treated with combination therapy had significantly improved functional activity compared to the patients in the control group. The null hypothesis was, therefore, rejected at the 5% level of significance.

Table 4. 13 Post-treatment changes between the CT and control groups following 12 weeks of Intervention

Variables	Combination Therapy Group (n=33) M±(SD)	Control Group (n=32) M±(SD)	P-Value
VAS	2.60±1.10	6.24±3.12	0.001
WOMAC (%)			
Pain	09.96± (3.88)	14.17(±13.38)	0.001
Stiffness	1.13(±2.06)	4.33(±0.80)	0.004
PF	45.77(±9.08)	49.09s(±16.22)	0.006

WOMAC, Western Ontario and McMaster Universities Arthritis Index; M, Mean; SD, Standard Deviation; * Denotes significance p<0.05. P values are for parametric test Independent sample *t*-test*)* for comparison groups *indicates significance

4.7.3 Health-related Quality of Life

Table 4.14 shows changes in QoL between baseline and post-treatment in the CT and control groups, following 12 weeks of treatment. There were statistically significant differences in all the domains from baseline to post-treatment in the CT group (p<0.05). In the control group, the emotional well-being did not change significantly from baseline to post-treatment and physical functioning scores deteriorated significantly. Between-group comparison at follow-up showed significant differences in all the domains between the two groups (Table 4.15). The second research question has been answered as increasing values for the domains of the SF-36 health survey show that CT influenced QoL in patients with knee OA. The null hypothesis stated that there will be no difference in QoL between CT and control group in patients with knee OA. The independent sample *t*-test was conducted to test this hypothesis,

and it was found that QoL generally improved significantly following the use of CT. Since the observed p-value is less than 0.05, the hypothesis was, therefore, rejected.

Table 4. 14 Baseline to post-intervention changes in SF-36 domains following 12 weeks of intervention in the CT and Control groups

	Combination Therapy Group			Control Group		
Variables	Pre-treatment	Post-treatment	P-Values	Pre-treatment	Post-treatment	P-Values
	M±(SD) (n=33)	M±(SD) (n=33)		M±(SD) (n=32)	M±(SD) (n=32)	
PF	54.57(±4.76)	80.07(±07)	<0.05	52.70(±4.88)	55.52(±52)	0.001*
RLPH	52.38(±5.62)	79.82(±7.87)	<0.05	52.42(±7.35)	54.05(±8.13)	0.001*
RLEP	67.09(±10.11)	83.70(±12.66)	0.012	66.76(±5.57)	68.60(±5.99)	0.001*
E/F	60.98(±7.64)	65.14(±16.37)	0.004	62.64(±6.70)	69.93(±9.05)	0.017*
EWB	65.67(±10.93)	78.37(±11.68)	0.011	65.55(±6.52)	65.63(±11.46)	0.678
SF	57.65(8.57)	75.24(±10.40)	< 0.05	57.95(±5.71)	58.18(±10.25)	0.912
Pain	51.54(±7.67)	72.42(±8.88)	<0.05	50.92(± 5.49)	53.33(±6.49)	0.003*
GH	50.82(±6.94)	80.13(±11.69)	<0.05	51.57(±4.17)	52.70(±11.69)	0.006*
PCS	52.37(±1.66)	78.27(±4.93)	<0.05	51.62(±2.56)	55.49(±3.49)	0.034*
MCS	63.10(±2.42)	72.90(±14.08)	<0.05	63.29(±1.62)	68.96(±5.60)	0.023*

***PCS**, Physical Component Summary; **MCS**, Mental Component Summary; **PF**, physical function; **RLPH**, role of limitation due to physical health; **RLEP**, role of limitation due to emotional problems; **E/F**, energy/fatigue; **EWB**, emotional well-being; **SF**, social functioning ;**GH**, general health; WOMAC, Western Ontario and McMaster Universities Arthritis Index; CI, confidence interval; **M**, Mean; **SD**, Standard Deviation; *Denotes significance p<0.05.The P values are for parametric test, paired t-test) for comparison groups *indicates statistical significance.*

Table 4. 15 Post-treatment Changes in QoL between the two groups (CT and Control)

Variables (%)	Combination Therapy Group	Control Group	P-Values
	M±(SD) (n=33)	M±(SD) (n=32)	
PF	80.07(±07)	55.52(±52)	0.001*
RLPH	79.82(±7.87)	54.05(±8.13)	0.002*
RLEP	83.70(±12.66)	68.60(±5.99)	0.011*
E/F	65.14(±16.37)	63.93(±9.05)	0.002*
EWB	78.37(±11.68)	65.63(±11.46)	0.001*
SF	75.24(±10.40)	58.18(±10.25)	0.001*
Pain	72.42(±8.88)	53.33(±6.49)	0.001*
GH	80.13(±11.69)	52.70(±11.69)	0.002*
PCS	78.27(±4.93)	55.49(±3.49)	0.005*
MCS	72.90(±14.08)	68.96(±5.60)	0.001*

***PCS**, Physical Component Summary; **MCS**, Mental Component Summary; **PF**, physical function; **RLPH**, role of limitation due to physical health; **RLEP**, role of limitation due to emotional problems; **E/F**, energy/fatigue; **EWB**, emotional well-being; **SF**, social functioning ;**GH**, general health; **WOMAC**, Western Ontario and McMaster Universities Arthritis Index; CI, confidence interval; **M**, Mean; **SD**, Standard Deviation; *Denotes significance p<0.05.The P values are for parametric test Independent sample t-test) for comparison groups *indicates statistical significance.*

4.8.1 Null Hypothesis 3

There will be no significant difference in pain, functional activity measures, and HRQoL between the interferential current therapy group and the control group in patients with knee OA.

4.8.2 Pain Severity

An independent sample *t*-test was conducted to compare post-treatment pain intensity scores between the IFC and control groups. Table 4.16 shows the pre-post treatment changes in VAS scores between the two groups. There was significant ($p<0.05$) decrease in the mean VAS score of IFC (2.23 ± 1.01) compared to the control (6.24±3.12) group. Thus, participants with knee OA treated with IFC had significantly lower pain intensity compared to those in the control group. Therefore, the use of IFC improves pain in patients with knee OA.

Table 4. 16 Baseline to post-intervention changes in measures of VAS and WOMAC scores following 12 weeks of intervention in the two groups

Variables	IFC Group			Control Group		
	Pre-treatment M±(SD) (n=34)	Post-treatment M±(SD) (n=34)	P-Values	Pre-treatment M±(SD) (n=32)	Post-treatment M±(SD) (n=32)	P-Values
VAS	7.32(±1.58)	2.23(±1.01)	0.001	7.00(±1.33)	6.24±3.12)	0.042
WOMAC						
Pain	18.80(±2.17)	10.17(± 2.19)	0.035	18.80(± 2.38)	14.17(± 13.38)	0.001
Stiffness	5.73(±1.05)	2.23(±1.38)	0.011	05.93(±1.41)	04.33(±0.80)	0.043
PF	56.33(±8.49)	51.03(± 7.66)	0.011	56.60(± 5.73)	49.09(±16.22)	0.001

WOMAC, Western Ontario and McMaster Universities Arthritis Index; M, Mean; SD, Standard Deviation; *Denotes significance p<0.05. P values are for parametric test Independent sample *t*-test*)* for comparison groups *indicates statistical significance.

4.8.3 Functional Activity

An independent sample *t*-test was conducted to compare functional activity between the IFC group and the control group. There were significant differences (p<0.05) in total WOMAC scores in the IFC group compared to the control group (Table 4.16). The mean score for physical function in the IFC group (M=51.03, SD±7.66) was significantly different with that of the control group (M=49.09, SD ±16.22). Between-group comparison at follow-up showed significant differences on all the WOMAC subscales between the two groups (Table 4.17). The null hypothesis stated that there will be no difference in functional activity between the IFC group and the control group in patients with knee OA. The null hypothesis was tested using an independent sample *t*-test, and significant higher values of WOMAC physical function subscale scores were found following the use of IFC. This result indicated that patients treated with IFC had significantly improved functional activity compared with the patients in the control group. The null hypothesis was, therefore, rejected at the 5% level of significance.

Table 4. 17 Post-intervention changes in measures of VAS and WOMAC scores following 12 weeks of intervention in both groups

Variables	IFC Group M±(SD) (n=34)	Control Group M±(SD) (n=32)	P-Values
VAS	2.23±1.01	6.24±3.12	0.002
WOMAC			
Pain	10.17 ± 2.19	14.17 ± 13.38	0.001
Stiffness	2.33 ±1.38	4.33 ±0.80	0.034
PF	51.03± 7.16	49.09 ±8.06	0.041

WOMAC, Western Ontario and McMaster Universities Arthritis Index; **M**, Mean; **SD**, Standard Deviation; * Denotes significance p<0.05. P values are for parametric test (Paired sample *t*-test*)* for comparison groups *indicates statistical significance.

4.8.4 Health-related Quality of Life

Table 4.18 shows changes in participants' HRQoL scores from baseline to post treatment in the IFC and control groups. There were significant improvements in all the domains of the SF-36 health survey from baseline to post-treatment in the IFC group (P<0.05). The highest increase was in the GH domain (from a mean of 66.67 to 86.21%). In the control group, scores on the domains either deteriorated significantly (EWB, PCS and MCS) or did not change (bodily pain and E/F) from baseline to post-treatment. Between-group comparison at follow-up showed significant differences in all the domains between the two groups (Table 4.19). Hypothesis 3 sought to test whether IFC significantly influences QoL among patients with knee OA. The null hypothesis stated that there will be no difference in QoL between the IFC group and the control group in patients with knee OA. The independent sample *t*-test was conducted to test this hypothesis and it was found that QoL generally improved significantly following the use of IFC. This hypothesis was, therefore, rejected at 5% level of significant.

Table 4. 18 Changes in Participants' Health-related Quality of Life (HRQoL) scores from Baseline to follow-up in each of the two groups

	IFC Group (n=34)			Control Group (n=32)		
Variables	Pre-treatment	Post-treatment	P-Values	Pre-treatment	Post-treatment	P-Values
	M±(SD)	M±(SD)		M±(SD)	M±(SD)	
PF	64.83(±15.51)	67.35(±22.73)	<0.05*	60.23(±19.52)	62.60(±13.30)	0.001*
RLPH	43.33(±19.52)	56.3 (±27.53)	< 0.05	57.61(±23.92)	34.48(±31.48)	0.023*
RLEP	65.53(±39.62)	68.73(± 34.13)	<0.05	59.26(±32.17)	54.54(±40.65)	0.043*
E/F	64.08(±22.78)	66.73(± 16.18)	<0.05	64.65(±14.98)	65.07(±16.57)	0.231
EWB	74.27(±17.49)	78.90 (± 17.41)	<0.05	67.87(±17.28)	66.84(±17.09)	0.471
SF	75.92(±13.19)	79.50 (± 20.91)	<0.05	69.53(±19.06)	75.70(±20.67)	<0.05*
Pain	67.17(±13.19)	71.50(± 15.97)	<0.05	68.67(±14.78)	68.00(±10.75)	0.960
GH	66.67(±24.36)	86.21 (± 13.29)	0.012	57.93(±13.29)	51.44(±09.25)	<0.05*
PCS	59.27(±13.67)	67.91(± 10.68)	0.011	58.39(±9.93)	59.25(± 9.17)	0.741
MCS	65.86(±16.62)	75.56**(**±12.30)	0.023	64.23(±11.38	66.20(±8.45)	<0.05*

***PCS**, Physical Component Summary; **MCS**, Mental Component Summary; **PF**, physical function; **RLPH**, role of limitation due to physical health; **RLEP**, role of limitation due to emotional problems; **E/F**, energy/fatigue; **EWB**, emotional well-being; **SF**, social functioning ;**GH**, general health; WOMAC, Western Ontario and McMaster Universities Arthritis Index; CI, confidence interval; **M**, Mean; **SD**, Standard Deviation; *Denotes significance p<0.05.The P values are for parametric test, paired t-test) for comparison groups *indicates statistical significance.*

Table 4. 19 Changes in Participants' Health-related Quality of Life (HRQoL) scores between the two groups

Variables	IFC Group (n=34)	Control Group (n=32)	P-Value
PF	67.35(±22.73)	62.60(±13.30)	<0.05*
RLPH	56.3 (±27.53)	34.48(±31.48)	0.012*
RLEP	68.73(± 34.13)	54.54(±40.65)	<0.05*
E/F	66.73(± 16.18)	65.07(±16.57)	<0.05*
EWB	78.90 (± 17.41)	66.84(±17.09)	0.021*
SF	79.50 (± 20.91)	75.70(±20.67)	<0.05*
Pain	71.50(± 15.97)	68.00(±10.75)	<0.05*
GH	76.21 (± 13.29)	51.44(±09.25)	0.011*
PCS	67.91(± 10.68)	59.25(± 9.17)	<0.05*
MCS	**75.56(**±12.30)	66.20(±8.45)	<0.05*

***PCS**, Physical Component Summary; **MCS**, Mental Component Summary; **PF**, physical function; **RLPH**, role of limitation due to physical health; **RLEP**, role of limitation due to emotional problems; **E/F**, energy/fatigue; **EWB**, emotional well-being; **SF**, social functioning ;**GH**, general health; WOMAC, Western Ontario and McMaster Universities Arthritis Index; CI, confidence interval; **M**, Mean; **SD**, Standard Deviation; *Denotes significance p<0.05.The P values are for parametric test, paired t-test) for comparison groups *indicates statistical significance.*

4.9.0 Null Hypothesis 4

There will be no significant difference in pain severity, functional activity and HRQoL between the therapeutic ultrasound group and the control group in patients with knee OA.

4.9.1 Pain Severity

An independent sample *t*-test was conducted to compare the baseline and post-treatment pain intensity scores between the therapeutic ultrasound group and the control group (Table 4.20). There was significant decrease ($p<0.05$) in the mean VAS scores of the two groups. Thus, there was improvement in pain severity post-treatment in the two groups. Between-group comparison at follow-up indicated a significant ($p<0.05$) decrease in the mean VAS score of the US (2.45±1.74) group compared to the control group (6.24±3.12) (Table 4.20). The participants with knee OA treated with US had significantly lower pain intensity compared to those in the control group. Therefore, use of US improves pain in patients with knee OA.

Table 4. 20 Baseline to post-treatment changes in VAS and WOMAC scores in the US and control groups

Variables	US Therapy Group (n=34)			Control Group (n=32)		
	Pre-treatment M±(SD)	Post-treatment M±(SD)	P-Values	Pre-treatment M±(SD)	Post-treatment M±(SD)	P-Values
VAS	7.05(±1.61)	2.45±1.74	0.011	7.00(±1.33)	6.24±3.12	0.048
WOMAC						
Pain	18.87(±3.09)	15.57± (3.44)	<0.05	18.800(±2.38)	14.17(±13.38)	<0.05
Stiffness	5.90(±1.27)	2.87(±1.25)	<0.05	5.93(±0.80)	4.33(±0.80)	< 0.05
PF	56.07(±7.35)	49.40(±7.12)	0.023	56.60(±5.73)	49.09(±16.22)	<0.05

WOMAC, Western Ontario and McMaster Universities Arthritis Index; M, Mean; SD, Standard Deviation; * Denotes significance p<0.05. P values are for parametric test (paired sample t-test) for comparison groups *indicates statistical significance.

4.9.2 Functional Activity

An independent sample *t*-test was calculated to compare functional activity between the US and the control group post-treatment (Table 4.20). There were significant differences ($p<0.05$) in all the 3 sub-scales of the WOMAC index in the US group compared to the control group. The mean scores of the US group, i.e. pain 15.57(±3.44), stiffness 2.87(±1.25) and physical function 49.40(±7.12) were significantly higher than those of the control group i.e. pain 14.17(±13.38), stiffness 4.33(±0.80) and physical function 49.09 (±16.22). Between-group comparison at follow-up indicated significant differences ($p<0.05$) between the two groups (Table 4.21). Hypothesis 4 stated that there will be significant effect of US on functional activity among patients with knee OA. The null hypothesis stated that there will be no significant difference in functional activity between the US group and the control group in patients with knee OA. This hypothesis was tested using the independent sample *t*-test, and significant higher values of the physical function subscale scores of WOMAC were found following the use of combination therapy. The null hypothesis was, therefore, rejected at the 5% level of significance.

Table 4. 21 Post-treatment changes between the US and control groups following 12 weeks of treatment

Variables	US Therapy Group (n=34) M±(SD)	Control Group (n=32) M±(SD)	P-Value
VAS	2.60(±1.10)	4.53(±1.04)	<0.05
WOMAC (%)			
Pain	3.30(±2.90)	11.76(±3.28)	<0.05
Stiffness	1.03(±0.93)	7.76(±11.04)	<0.05
PF	4.67(±3.38)	54.10(±5.97)	<0.05

WOMAC, Western Ontario and McMaster Universities Arthritis Index; M, Mean; SD, Standard Deviation; * Denotes significance p<0.05. P values are for parametric test Independent sample t-test) for comparison groups *indicates statistical significance.

4.9.3 Health-related Quality of Life

The domains of the SF-36 health survey improved significantly from baseline to post-treatment in the US group (P<0.05), with the exception of mental component summary. The highest increase was in the GH domain (from a mean of 50.82 to 72.33) (Table 4.22). In the control group, the scores on the domains either deteriorated slightly (RLPH, GH and PCS), while EWB and pain remained almost the same from baseline to post-treatment (Table 4.22). Between-group comparison at follow-up showed significant differences in all the domains with the exception of bodily pain and social function (Table 4.22). Hypothesis 4 sought to test whether US significantly influences QoL among patients with knee OA. The null hypothesis stated that there will be no difference in QoL between the US group and the control group in patients with knee OA. The independent sample *t*-test was conducted to test this null hypothesis, and it was found that QoL generally improved significantly following the use of therapeutic ultrasound. Since the observed p-value is less than 0.05, the null hypothesis was, therefore, rejected.

Table 4. 22 Baseline to post-treatment changes in QoL following 12 weeks of intervention in the US and control groups

Variables	US Therapy Group(n=34)		P-value	Control Group(n=32)		P-value
	Pre-treatment	Post-treatment		Pre-treatment	Post-treatment	
PF	54.57(±4.76)	69.67(±14.61)	<0.05*	55.52(±52)	57.00(±12.97)	<0.05*
RLPH	52.38(±5.62)	41.833(±34.38)	<0.05*	52.42(±7.35)	55.00(30.16)	<0.05*
RLEP	67.09(±10.11)	72.97(±41.68)	<0.05*	66.76(±5.57)	65.89(±37.86)	0.93
E/F	60.98(±7.64)	72.10(±17.24)	<0.05*	62.64(±6.70)	66.25(20.14)	<0.05*
EWB	65.67(±10.93)	69.07(±16.66)	<0.05*	65.55(±6.52)	65.87(±18.15)	0.86
SF	57.65(8.57)	71.25(±21.83)	<0.05*	57.95(±5.71)	68.58(19.61)	<0.05*
Pain	51.54(±7.67)	53.92(±13.61)	<0.05*	50.92(± 5.49)	50.67(±10.27)	0.68
GH	50.82(±6.94)	72.33(±21.08)	<0.05*	51.57(±4.17)	52.70(±9.49)	0.97
PCS	52.37(±1.66)	59.34(±9.18)	<0.05*	51.62(±2.56)	52.70(±21.08)	0.78
MCS	63.10(±2.42)	68.69(±11.51)	0.601	63.29(±1.62)	65.66(±9.64)	<0.05*

*PCS, Physical Component Summary; MCS, Mental Component Summary; PF, physical function; RLPH, role of limitation due to physical health; RLEP, role of limitation due to emotional problems; EF, energy/fatigue; EWB, emotional well-being; SF, social functioning ;GH, general health; WOMAC, Western Ontario and McMaster Universities Arthritis Index; CI, confidence interval; M, Mean; SD, Standard Deviation; *Denotes significance p<0.05.The P values are for parametric (paired t-test) for comparison within each group *indicates statistical significance.*

4.10. Secondary Outcomes at Follow-up

4.10.1 Knee Goniometry

Table 4.23 shows post-treatment mean scores of both active and passive knee flexion and extension of the participants from the four groups. One-way ANOVA was used to compare the mean scores for ROM between the study groups. No significant difference ($p<0.05$) was found between the experimental groups (US, IFC, & CT) and the control group. Thus, participants in the experimental group had no significant improvement in range of motion (active flexion, extension and passive flexion, extension) post-treatment.

Table 4. 23 Baseline to post-intervention changes in Active Flexion, Extension and Passive flexion and Extension scores following 12 weeks of intervention between the groups

Variable	Pre-intervention					Post-intervention				
(Deree)	US (n=34)	IFC (n=34)	CT (n=33)	Control (n=32)	P- valu	US (n=34)	IFC (n=34)	CT (n=33)	Control (n=32)	P- valu
PreActFlx	124.46±(7.76)	124.22(±4.85)	123.57(±6.16)	124.20(±5.12)	0.950	129.01(±4.78)	127.36(±3.46)	125.28(±3.38)	127.14(±4.82)	0.090
PrePassFlx	120.87±13.62)	118.76(±5.90)	118.59(±4.67)	118.69(±3.10)	0.635	126.77(±5.91)	124.21(±4.11)	122.69(±3.32)	124.53(±4.50)	0.080
PreActExt	127.58(±8.09)	128.54(±5.57)	128.19(±6.13)	128.59(±4.30)	0.916	133.24(±6.67)	131.97(±3.98)	131.48(±5.50)	136.30(±4.80)	0.030*
PrePassExt	124.92(±8.27)	123.97(±6.02)	124.19(±5.42)	124.31(±1.64)	0.932	130.21(±6.54)	128.82(±4.23)	128.67(±5.43)	134.67(±4.49)	0.001*

PreActFlx: pre-active flexion; **PrePassFlx:** pre-passive flexion; **PreActExt: pre**-active extension; **PrePassExt: pre**-passive extension. M, Mean; SD, Standard Deviation. * p>0.05 .P values are for parametric test (ANOVA) for comparison among the four groups *indicates statistical significance

4.11.0 Summary

This chapter presented the results and findings of this study. The results of the analyses indicate a reduced level of pain severity, improved functional activity and quality of life among the study participants with knee OA in the experimental (US, IFC and CT) groups compared with the control group. Similarly, knee ROM, both active and passive flexion and extension were reported not to have improved in all experimental groups compared to the control group. Also, comparison of the effect of each modality on pain, functional activity, and QoL with the control showed that there were improvements in all the dependent variables in each group. Thus, generally, the study data supports the four study hypotheses and so these were rejected at the 5% level of significance. A detailed discussion of results from the study is presented in the next chapter.

CHAPTER 5: DISCUSSION

5.1 Introduction

The focus of this study was to investigate the effects of electrotherapy combination (CT = US + IFC) on pain, physical activity and health-related quality of life in individuals with knee osteoarthritis. The treatment was administered for 12 weeks and elicited improvements in pain severity, functional activity, and quality of life of the participants in the experimental groups, with some significant improvement in some outcome measures in the control group.

This chapter discusses the findings of the study, starting with a discussion of the changes in primary outcome measures within the study samples. Precisely, the results pertaining to the primary outcomes are reviewed in relation to previous literature. The outcomes of the study are presented to demonstrate how they support or differ from existing literature, and contribute to the existing body of knowledge. An attempt is also made to discuss the influence of electrotherapy (specifically the use of CT, US and IFC) on pain severity, physical function and QoL in the management of patients with knee OA. Also included is a discussion of other variables of secondary importance that relate to the knee joint range of motion post-treatment. Finally, the chapter concludes with a summary of the discussion.

5.2 Primary Outcome Measures

The outcomes of this study show more significant improvements in pain severity, physical activity and quality of life of participants with knee osteoarthritis treated with electrotherapy combination (CT: US & IFC) when compared to the control group that received IRR. One of the primary outcomes was the post-treatment improvement in the quality of life scores of the participants in the experimental group, measured using the SF-36 health survey, compared with the control group. Similarly, more reductions in pain severity and improved functional activity were recorded in all the experimental groups compared to the control. No modality was better than the other among the experimental groups when compared in terms of improvement in pain severity, physical function and QoL. Also, better improvements in pain severity, functional activity, and QoL were found when individual modalities were compared with the control group. However, significant improvements were noticed in some outcome measures in the control group but more effective in the experimental groups.

The result of the interventions on pain and functional activity were evaluated using the VAS and WOMAC index. These findings support the hypothesis that electrotherapy (US, IFC, & CT) improves pain, functional activity and HRQoL in patients with knee OA.

The effects of electrotherapy such as US therapy, IFC and other forms of electrical stimulation on musculoskeletal disorders, including knee OA, have been reported. Electrotherapy plays an important role in the rehabilitation of musculoskeletal conditions by reducing pain, improving physical function, increasing joint range of motion and increasing quality of life of individuals (Eftekharsadat et al., 2015, Adhya et al., 2014). These might collectively necessitate the use of less pharmacological agents and produce effects that prevent or delay disabilities and other related complications, which are supported by the current study.

This study has shown that electrotherapy (US, IFC, and CT) is an important physical modality that can be used to relieve pain, improve physical activity and quality of life in patients with knee osteoarthritis. Similarly, it has shown that none of the modalities in the experimental group was more effective than the other in terms of improvement in pain severity, functional activity and QoL of patients with knee OA. Findings from this study support the hypotheses that the use of electrotherapy modalities (US, IFC &CT) significantly improves functional activity and quality of life compared to the control in patients with osteoarthritis.

The outcomes of this study support the systematic review study conducted by Rutjes et al. (2010) which compared the therapeutic effects of US on pain severity and functions in patients with knee OA with sham or no intervention. They concluded that US was of benefit in improving pain and functions in patients with knee OA. Other studies have also shown that US is a safe and effective therapeutic physical modality for pain relief and improvement of functions in patients with knee OA (Özgönenel et al., 2009, Ulus et al., 2012, Yıldırıım et al., 2015).

In contrast, some studies in the literature report that the use of US in addition to other physical therapy approach has no further significant improvement on pain, physical function, and ambulatory (Cakir et al., 2014, Ulus et al., 2012).

5.2.1 Therapeutic Ultrasound and Knee OA

Therapeutic ultrasound is one of the electrotherapy therapeutic heating modalities used in physical therapy clinics. It is produced by a transducer (treatment head) that converts electrical energy to ultrasound through the use of the piezoelectric principle.

The finding of this study is in conformity with the findings of the systematic review and meta-analysis study conducted by Zhang et al. (2016), which investigated the effects of

therapeutic ultrasound on pain, physical function and safety outcomes in patients with knee osteoarthritis compared to sham or no intervention. The authors concluded that US is beneficial for relieving knee pain and improving physical functions in patients with knee osteoarthritis and could be a safe treatment modality. In another systematic review conducted by Zeng et al. (2014) to investigate the efficacy of continuous and pulsed ultrasound (US) in the management of knee osteoarthritis, they concluded that continuous therapeutic ultrasound could only be considered as a pain relief treatment in the management of knee OA. The study also assured that none of these modes is dangerous. Özgönenel et al. (2009) conducted a randomized, double-blind clinical trial to assess the effectiveness of US in knee OA. They reported that US is a safe and effective therapeutic modality that improves pain and functions in patients with knee OA. Similarly, in a randomized, double blind, placebo controlled study, conducted to determine the effectiveness of therapeutic ultrasound on pain, stiffness and functional activity of a patient with knee OA, Kapidzic (2011) concluded that continuous US compared with placebo showed significant improvement in pain, joint stiffness, and level of physical functions. Similarly, therapeutic ultrasound was found to improve pain and physical activity in the short term in patients with knee OA (Yeğin et al., 2017).

Welch et al. (2001), reported contrary findings in a systematic review conducted to compare the use of therapeutic ultrasound and placebo or short wave diathermy in patients with knee OA. The authors concluded that the use of US appears to have no therapeutic benefit over placebo or short-wave diathermy for patients with knee OA.

It was reported that mechanical effects and/or thermal effects aimed at heating the deeper tissues to increase blood flow, local metabolism, tissue regeneration and collagen elasticity, and decrease inflammatory response and/or enhance soft tissue healing (Bailey et al., 2003).

5.2.2 Interferential Current Therapy and Knee OA

Various randomized controlled trials and systematic reviews have been conducted to evaluate the efficacy of IFC on pain and physical functions in individuals with knee osteoarthritis (Gundog et al., 2012, Eftekharsadat et al., 2015, Adhya et al., 2014, Zeng et al., 2015). A review of high quality randomized controlled trials has shown evidence to support the use of IFC in the management of knee osteoarthritis (Atamaz et al., 2012). For instance, Gundog et al. (2012) conducted a randomized and single-blind study to assess the effectiveness of different amplitude-modulated frequencies of interferential current and sham IFC on knee osteoarthritis, and treatments were rendered 5 times for 3 weeks. The authors concluded that

IFC improved pain and disability outcomes when compared with a sham group in the management of patients with knee osteoarthritis. In another randomized, multi-centered, controlled study, Burch et al. (2008) reported significant improvement in pain outcome and total WOMAC index scores including pain, stiffness and physical function in patients with knee OA. In earlier studies on knee OA, the efficacy of IFC was partly supported, but the studies failed to include controls to adjust for the placebo effect (Shafshak et al., 1991, Itoh et al., 2008).

The therapeutic effects of IFC in other conditions such as non-specific low back pain have been evaluated and showed a significant improvement in pain and disability (Lara-Palomo et al., 2013). The use of IFC was found to be a useful intervention for immediate improvement of spasticity, balance, and gait in individuals with chronic stroke (Suh et al., 2014). Walker et al. (2006) reported significant improvements in pain severity when IFC was used on patients with psoriatic arthritis. In our study, the IFC treatment indicated similar positive outcomes on individuals with knee OA, and is consistent with the literature.

Unlike our findings and the above-reported research, a few clinical studies did not show positive results for IFC compared with control groups in improving pain and functional outcomes. Fuentes et al. (2016) conducted a systematic review and meta-analysis to analyze the available information on the efficacy of IFC in the management of musculoskeletal pain. They reported that treatment with IFC alone did not produce significantly better results than a placebo or other therapy at the end of 12 weeks treatment. However, the author reported that the use of IFC as a supplement to another therapy seemed to be more therapeutically effective in reducing pain and more effective than a placebo following a 3-month intervention. The author concluded that due to the heterogeneity across the study samples and methodological limitations, analgesic efficacy could not be concluded.

There is evidence that IFC attains electro-analgesic effects as explained through the “Pain Gate Theory” postulated by Melzack and Wall (1967). The theory explains that activation of afferent smaller nerve fibers causes pain, and that stimulating the larger diameter nerve fibers leads to inhibition of nociceptive impulses from the smaller diameter nerve fibers where the pain is reduced. This explains a physiological “gating mechanism” at the dorsal horn of the spinal cord. The ‘gate’ opens and closes to allow or inhibit transmission of nociceptive impulses to the higher center of the brain where it will be processed.

5.2.3 Combination Therapy and Knee OA

In patients with OA, pain is the primary and most important and frequent clinical symptom that leads to limited functional activity and poor quality of life (Rutjes et al., 2010, Zhang and Jordan, 2010). The primary goal of OA management is to alleviate the pain, improve functional activity and quality of life of the individuals (Zhang et al., 2009).

In the current study, the significant pain improvement reported by the combination therapy group may be attributed to the combined effects of the electro-analgesia of IFC (Gundog et al., 2012) and the therapeutic effects of continuous US (Yeğin et al., 2017). Previous studies showed the effectiveness of CT in fibromyalgia pain (Moretti et al., 2012, Almeida et al., 2003), but it was not assessed as musculoskeletal pain due to knee osteoarthritis.
Our findings are also supported by a study conducted by S˘ varcova et al. (1988), who studied the combined effects of therapeutic ultrasound, galvanic current and shortwave diathermy in patients with knee osteoarthritis. They reported significant improvement in pain level.

The mechanism by which CT relieves pain is not totally understood. There is evidence, however, that IFC achieves its electro-analgesic effect through the activation of large diameter afferent nerve fibers that inhibit the nociceptive impulses into the posterior horn of the spinal cord through smaller diameter nerves that carry painful impulses (Samuel and Maiya, 2015, Gundog et al., 2012). Pain in OA is believed to originate from both nociceptive, neuropathic pathways as well as from unusual excitability in the nociceptive pathways of both the peripheral and central nervous systems (Dray and Read, 2007). The pain is proven to be associated with central sensitization as a result of continued nociceptive activities from the affected knee that lead to prolonged hyper excitability of pain in the CNS (Woolf, 2011, Mease et al., 2011). Furthermore, IFC may limit the prolonged abnormal hyperexcitation that leads to central sensitization pain seen in patients with knee OA. IFC also achieves its electro-analgesic effects by blocking nociceptive impulses as explained by Melzack and Wall (1967).

Watson (2009) explained the possible mechanism through which the CT exerts its therapeutic effects. When US is applied to a resting nerve cell membrane, it reduces the membrane potential by enhancing its permeability to various ions especially Na+ Ca+. Due to this enhanced permeability, the nerve membrane is adjusted to its closest threshold point of depolarization even though it does not usually make the nerve to fire. When IFC is simultaneously applied with US, it takes a smaller current of IFC than usual to induce

depolarization to generate action potential due to the effects of US. This is the likely mechanism through which the combination therapy achieves its desired therapeutic effects with fewer intensities and smaller treatment durations.

Studies have shown that the application of continuous US therapy produces thermal effects (Ulus et al., 2012, Johns, 2002b). Thermal therapies are physiologically known to produce an increase in tissue metabolism, collagen elasticity, improve capillary blood flow and reduce muscle spasm (Baker et al., 2001, Benjaboonyanupap et al., 2015).

Yeğin et al. (2017) reported that US is an effective treatment modality that reduces pain and improves physical function in the short term. In another study, Zeng et al. (2014) reported that continuous US could be used as an effective pain relief in the management of knee osteoarthritis. Other studies (Loyola-Sánchez et al., 2010, Jia et al., 2016) have also shown that US is an effective modality for reducing pain and improving functional activity and quality of life in the management of patients with knee OA.

However, some studies have reported contrary findings to those in this study. Welch et al. (2001) conducted a systematic review and reported that US therapy has no beneficial effects on pain and function in the management of patients with osteoarthritis when compared with a placebo and shortwave diathermy. In addition, some controlled clinical studies have reported that US has no benefits in improving pain or functional activity in the management of knee osteoarthritis (Cakir et al., 2014, Ulus et al., 2012).

To the best of our knowledge, no literature has reported that CT is unsafe. In all the available clinical studies on the use of CT on musculoskeletal disorders, no single study reported side effects, either in the CT or in the control group (Almeida et al., 2003, Moretti et al., 2012, Çıtak-Karakaya et al., 2006). Similarly, in the current study, no side effects occurred during or after the CT treatment. Thus, the use of combination therapy was not associated with any negative or adverse effects in the management of knee OA.

According to the findings in this study, CT could provide additional benefits in improving pain, physical functioning, and quality of life (QoL) in the rehabilitation of patients with knee osteoarthritis. To our knowledge, no previous study has been conducted to assess the therapeutic effects of CT on QoL, functional activity and pain in patients with knee osteoarthritis. Therefore, the findings of this study will hopefully contribute to the growing clinical evidence on the rehabilitation of patients with knee OA.

However, the control group received IRR treatment, which was also a recognized intervention in the management of patients with OA. The little significant improvements seen in some outcome measures in the control might be attributed to the therapeutic effect of the IRR. Infrared radiation (IRR) which is a heating modality with wavelength ranging from 750nm to 1 mm on the electromagnetic spectrum. Infrared wavelengths nearer to visible light are referred to as near infrared and cause thermal effects which penetrate about 5-10mm into soft tissue (Schieke et al., 2003). The biological phototherapy effect of this heating modality was found to improve microcirculation by increasing arterioles diameter and blood flow velocity (Komori et al., 2009). Studies have also demonstrated an effect of increased vasodilatation, increase in blood flow and improved rheologic characteristics which are facilitated by increasing nitrogen oxidize (NO), prostacyclin and endothelial-derived benefits provided by endothelial cells (Samoilova et al., 2008). The concomitant effect of these by the use of IRR for patients with knee OA is that there is a reduction in pain with improvement in functional activities and their quality of life (Gur et al., 2003, Stelian et al., 1992).

5.3.1 Knee Range of Motion and Electrotherapy

In recent studies, it has been shown that various electrotherapy modalities have been used to relieve pain and improve functional activity in individuals with knee osteoarthritis. For instance, Eftekharsadat et al. (2015) conducted a randomized controlled clinical study with the aim of evaluating the therapeutic effectiveness of interferential current therapy and action potential stimulation (APS) in the management of knee osteoarthritis. They concluded that short-term use of IFC and APS significantly relieved pain and improved physical functions in patients with knee OA. IFC could therefore be of benefit in improving pain and disability in patients with knee OA (Gundog et al., 2012).

In this report, no significant difference was found among the experimental groups and the control regarding knee ROM after 12 weeks interventions. It is believed that there is correlation between pain and movement(Asheghan et al., 2016). Pain is an important factor restricting movement, but a limitation in movement may result in more pain. It is also known that when pain is decreased, muscle spasm would also reduce freer joint mobility. However, our findings demonstrated a positive correlation between pain relief and the range of motion in patients with knee OA. The improvements seen in clinical symptoms in the various treatment outcomes (pain, QoL, and physical function) for people with knee OA could not be explained by a simple linear relationship.

In the present study, a placebo group was included as a control group. VAS is often used in clinical research to measure the intensity or frequency of various pain symptoms. Reduction in its values means a reduction in pain perception; WOMAC is a specific outcome measure designed for patients with OA. Recording drastic significant improvement in WOMAC subscales is an indication of good findings that may not possibly be observed in a placebo or control group. Therefore, we believe CT, IFC & US could be used to improve patient condition in individuals with knee OA.

CHAPTER 6 CONCLUSION

6.1 Introduction

This chapter presents the conclusions from the research findings. The chapter begins with an introduction which is followed by the contributions of the study and then the conclusions on the results. Next, the limitations of the research are presented. The chapter closes with recommendations for future studies and implications for clinical practice and research.

6.2 Contributions of the study

The purpose of this study was to investigate the therapeutic efficacy of electrotherapy (US, IF and CT) on pain, functional activity and quality of life in patients with knee osteoarthritis. The study contributes to the body of knowledge as it is among the very few that formally assess the therapeutic effects of simultaneous application of therapeutic ultrasound and interferential current therapy on pain, physical activity and QoL in patients with knee OA. This is an area that is generally under-researched, or most of the available information is anecdotal or based on the experiences of those who use the modality frequently. Findings from the literature review provided little in terms of the direction for the investigation of the present study, particularly with regard to methodology, as very little documented information was available.

Osteoarthritis is the most common degenerative articular disease that leads to disability and remains a leading cause of joint pain, physical impairment and poor quality of life in adults worldwide. The goal of the treatment is to alleviate pain, improve physical function, and quality of life. In patients with knee OA, QoL is an important outcome measure that estimates the degree of affectation to individuals and evaluates the effectiveness of treatment.

A pilot for application of the CT was also carried out before the main treatment in order to test the feasibility of the study, recruitment of participants, research tool and data analysis and other logistics. Two important research questions were formed concerning the primary outcomes and answers were provided to these questions using quantitative research procedures discussed under chapter three (methodology). A summary of the major research findings follow.

The influence of electrotherapy on pain, functional activity and quality of life in patients with knee OA was examined and the electrotherapeutic modalities (US, IFC &CT) were found to be effective physical therapy agents that could be used in the rehabilitation of patients with knee osteoarthritis.

Hypothesis one tested whether there were significant effects of electrotherapy on pain, functional activity and QoL measures among patients with knee OA. The null hypothesis stated that there would be no difference in pain, functional activity and QoL measures between electrotherapy groups (US, IFC & CT) and the control group of patients with knee OA. Significant differences were observed between the outcomes of the electrotherapy groups and the control group. The hypothesis was, therefore, rejected.

It was further revealed that no modality was superior to others in terms of effectiveness on all the assessed dependent variables. Secondary investigations were also carried out to determine the effect of electrotherapy on knee range of motion (active and passive) in patients with knee OA. Both active and passive knee ROM did not significantly increase in the electrotherapy (experiential) groups and the control from baseline to post-intervention. Between-group differences showed no significant differences, i.e. no therapeutic modality was found to be effective in terms of knee ROM.

Hypothesis two stated that combination therapy significantly influences pain, functional activity and QoL among patients with knee OA. The null hypothesis stated that there would be no difference in pain, functional activity, and QoL between the combination therapy group and the control group in patients with knee OA. The values for VAS, total WOMAC index and the SF-36 scores significantly improved in the CT group post-treatment. The null hypothesis was thus rejected. The CT was found to improve participants' pain, physical function and QoL positively and significantly. Between-group comparison at follow-up showed significant differences on all the domains of the SF-36 questionnaire. Thus, CT is an effective electrotherapeutic modality that can improve the quality of life of patients with knee OA.

Hypothesis three sought to test whether IFC significantly influences pain, functional activity and QoL among patients with knee OA. The null hypothesis stated that there would be no difference in pain severity, functional activity and QoL between the IFC group and control group in patients with knee OA. The values for VAS, total WOMAC index and the SF-36 scores significantly changed following treatment with IFC. This hypothesis was, therefore, rejected. Participants' were found to improve in pain severity, functional activity and QoL. Between-group comparison at follow-up showed significant differences on all the domains of the SF-36 questionnaire. Thus, IFC can be used to improve pain, functional activity and QoL in patients with knee OA.

Hypothesis four tested whether therapeutic ultrasound (US) significantly influences pain, functional activity and QoL in patients with knee OA. The null hypothesis stated that there would be no difference in pain, functional activity and QoL between the US and control groups in patients with knee OA. The values for VAS, total WOMAC index and SF-36 scores significantly improved in the US group post-treatment. The null hypothesis was thus rejected. It was found that US improved participants' pain, physical function and QoL positively and significantly. Between-group comparison at follow-up showed significant differences on all the domains of the SF-36 questionnaire. This result shows that the use of US can improve pain, functional activity, and quality of life of patients with knee OA.

6.3 Conclusions

Based on the findings of this study, it was concluded that the use of electrotherapy (US, IFC, and CT) is beneficial in alleviating pain, improving functional activity and improving quality of life in patients with knee osteoarthritis. The findings would reduce the use of pharmacological agents with their associated negative effects. Such adverse effects include polypharmacy and even the cost of the management of the patient with knee osteoarthritis. Also, it provides evidence-based results for the treatment of knee osteoarthritis.

6.4 Study Limitation

With respect to study inclusion and exclusion criteria, getting outpatients who had clinical symptoms for at least three months and grade II and III OA according to the Kellgren-Lawrence grade and who were approved to participate in a singular treatment regimen for 12 weeks was extremely difficult. This explains the small sample size. There is therefore a need for a future study with a larger sample size.

6.5 Implications and Recommendations

The major implication of the study findings to clinical practice is that it provides empirical evidence as to the benefits of US, IFC and CT in relieving pain, and improving functional activity, and QoL in patients with knee osteoarthritis. Of particular significance is the use of combination therapy (simultaneous application of interferential current therapy and therapeutic ultrasound), which has limited or no literature as regards its clinical importance, in the rehabilitation of patients with knee OA. The major findings of this study did not lead to any direct policy implications but probably offer some opportunities for future research, both in terms of protocol development for the use of US, IFC and CT and the actual electrotherapy application in the rehabilitation of patients with knee OA. These study findings have

implications for improving the use and delivery of electrotherapy in the rehabilitation management of the commonest cause of disability in elderly individuals, to reduce pain, improve activities of daily living and quality of life.

6.5.1 Recommendations Related to the Use of Combination Therapy

Future randomized controlled trial research is necessary to investigate how the use of CT changes HRQoL over time and its relation to other clinical outcomes. The combination therapy should be compared to the standard physical therapy treatment of knee osteoarthritis to assess whether the improvements in pain, physical activity and quality of life are as effective as the standard physiotherapy treatment of knee OA. It is also recommended that the efficacy of combination therapy and other electrotherapy treatments should be compared to the pharmacological treatments in patients with knee osteoarthritis.

6.5.2 Recommendations Related to Future Research

To address the weaknesses of the present study, future research should focus on the following:

Future study should be conducted to evaluate all the clinical indices (including quadriceps muscles strength) and changes. Studies should be conducted with larger sample sizes to ascertain the present study findings. There is a need for further study to compare cost effectiveness of pharmacological treatment against physiotherapy treatment of patients with knee OA, in particular, the use of combination therapy.

APPENDICES

APPENDIX A1: INFORMATION SHEET (ULTRASOUND THERAPY GROUP)

Date:

Dear Participant,

My name is Zubair Usman, a Ph.D. student in the Department of Physiotherapy, School of Health Sciences, Westville Campus, University of KwaZulu-Natal (+27610276424, +2348034505780, zubees2000@yahoo.com, zubs1235@gmail.com).

You are invited to consider participating in a study that involves the use of electrotherapy modalities – therapeutic ultrasound (US), interferential therapy current (IFC). The aim and purpose of this research are to find out the efficacy of electrotherapy modalities (Therapeutic ultrasound and Interferential therapy current) on the pain, functional activity and quality of life of patients with knee osteoarthritis.

The study is expected to enroll 120 patients – 30 each in four groups – from the Physiotherapy Departments of Rasheed Shekoni Specialist Hospital; Dutse General Hospital, Dutse, and Federal Medical Centre, Birnin Kudu, Jigawa State, North-west Nigeria. This involves the following procedures:

Health Screening

You will undergo comprehensive medical examination that involves your medical history and a review of the body system before participation in this study. You will be required to undergo physical examination (to be conducted by the study physician), which will involve checking the function or integrity of the joint range of motion, circulation, blood vessels, lungs, muscles and bones among others. You will be allowed to take some other medications for other comorbidities.

Anthropometrics Measurement

You will undergo some physical measurements prior to the commencement of the study. These include your height (meter) using a Standiometre, weight (Kg) using a weighing scale; based on these, your Body Mass Index (BMI) will be calculated in meters/kilograms square (m/kg^2).

You will be asked to wear light clothing for your body stature (height) and body mass (weight) to be measured accurately.

Measurement of Health-related Quality of Life

You will be required to answer some questions related to your health status before and after the 12-week period of intervention/treatment. Prior to providing answers to these questions, you will be given careful explanations about the questions and adequate instructions on how they should be answered. However, a Hausa translated version will also be available for better understanding.

Pain Assessment

Clinical assessment of your knee pain will be conducted at baseline and at the end of the study period. Primarily, pain perception will be assessed with the Visual Analogue Scale (VAS). VAS is a straight horizontal line drawn on a sheet of paper with fixed length, usually 10-cm (i.e. 100mm). The ends are defined as the extreme limits of the parameter to be measured with anchor points 0 (no pain) and 10 (maximum pain). You will be asked to indicate the level of your pain perception on the drawn horizontal line. The indicated number will be recorded as your level of pain perception.

Measurement of Knee Range of Motion (ROM)

You will be asked to raise your clothes to halfway up your thighs to allow for the measurement of your knee's range of motions. This will be done in the treatment cubicle while you are comfortably positioned on the treatment plinth. Assisted active ROM will be measured with a large plastic goniometer (Baseline Goniometer, 12"®, USA) with 25-cm movable arms, marked in 1^{o} increase. You will be asked to fully extend and bend your knee while the movable plastic arm of the goniometer is attached to your leg. As you move the leg, the goniometer readings will be noted and recorded. This procedure will be conducted prior to the commencement of the treatment procedure and at the end of the 1^{st}, 2^{nd} and 3^{rd} months of the study.

Intervention (Procedures)

You will be lectured on the significance of early identification of the complications associated with your condition (knee pain). You will be required to attend the treatment sessions 3 times a week. Each treatment session will last for 30 minutes. The period of your

participation, if you choose to enroll and remain in the study, is expected to be 3 months. The researcher received bursary (Research Scholarship) from the College of Health Sciences, University of KwaZulu-Natal.

Therapeutic Ultrasound Treatment

The therapeutic ultrasound treatment will be for a duration of 15 minutes while moving the sound head (transducer) in longitudinal strokes on the affected knee. Equipment calibration will be checked before the study begins and during the treatment; the transducer will be in direct contact with your skin and a water-based gel will provide an optimal couple. The unaffected knee will not receive treatment. Ultrasound treatment produces mild heat; patients typically report a pleasant warm sensation during treatment.

The study may involve the following discomforts:

The research does not potentially involve any risk or harm. However, in case of any eventualities resulting from comorbidity, proper and prompt medical attention will be given to any participant. Already, arrangements have been made with the Accident and Emergency units of the hospitals where the research will be conducted. Also, psychosocial interventions will be put in place where necessary.

This study has been ethically reviewed and approved by: the UKZN Biomedical Research Ethics Committee University of KwaZulu-Natal, Durban, South Africa; Rasheed Shekoni Specialist Hospital, Dutse; General Hospital, Dutse and the Federal Medical Centre, Birnin Kudu.

In the event of any problem or concern/question you may contact the researcher at:

Department of Physiotherapy

Rasheed Shekoni Specialist Hospital,

Dutse, Jigawa State, Nigeria.

Tel: +2348034505780

Email: zubees2000@yahoo.com

Or the UKZN Biomedical Research Ethics Committee contact details as follows:

BIOMEDICAL RESEARCH ETHICS ADMINISTRATION

Research Office, Westville Campus

Govan Mbeki Building
Private Bag X 54001
Durban
4000

KwaZulu-Natal, SOUTH AFRICA

Tel: 27 31 2604769 - Fax: 27 31 2604609

Email: BREC@ukzn.ac.za

APPENDIX A2: INFORMATION SHEET (INTERFERENTIAL THERAPY GROUP)

Date:

Dear Participant,

My name is Zubair Usman, a Ph.D. student of the Department of Physiotherapy, School of Health Sciences, Westville Campus, University of KwaZulu-Natal (+27610276424, +2348034505780, zubees2000@yahoo.com, zubs1235@gmail.com).

You are invited to consider participating in a study that involves the use of electrotherapy modalities – therapeutic ultrasound (US). The aim and purpose of this research is to find out the effects of electrotherapy modalities (Therapeutic ultrasound and Interferential therapy current) on pain, functional activity, and the health-related quality of life of patients with knee osteoarthritis. The study is expected to enroll 140 patients – 35 each in four groups, from the Physiotherapy Departments of Rasheed Shekoni Specialist Hospital, Dutse General Hospital, Dutse and Federal Medical Centre, Birnin Kudu, Jigawa State, Northwestern Nigeria.

This will involve the following procedures:

Health Screening

You will undergo comprehensive medical screening including medical history and a physical examination before participation in this study. You will be required to undergo a physical examination (to be conducted by the study physician), which will involve checking the functions and integrity of the joint, range of motion, circulation, blood vessels, lungs and muscles and bones among others. You will be asked to wear light clothing to enable easy and accurate measurement of your body height and mass (weight).

Anthropometrics Measurement

You will undergo some physical measurements prior to the commencement of the study. These include your height (meter) using a Stadiometre, weight (Kg) using a weighing scale and based on these, your Body Mass Index (BMI) will be calculated in meter/kilograms square(m/kg^2).

Measurement of Health-related Quality of Life

You will be required to answer some questions related to your health status before and after the 12-week period of treatment. Prior to providing answers to these questions, you will be given careful explanations about the questions and adequate instructions on how they should be answered. However, a Hausa translated version is also available for better understanding.

Pain Assessment

Clinical assessment of your knee pain will be conducted at the baseline and at the end of the study period. Primarily, pain perception will be assessed with Visual Analogue Scale (VAS). VAS is a straight horizontal line drawn on a sheet of paper with fixed length, usually 10-cm (i.e. 100mm). The ends are defined as the extreme limits of the parameter to be measured with anchor points 0 (no pain) and 10 (maximum pain).You will be asked to indicate the level of your pain perception on the drawn horizontal line. The indicated number will be recorded as your level of pain perception.

Measurement of Knee Range of Motion (ROM)

You will be asked to raise your clothes to halfway up your thigh to allow for measurement of your knee range of motion. This will be done in the treatment cubicle while you are comfortably positioned on the treatment plinth. Assisted active ROM will be measured with a large plastic goniometer (Baseline Goniometer, 12”®, USA) with 25-cm movable arms, marked in 1^{o} increase. You will be asked to fully extend and bend your knee while the movable plastic arm of the Goniometer is attached to your leg as you move the leg. The goniometer readings will be noted and recorded .This procedure will be conducted before the treatment commences and at the end of the study.

Intervention (Procedures)

Inferential Therapy Current Treatment

You will be asked to lie down on your back comfortably with the knees flexed at 20-30 degrees over a pillow on a treatment couch in a ventilated treatment cubicle. The affected knee will be cleaned with an antiseptic (methylated spirit). Treatment parameters will be set based on the treatment settings. The interferential current will be applied to the affected area using four electrodes, padded (8 x $6cm^2$) placed anterior-posterior and mediolateral to the knee. The four electrodes will be connected to the two channels of the Sonicator Plus 920® Inferential Therapy Curry Machine (Mettle Electronics Corp; Anaheim, CA USA).

During the treatment you will be expected to experience a tingling or 'pins and needles' sensation at the contact area of the electrodes, and you may also feel the tingling sensation throughout the area being treated. The intensity of the current will be increased within your comfort level. A stronger intensity will usually have more beneficial effect but the intensity should not be turned too high to be uncomfortable for you.

The study may involve the following discomforts:

The research does not potentially involve any serious risk or harm apart from a mild tingling and needlelike sensation as a result of interferential therapy application. In case of any eventualities resulting from comorbidity or injuries, proper and prompt medical attention will be given to participants. Arrangements have been made with the Accident and Emergency units of the hospitals where the research will be conducted. Also, psychosocial interventions have been put in place where necessary.

This study has been ethically reviewed and approved by: the UKZN Biomedical Research Ethics Committee University of KwaZulu-Natal,Durban, South Africa and that of Rasheed Shekoni Specialist Hospital, Dutse, General Hospital Dutse and the Federal Medical Centre, Birnin Kudu, respectively.

In the event of any problem or concern/question you may contact the researcher at:

Department of Physiotherapy

Rasheed Shekoni Specialist Hospital

Dutse, Jigawa State, Nigeria

Tel: +2348034505780; +27610276424

Email: zubees2000@yahoo.com

or his supervisor (Dr S.S. Maharaj at the Department of Physiotherapy, School of Health Sciences, Westville Campus, University of KwaZulu-Natal, +27312607938, mahrajss@ukzn.ac.za).

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Durban 4000 KwaZulu-Natal, SOUTH AFRICA

Tel: 27 31 2604769 - Fax: 27 31 2604609

Email: BREC@ukzn.ac.za

APPENDIX A3: INFORMATION SHEET (COMBINATION THERAPY GROUP)

Date:

Dear Participant,

My name is Zubair Usman, a Ph.D. student of the Department of Physiotherapy, School of Health Sciences, Westville Campus, University of KwaZulu-Natal (+27610276424, +2348034505780), zubees2000@yahoo.com, zubs1235@gmail.com).

You are invited to consider participating in a study that involves the use of electrotherapy modalities – therapeutic ultrasound (US). The aim and purpose of this research is to find out the effects of electrotherapy modalities (Therapeutic ultrasound and Interferential therapy current) on the pain, joint range of motion (ROM), functional activities and the health-related quality of life of patients with knee osteoarthritis. The study is expected to enroll 120 patients-30 patients each in four groups from the Physiotherapy Departments of Rasheed Shekoni Specialist Hospital, Dutse, General Hospital Dutse, and Federal Medical Centre, Birnin Kudu, Jigawa State, Northwestern Nigeria.

This will involve the following procedures:

Anthropometrics Measurement

You will undergo some physical measurements prior to the commencement of the study. These include your height (meter) using a Stadiometre, weight (Kg) using a weighing scale, and based on these, your Body Mass Index (BMI) will be calculated in meters/kilograms square(m/kg^2).

Health Screening

You will undergo comprehensive medical screening which includes your medical history and a physical examination before participation in this study. You will be required to undergo a physical examination (to be conducted by the study physician), which will involve: checking the function and integrity of the joint, range of motion, circulation, blood vessels, lungs, muscles and bones among others. You will be asked to wear light clothing to ease the measurement of your body stature (height) and body mass (weight) accurately.

Measurement of Health-related Quality of Life

You will be required to answer some questions relating to your health status before and after the 12-week period of treatment. Prior to providing answers to these questions, you will be given careful explanations about the questions and adequate instructions on how they should be answered. However, a Hausa translated version is also available for better understanding.

Pain Assessment

Clinical assessment of your knee pain will be conducted at baseline and at the end of the study period. Primarily, pain perception will be assessed with a Visual Analogue Scale (VAS). VAS is a straight horizontal line drawn on a sheet of paper with fixed length, usually 10-cm (i.e. 100mm). The ends are defined as the extreme limits of the parameter to be measured with anchor points 0 (no pain) and 10 (maximum pain). You will asked to indicate the level of your pain perception on the drawn horizontal line. The indicated number will be recorded as your level of pain perception.

Measurement of Knee Range of Motion (ROM)

You will be asked to raise your clothes to halfway up your thigh to allow for measurement of your knee's range of motion. This will be conducted in the treatment cubicle while you are comfortably positioned on the treatment plinth. Assisted active ROM will be measured with a large plastic goniometer (Baseline Goniometer, 12"®, USA) with 25-cm movable arms, marked in 1^{o} increase. You will be asked to fully extend and bend your knee while the movable plastic arm of the goniometer is attached to your leg. As you move the leg, the goniometer readings will be noted and recorded. This procedure will be conducted prior to the commencement of the treatment procedures, and at the end of the study period.

Intervention (Procedures)

You will be informed on the significance of early identification of the complications associated with your condition (knee pain). You will be required to attend the treatment sessions 3 times every week. Each treatment session will last for at least 30 minutes. The period of your participation, if you choose to enroll and remain in the study, is expected to be 3 months. The researcher received bursary (Research Scholarship) from the College of Health Sciences, University of KwaZulu-Natal.

Electro-diagnosis

Combination therapy with continuous US and interferential current therapy will simultaneously be applied to your painful knee. You are expected to undergo electro-diagnosis of the painful area by means of continuous US (1MHz; 0.5W/cm2) and IFC (4000Hz; AMF-100Hz) intensity in the tactile sensation threshold. These procedures will help in mapping the exact painful point of your knee that needs to be treated. It also ensures accurate localization of US treatment – to provide increased accuracy/effectiveness in treating deeper lesions.

You will be positioned supine on a treatment couch with knee sub-flexed and placed over a pillow comfortably. Following the electro-diagnosis, the two electrodes are placed either front and back, or side-by-side on your knee. However, this is followed by the simultaneous application of continues modes of US and bipolar IFC with below treatment parameters. You may experience a mix of comfortable, warm and tingling sensations at the area of the treatment.

This study has been ethically reviewed and approved by the UKZN Biomedical Research Ethics Committee of the University of KwaZulu-Natal, Durban, South Africa and that of Rasheed Shekoni Specialist Hospital, Dutse, the General Hospital, Dutse and the Federal Medical Centre, Birnin Kudu, respectively.

In the event of any problem or concern/question you may contact the researcher at

Department of Physiotherapy

Rasheed Shekoni Specialist Hospital

Dutse Jigawa State Nigeria

Tel: +2348034505780; +27610726424

Email: zubees2000@yahoo.com

or his supervisor (Dr S.S. Maharaj at the Department of Physiotherapy, School of Health Sciences, Westville Campus, University of KwaZulu-Natal, +27312607938, mahrajss@ukzn.ac.za).

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Tel: 27 31 2604769 - Fax: 27 31 2604609

Email: BREC@ukzn.ac.za

APPENDIX A4: INFORMATION SHEET (CONTROL THERAPY GROUP)

Date:

Dear Participant,

My name is Zubair Usman, a Ph.D. student in the Department of Physiotherapy, School of Health Sciences, Westville Campus, University of KwaZulu-Natal (+27610276424, +2348034505780, zubees2000@yahoo.com, zubs1235@gmail.com).

You are invited to consider participating in a study that involves the use of electrotherapy modalities – therapeutic ultrasound (US). The aim and purpose of this research is to find out the effects of electrotherapy modalities (Therapeutic ultrasound and Interferential therapy current) on the pain, joint range of motion (ROM), functional activity and the health-related quality of life of patients with knee osteoarthritis. The study is expected to enroll 120 patients-30 each in four groups from the Physiotherapy Departments of Rasheed Shekoni Specialist Hospital, Dutse; the General Hospital, Dutse, and Federal Medical Centre, Birnin Kudu, Jigawa State, Northwestern Nigeria.

This will involve the following procedures:

Health Screening

You will undergo comprehensive medical screening including your medical history before participation in this study. You will be required to undergo a physical examination (to be conducted by the study physician), which will involve: checking the functions and integrity of the joint, range of motion, circulation, blood vessels, lungs, muscles and bones among others. You will be asked to wear light clothing to enable easy and accurate measurement of your body stature (height) and body mass (weight).

Anthropometrics Measurement

You will undergo some physical measurements prior to the commencement of the study. These will include your height (meter) using a Stadiometre, weight (Kg) using a weighing scale and based on these your Body Mass Index (BMI) will be calculated in meters/kilograms square(m/kg^2).

Measurement of Health-related Quality of Life

You will be required to answer some questions relating to your health status before and after the 12-week period of treatment. Prior to providing answers to these questions, you will be given careful explanations about the questions and adequate instructions on how they should be answered. However, a Hausa translated version is also available for better understanding.

Pain Assessment

Clinical assessment of your knee pain will be conducted at baseline and at the end of the study period. Primarily, pain perception will be assessed with a Visual Analogue Scale (VAS). VAS is a straight horizontal line drawn on a sheet of paper with fixed length, usually 10-cm (i.e. 100mm). The ends are defined as the extreme limits of the parameter to be measured with anchor points 0 (no pain) and 10 (maximum pain). You will be asked to indicate your level of pain perception on the drawn horizontal line. The indicated number will be recorded as your level of pain perception.

Measurement of Knee Range of Motion (ROM)

You will be asked to raise your clothes to halfway up your thigh to allow for measurement of your knee range of motion. This will be done in the treatment cubicle while you are comfortably positioned on the treatment plinth. Assisted active ROM will be measured with a large plastic goniometer (Baseline Goniometer, 12”®, USA) with 25-cm movable arms, marked in 1^{o} increase. You will be asked to fully extend and bend your knee while the movable plastic arm of the goniometer is attached to your leg. As you move the leg, the goniometer readings will be noted and recorded. This procedure will be conducted before the treatment procedure commences and at the end of the study.

Intervention (Procedures)

You will be informed on the significance of early identification of the complications associated with your condition (knee pains). You will be required to attend the treatment sessions 3 times every week. Each treatment session will last for at least 30 minutes. The period of your participation, if you choose to enroll and remain in the study, is expected to be 3 months. The researcher received bursary (Research Scholarship) from the College of Health Sciences, University of KwaZulu-Natal.

Infra-Red Radiations Treatment

You will be asked to lay on your back on the treatment plinth with your knee semi-flexed over a pillow. You will also be asked to move your clothes off the area to be treated. The affected knee will be placed directly under the source of infra-red light at 90^0 for maximum absorption of the radiation. You are expected to experience a comfortable warmth. However, in case it is too hot, please let the researcher know. Each session of the treatment will last for 15 minutes and you are expected to receive this treatment 3 times a week for a period of 12 weeks.

The study may involve the following discomforts:

The only hazard in most cases is that prolonged exposure to a very high level of infra-red radiation could result in a burn, as in exposure to a hot stove or any heat source.

Apart from the above-mentioned hazard, the research does not potentially involve any risk or harm. However, in case of any eventuality resulting from comorbidity, proper and prompt medical attention will be given to the participant. Arrangements had been made with the Accident and Emergency units of the hospitals where the research will be conducted. Also, psychosocial interventions are put in place where necessary.

This study has been ethically reviewed and approved by the UKZN Biomedical Research Ethics Committee of the University of KwaZulu-Natal, Durban, South Africa and that of Rasheed Shakoni Specialist Hospital, Dutse; General Hospital, Dutse and the Federal Medical Centre, Birnin Kudu, respectively.

In the event of any problem or concern/question you may contact the researcher at

Department of Physiotherapy

Rasheed Shekoni Specialist Hospital

Dutse, Jigawa State, Nigeria

Tel: +2348034505780; +27610726424

Email: zubees2000@yahoo.com

or his supervisor (Dr S.S. Maharaj at the Department of Physiotherapy, School of Health Sciences, Westville Campus, University of KwaZulu-Natal, +27312607938, mahrajss@ukzn.ac.za).

Or the UKZN Biomedical Research Ethics Committee, contact details as follows:

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Private Bag X 54001
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4000

KwaZulu-Natal, South Africa

Tel: 27 31 2604769 - Fax: 27 31 2604609

Email: BREC@ukzn.ac.za

Withdrawal from the Study

Participation in this research is voluntary and you will not incur any cost as a result of your participation. Transportation costs (to and from the data collection site) will be reimbursed at the end of each week and you may withdraw from participating at any point. In the event of refusal/withdrawal of participation, you will not incur any penalty or loss of treatment or other benefit to which you are normally entitled. Should you decide to withdraw your participation from the study, there are no potential consequences. For orderly withdrawal, once you indicate your intention, a form will be given to you to fill stating reasons for your withdrawal and that you are not under any obligation to continue and that you will not incur any penalty for your decision

All data generated from this study will remain confidential and no report will contain any reference to your name. Upon entering the data into the computer, the data set will be coded. All personal information will be kept on a separate database which only the researcher can use. Clinical data recorded on paper will be stored in a locked filing cabinet and data saved on the computer will be protected using a password (key). All paper records will be kept for a period of 5 years and will then be destroyed using crosscut paper shredder. All stored samples will be disposed of appropriately in the laboratory one year after the research.

APPENDIX B: CONSENT TO PARTICIPATE IN RESEARCH

I ……. have been informed about the study entitled **"Effect of Electrotherapy on Health Quality of Life of Patients with Knee Osteoarthritis"** ***by*** Zubair Usman.

I understand the purpose and procedures of the study.

I have been given the opportunity to answer questions about the study and have had answers to my satisfaction.

I understand that I will sign this consent form and that the signed copy will be given to me.

I declare that my participation in this study is entirely voluntary and that I may withdraw at any time without affecting any treatment or care that I would usually be entitled to.

I have been informed about any available compensation or medical treatment if injury occurs to me as a result of study-related procedures.

If I have further questions/concerns or queries related to the study I understand that I may contact the researcher at the Department of Physiotherapy, Rasheed Shekoni Specialist Hospital, +2348034505780, zubees2000@yahoo.com, zubs1235@gmail.com) or his supervisor (Dr. S.S. Maharaj at the Department of Physiotherapy, School of Health Sciences, Westville Campus, University of KwaZulu-Natal, +27312607938, mahrajss@ukzn.ac.za).

If I have any questions or concerns about my rights as a study participant, or if I am concerned about an aspect of the study or the researchers then I may contact:

BIOMEDICAL RESEARCH ETHICS ADMINISTRATION

Research Office, Westville Campus

Govan Mbeki Building

Private Bag X 54001 Durban 4000

KwaZulu-Natal, SOUTH AFRICA 190

Tel: 27 31 2604769 - Fax: 27 31 2604609

Email: BREC@ukzn.ac.za

_____ _____

Signature of Participant **Date**

_____ _____

Signature of Witness **Date**

(Where applicable)

_____ _____

Signature of Investigator **Date**

APPENDIX C

Hausa Translated Version of SF-36

SF-36 TAMBAYOYI A KAN BAYANIN LAFIYARKA

Suna----------

Kwanan wata----------

1. Gaba daya kana iya cewa lafiyar jikinka ta zama:**(ka zagaye daya daga ciki)**
   a. Ingantacciya ce kwarai
   b. Ingantacciya ce sosaai
   c. Ingantacciya ce
   d. Ba laifi
   e. Ba kyau
2. Idan ka kwatanta da bara, yaya za ka bayyana lafiyarka (a kan mizani) a bana? (**zagaye amsarka**)
   a. Na fi jin dadin bana sosai a kan bara
   b. Kusan bana ta fi bara
   c. Da bara da bana kusan duk daya ne
   d. Kusan ta bana tafi ta bara tabarbarewa
   e. Abin ya baci sosai a kan bara
3. Ga jerin wadansu aikace-aikace da zaka iya aiwatarwa a rana guda. Shin lafiyar jikinka takan hana ka aiwatar da wasu? (**ka nuna amsar kowacce tambaya da alamar X a cikin akwaatin da ya dace**)

Aikace-aikace	**E! tana hana ni sosai**	**E! tana dan hana ni**	**A'a! ba ta hana ni ko kadan**
a. Matsanantan ayyyukan.kamar gudu, daga abu mai nauyi, motsa jiki mai tsanani			
b. Matsakaitan ayyuka kamar motsa tebur, tura kujera da sauransu			

c. Dagawa ko kuma daukan kwali da kaya			
d. Hawa kan bene sau da yawa			
e. Hawa kan bene sau daya			
f. Sunkuyawa, durkusawa ko tsugunawa			
g. Tafiyar- kafa sama da mil guda			
h. Tafiyar -kafa mai dan nisa			
i. Tafiyar- kafa marar nisa			
j. Wanka ko sanya tufafi			

4. A tsawon sati hudu da suka wuce, ka samu wata matsala a game da harkar gudanar da aikinka, ko kuma harkokinka na yau da kullun a sakamakon matsalar lafiyar gabobin jikinka? **(ka nuna amsar kowacce tambaya da sanya alamar X a kwatin da ya dace)**.

	E!	**A'a!**
a. Raguwar lokacin da kake baiwa aiki ko sauran harkokika		
b. Rashin cimma burinka a abubuwaka kamar yadda kake so		
c. Baka iya aiwatar da ayyukaka kamar da		
d. Kana samun wahalar aiwatar da ayyukan da ka sa a gaba		

5. A tsawon sati hudu da suka wuce, ka samu wata matsala a game da harkar aikinka ko kuma harkokinka na yau da kullun a sakamakon wata damuwa (bacin-rai ko juyayi)? **(ka nuna amsar kowacce tambaya da alamar X)**

	E!	**A'a!**
a. Raguwar lokacin da kake ba wa aikinka ko sauran harkokinka		

b. Rashin cimma burina a abubuwana kamar yadda kake so		
c. Kasa aiwatar da ayyukana cikin nutsuwa kamar da		

6. A tsawon sati hudu da suka wuce, ta yaya matsalar damuwa ko kuma lafiyar gabobin jikinka suka shafi harkokin zamantakewarka da iyalinka, ko da abokanka ko da makwautanka? **(ka zagaye amsarka)**.

   a. Babu kwata-kwata

   b. Kadan

   c. Matsakaici

   d. Da dan yawa

   e. Da yawa sosai

7. Ya ya tsanantar ciwon jiki a tsawon sati hudu da suka wuce? (**ka zagaye amsarka**)
   a. Babu
   b. Dan kadan
   c. Kadan
   d. Matsakaici
   e. Matsananci
   f. Matsananci sosai
8. A tsawon sati huxu da suka wuce, ta yaya zogi ko ciwo ya shafi harkokin aikinka na yau da kullun (a gida ko a waje)?
   a. Babu kwata-kwata
   b. Kadan
   c. Matsakaici
   d. Da dan yawa
   e. Da yawa sosai
9. Wadannan tambayoyin masu zuwa sun shafi yadda kake ji, da kuma yadda abubuwa suka kasance maka a tsawon sati hudu da suka wuce. A kowacce tambaya ana so ka bayar da amsar da ta yi kusa da yadda kake ji a ranka. **(ka nuna amsar kowacce tambaya da alamar X)**

	Kowanne lokaci	**Mafi yawancin lokuta**	**A lokuta da dama**	**Wani lokaci**	**A lokuta ‘yan kadan**	**Babu a kowanne lokaci**
a. Zama cikin annashuwa?						
b. Zama cikin halin tsorata da fargaba?						
c. Kasancewa cikin halin bakin ciki ko rashin walwala ta yadda babu wani abu da zai iya sa ka jin annashuwa						
d. Zama cikin nutsuwa da kwanciyar hankali?						
e. Jin kuzari sosai?						
f. Karayar zuciya da rashin tabbas.						
g. Matsananciyar gajiya?						
h. Zama cikin farin ciki?						
i .Kasancewa cikin halin gajiya?						

10. A sati hudu da suka wuce, tsawon wani lokaci ne matsalar damuwa da kuma lafiyar gabobin jikinka suka shafi harkokin zamantakewarka (kamar ziya tare da abokai, dangi da sauransu)? (**zagaye amsarka)**

    a. Kowanne lokaci

    b. Mafi yawancin lokuta

c. Wani lokaci

d. A lokuta 'yan kadan

e. Babu a kowanne lokaci

11. Yaya gaskiyar ko kuma akasin gaskiyar wadannan bayanai a game da kai?

	Ba shakka gaskiya ne	**Lokuta da yawa gaskiya ne**	**Ban sani ba**	**Lokuta da yawa ba gakiya ba ne**	**Ba gaskiya ba ne**
a. Ina saurin kamuwa da rashin lafiya fiye da kowa					
b. Ina da koshin lafiya daidai da kowa					
c. Ina tsammanin rashin lafiyata zai tsananta					
d. Lafiyata ingantacciya ce sosai					

Appendix D

The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)

Name: _____ Date:

Instructions: Please rate the activities in each category according to the following

Scale of difficulty: 0 = None, 1 = Slight, 2 = Moderate, 3 = Very, 4 = Extremely

Circle one number for each activity

	1. Walking	0	1	2	3	4
	2. Stair Climbing	0	1	2	3	4
	3. Nocturnal	0	1	2	3	4
	4. Rest	0	1	2	3	4
	4. Walking	0	1	2	3	4
	5. Weight bearing	0	1	2	3	4
Stiffness	1. Morning Stiffness	0	1	2	3	4
	2. Stiffness occurring later in the day	0	1	2	3	4
Physical Functions	1. Descending stairs	0	1	2	3	4
	2. Ascending stairs	0	1	2	3	4
	3. Rising from sitting	0	1	2	3	4
	4. Standing	0	1	2	3	4
	5. Bending	0	1	2	3	4
	6. Walking on flat surface	0	1	2	3	4
	7. Getting in /out of car	0	1	2	3	4
	8. Going shopping	0	1	2	3	4

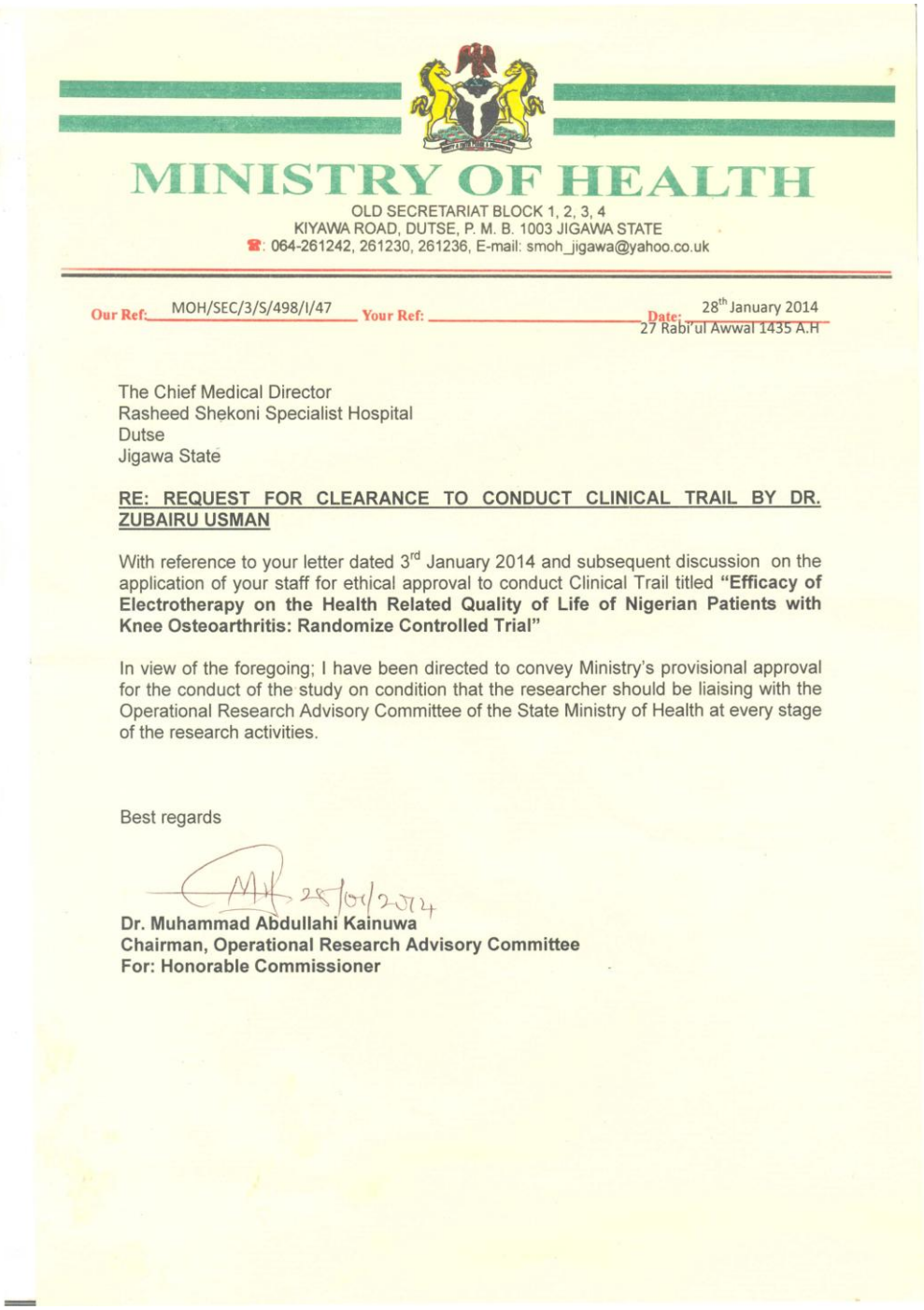
9. Putting on socks	**0**	**1**	**2**	**3**	**4**
10. Lying in bed	**0**	**1**	**2**	**3**	**4**
11. Taking off socks	**0**	**1**	**2**	**3**	**4**
12. Rising from bed	**0**	**1**	**2**	**3**	**4**
13. Getting in/out of bath	**0**	**1**	**2**	**3**	**4**
14. Sitting	**0**	**1**	**2**	**3**	**4**
15. Getting in/out of toilet	**0**	**1**	**2**	**3**	**4**
16. Heavy domestic duties	**0**	**1**	**2**	**3**	**4**
17. Light domestic duties	**0**	**1**	**2**	**3**	**4**

Total Score:_____/96 =_____%

Comments /Interpretation (to be completed by the therapist):

APPENDIX E

Ethical Approval /Clearance from RSSH/ Jigawa State Ministry of Health, Jigawa State, Nigeria



MINISTRY OF HEALTH

OLD SECRETARIAT BLOCK 1, 2, 3, 4
KIYAWA ROAD, DUTSE, P. M. B. 1003 JIGAWA STATE
☎: 064-261242, 261230, 261236, E-mail: smoh_jigawa@yahoo.co.uk

Our Ref: MOH/SEC/3/S/498/I/47 Your Ref: _____ Date: 28th January 2014
27 Rabi'ul Awwal 1435 A.H

The Chief Medical Director
Rasheed Shekoni Specialist Hospital
Dutse
Jigawa State

RE: REQUEST FOR CLEARANCE TO CONDUCT CLINICAL TRAIL BY DR. ZUBAIRU USMAN

With reference to your letter dated 3rd January 2014 and subsequent discussion on the application of your staff for ethical approval to conduct Clinical Trail titled **"Efficacy of Electrotherapy on the Health Related Quality of Life of Nigerian Patients with Knee Osteoarthritis: Randomize Controlled Trial"**

In view of the foregoing; I have been directed to convey Ministry's provisional approval for the conduct of the study on condition that the researcher should be liaising with the Operational Research Advisory Committee of the State Ministry of Health at every stage of the research activities.

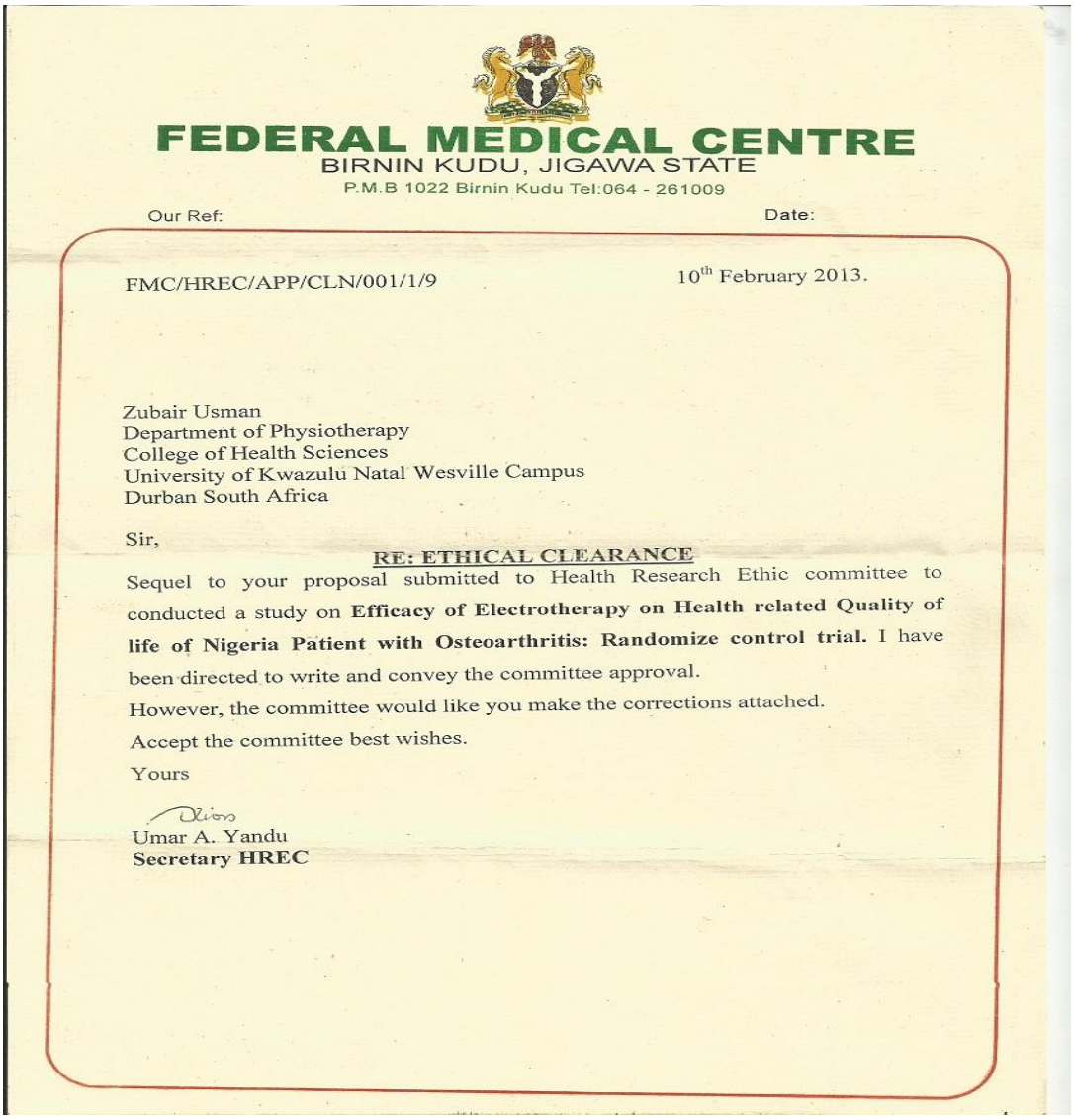
Best regards

28/01/2014

Dr. Muhammad Abdullahi Kainuwa
Chairman, Operational Research Advisory Committee
For: Honorable Commissioner

APPENDIX F

Ethical Approval /Clearance from the Federal Medical Centre, Birnin Kudu, Jigawa State, Nigeria



FEDERAL MEDICAL CENTRE
BIRNIN KUDU, JIGAWA STATE
P.M.B 1022 Birnin Kudu Tel:064 - 261009

Our Ref: Date:

FMC/HREC/APP/CLN/001/1/9 10th February 2013.

Zubair Usman
Department of Physiotherapy
College of Health Sciences
University of Kwazulu Natal Wesville Campus
Durban South Africa

Sir,

RE: ETHICAL CLEARANCE

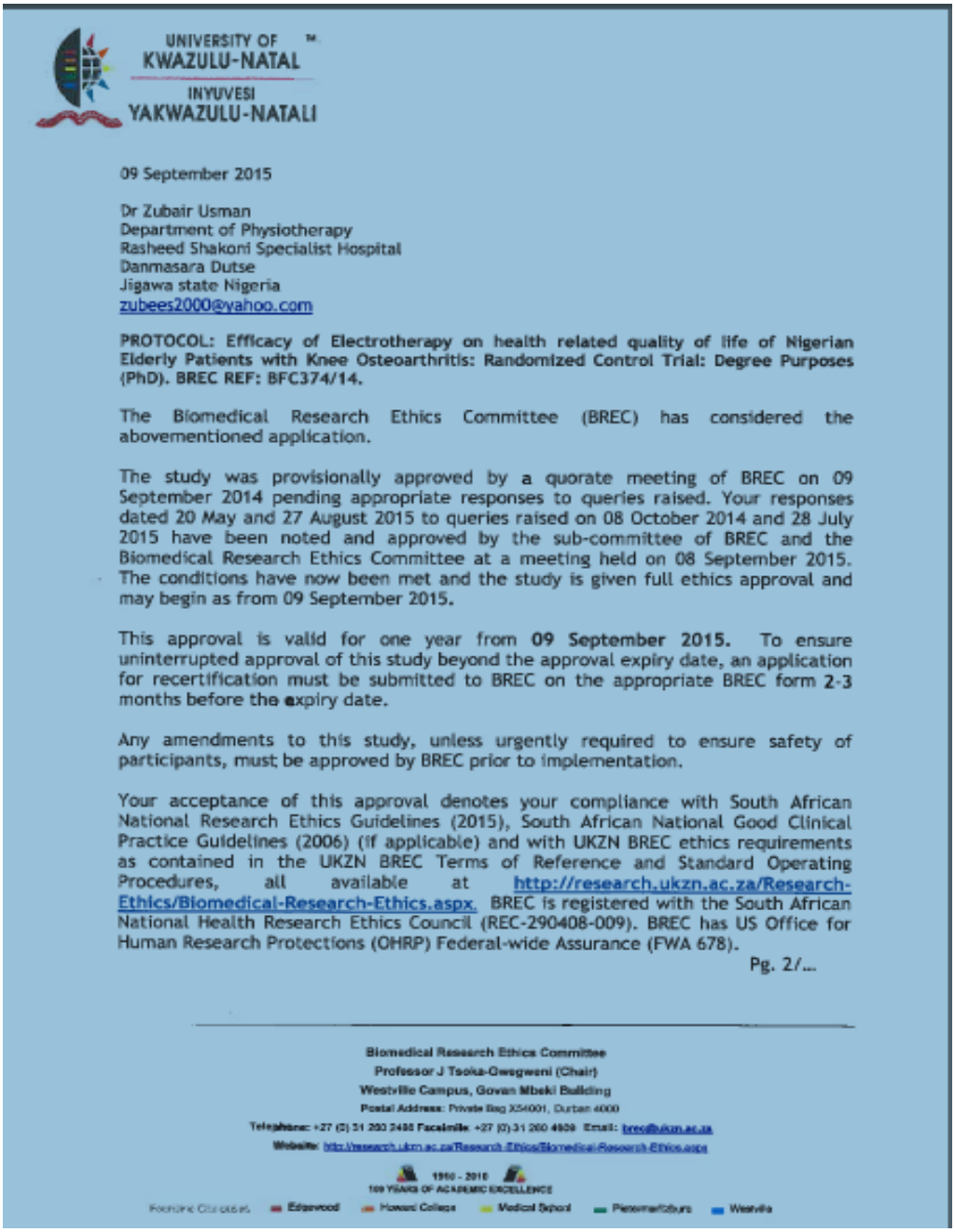
Sequel to your proposal submitted to Health Research Ethic committee to conducted a study on **Efficacy of Electrotherapy on Health related Quality of life of Nigeria Patient with Osteoarthritis: Randomize control trial.** I have been directed to write and convey the committee approval.

However, the committee would like you make the corrections attached.

Accept the committee best wishes.

Yours

Umar A. Yandu
Secretary HREC



UNIVERSITY OF KWAZULU-NATAL
INYUVESI YAKWAZULU-NATALI

09 September 2015

Dr Zubair Usman
Department of Physiotherapy
Rasheed Shakoni Specialist Hospital
Danmasara Dutse
Jigawa state Nigeria
zubees2000@yahoo.com

PROTOCOL: Efficacy of Electrotherapy on health related quality of life of Nigerian Elderly Patients with Knee Osteoarthritis: Randomized Control Trial: Degree Purposes (PhD). BREC REF: BFC374/14.

The Biomedical Research Ethics Committee (BREC) has considered the abovementioned application.

The study was provisionally approved by a quorate meeting of BREC on 09 September 2014 pending appropriate responses to queries raised. Your responses dated 20 May and 27 August 2015 to queries raised on 08 October 2014 and 28 July 2015 have been noted and approved by the sub-committee of BREC and the Biomedical Research Ethics Committee at a meeting held on 08 September 2015. The conditions have now been met and the study is given full ethics approval and may begin as from 09 September 2015.

This approval is valid for one year from **09 September 2015.** To ensure uninterrupted approval of this study beyond the approval expiry date, an application for recertification must be submitted to BREC on the appropriate BREC form 2-3 months before the expiry date.

Any amendments to this study, unless urgently required to ensure safety of participants, must be approved by BREC prior to implementation.

Your acceptance of this approval denotes your compliance with South African National Research Ethics Guidelines (2015), South African National Good Clinical Practice Guidelines (2006) (if applicable) and with UKZN BREC ethics requirements as contained in the UKZN BREC Terms of Reference and Standard Operating Procedures, all available at http://research.ukzn.ac.za/Research-Ethics/Biomedical-Research-Ethics.aspx. BREC is registered with the South African National Health Research Ethics Council (REC-290408-009). BREC has US Office for Human Research Protections (OHRP) Federal-wide Assurance (FWA 678).

Pg. 2/...

APPENDIX G

Ethical Approval /Clearance from BREC, University of KwaZulu-Natal, Durban, South Africa

The following Committee members were present at the meeting that took place on 09 September 2014:

Prof D Wassenaar	Chair
Dr C Aldous	Genetics
Prof R Bhimma	Paediatrics & Child Health
Prof A Coutsoudis	Paediatrics & Child Health
Dr R Gowender	Family Medicine
Dr T Hardcastle	Surgery - Trauma
Ms MP Mabaso	Lay member
Dr K Naidoo	Family Medicine
Dr G Nair	HIV - Medicine
Dr A Noorbhai	Surgery
Prof V Rambiritch	Pharmacology
Prof A Ross	External - DUT- Homoeopathy
Prof C Rout	Anaesthetics
Dr A Sather	External - Microbiology
Dr S Singh	Dentistry
Ms T Van Dou	Legal Member

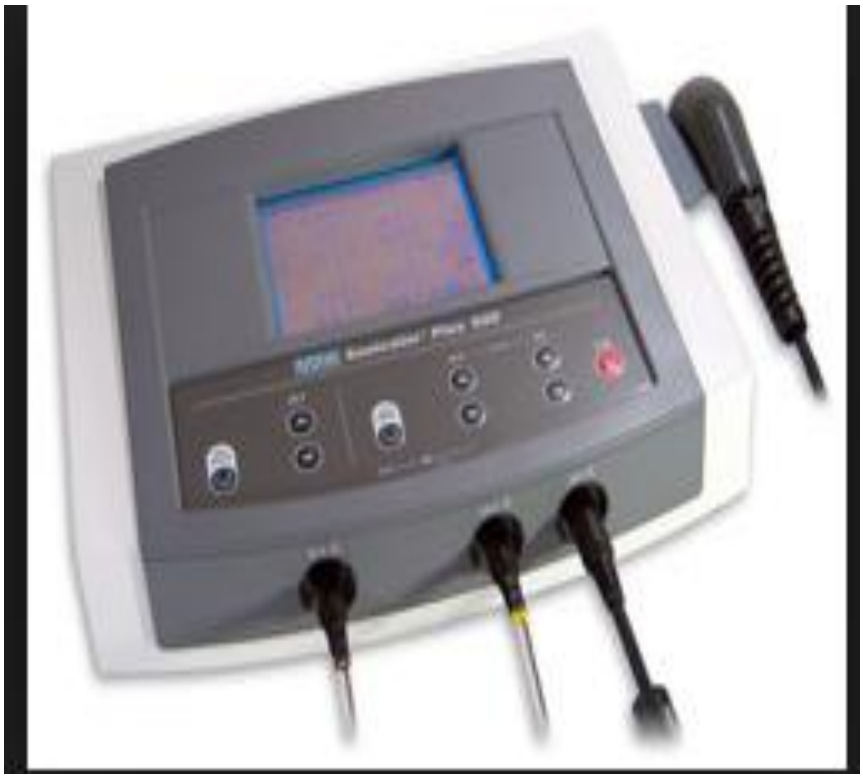
We wish you well with this study. We would appreciate receiving copies of all publications arising out of this study.

Yours sincerely

PROFESSOR J Toska-Gwegweni
Chair: Biomedical Research Ethics Committee

APPENDIX H

Sonicator Plus 920®,Complete Unit



Sonicator Plus 920® complete unit

APPENDIX I

Control Panel Descriptions

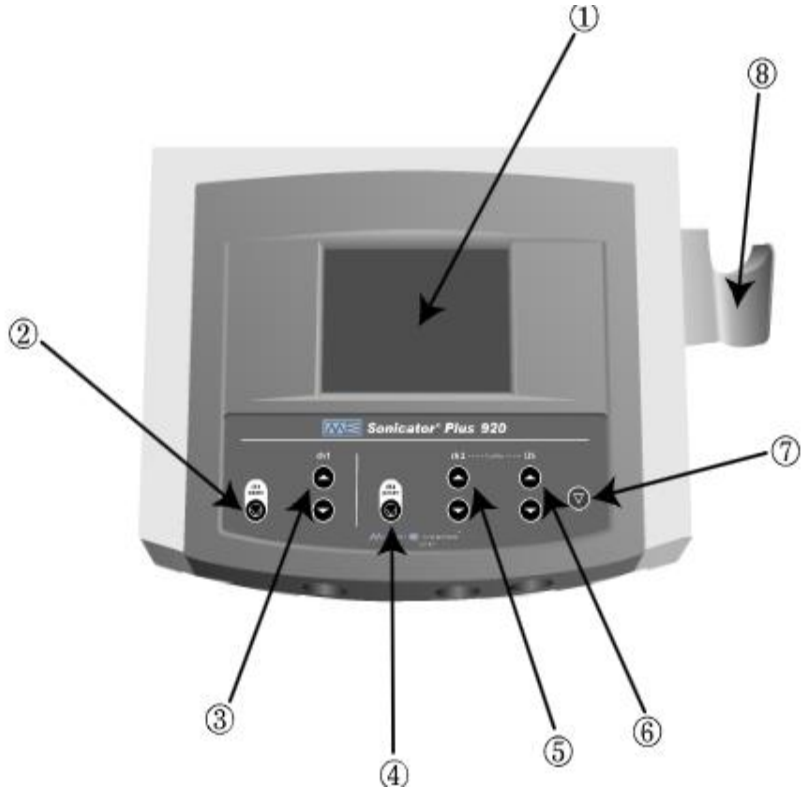


Figure 2:Sonicator Plus 920, top view.

1. Touch-screen LCD
2. CH1 pause control
3. CH1 intensity controls
4. CH2 pause control
5. CH2 intensity controls
6. Ultrasound intensity controls
7. Stop control
8. Ultrasound applicator cradle

APPENDIX J

PATIENT DEMOGRAPHIC DATA FORM

Please complete this form as accurately as possible and hand it to the Research Assistant

Title.....…**Surname**.....…**Forename**:……...……...…….....

Address:……...……...……

Hospital :.....Number:……**Phone Number**:……**E-mail Address:**……**Gender:**..... .....**Age:**.....**Height.....M)**.....**Weight (Kg)**.....**Calculated BMI (Kg/m^2)**:.....**Knee Extension (Passive)**.....**Knee Extension(Active)**.....**Knee Flexion (Passive)**..... **Knee Flexion (Active):**.....

Date:.....

APPENDIX K

PUBLICATION 1 (MANUSCRIPT)

Original manuscripts

Effects of Combination Therapy and Infrared Radiation on Pain, Physical Function, and Quality of Life in Subjects with Knee Osteoarthritis: A randomized controlled study.

Zubair Usman MSc, DPT, [a], *Sonill Sooknunan Maharaj Ph.D.* [b], *Bashir Kaka PhD* [c]

[a] *Department of Physiotherapy, Rasheed Shakoni Teaching Hospital Dutse, Jigawa State, Nigeria.*

[b] *Department of Physiotherapy, University of KwaZulu-Natal, Private Bag X54001, Durban 4000, South Africa. Email: maharajss@ukzn.ac.za*

[C] *Department of Physiotherapy, Faculty of Allied Health Sciences, Bayero University Kano, Nigeria.*

Corresponding Author: *Department of Physiotherapy, Rasheed Shakoni Teaching Hospital, Nigeria, P.M.B. 7200, Dutse, Jigawa State, Nigeria.*

Email: Zubees2000@yahoo.com; Tel., +2348034505780.

Background: Knee osteoarthritis (KOA) is a common degenerative articular disease that causes disability and poor quality of life in individuals. Electrotherapeutic agents such as therapeutic ultrasound (US), interferential current (IFC) and infrared radiation are used in treatment. It is not clear which of these agents is the best in improving the variables.

Objectives: The study aimed to compare the effects of the combined application of US and IFC and infrared radiation on pain, functional activity and QoL in people with KOA.

Method: This was a randomized controlled study. Sixty participants were randomized into two groups: the combination therapy group (CTG), and the infrared radiation group (IRG). Each group received 15 minutes treatment 3 times a week for 12 weeks**.** The Visual Analogue Scale was used to assess pain; the Western Ontario and McMaster Universities Osteoarthritis

Index was used for functional activity and the Short Form Health Survey questionnaire for QoL.

Result: Participants in the CTG had a significant ($p<0.05$) reduction in pain and a significant ($p < 0.05$) improvement in functional activity and QoL compared to the IRG.

Conclusion: The results of this study support the use of the combination of IFC and US to reduce pain, improve function and QoL in KOA patients.

Keywords: Combination Therapy; Interferential Current Therapy; Infrared Radiation; Knee Osteoarthritis; Therapeutic Ultrasound.

Introduction

Osteoarthritis (OA) is a progressive degenerative articular disease characterized by marginal osteophyte formation, destruction of joint cartilage and subchondral bone changes (Laxafoss et al., 2010, McKinnis, 2013). Clinical symptomology includes joint pain, loss of joint function, and limitation of joint range of motion (Heidari, 2011). OA mostly affects weight bearing joints such as the knee and hip. The disease rate increases with increase in age and obesity, with arthritis pain and dysfunction affecting patient's quality of life (Felson et al., 2000). OA is one of the commonest causes of disability among elderly individuals (Michael et al., 2010). It has been shown that 50% of people over the age of 65 have radiological features of OA, with roughly 10% of men and 18% of women suffering symptomatic OA (Woolf and Pfleger, 2003).

The aims of the knee OA treatment are to reduce pain and improve function or quality of life based on the ICF approach (Fitzcharles et al., 2010). Moreover, drug treatments for the elderly are often limited, producing suboptimal benefits because of comorbidities, polypharmacy, and the associated high risk of side effects of drugs (Fitzcharles et al., 2010, Walker et al., 2006). In order to limit the side effects of medication, non-pharmacological treatments, such as exercises and physical modalities, are recommended for the treatment of knee OA; in addition to the use of heat and cold, ultrasound, and inferential current (Thomas et al., 2009).

Interferential current (IFC) is characterized by the superimposition of two slightly different medium frequency currents (4,000 Hz), to form a new medium-frequency current with an amplitude modulation at low frequency (0–250 Hz)(Gadsby and Flowerdew, 1997, Gundog et al., 2012). It has been stated that amplitude modulated frequency (AMF) is the main electro-analgesic component of IFC (Noble et al., 2000a). IFC achieves its pain modulation by stimulating afferent large-diameter fibers. Studies have reported the effectiveness of IFC in the treatment of painful musculoskeletal problems such as sport injuries; bruises and swellings, low back pain, osteoarthritis, rheumatoid arthritis, and muscular pain (Jarit et al., 2003, Eftekharsadat et al., 2015, Lara-Palomo et al., 2013).

Therapeutic ultrasound is one of the most frequently applied electrotherapeutic modalities in orthopaedic physiotherapy (Wong et al., 2007). It produces thermal effects which increase tissue metabolism, collagen elasticity, and capillary blood flow and reduces skeletal muscle spasm (Kapidzic, 2011). Therapeutic ultrasound is often used in the management of knee osteoarthritis and it is believed to be effective in enhancing inflammatory response, tissue repair, and is absorbed especially in tissues with high collagen content (Atamaz et al., 2012). Besides the individual therapeutic effects of ultrasound and interferential current therapy, their combination (Combination therapy [CT]), is more effective than each of them applied separately in eliciting localized analgesia on previously detected painful areas (Jones et al., 2014).

Infrared radiation with wavelength range from 750 nm to 1 mm can stimulate the production of nitric oxide (NO), enhancing inflammatory response and tissue repair, and is absorbed especially in tissues with high collagen content (29.34**)** Clinical investigations of the efficacy of OA therapies should examine variables such as pain, function, disability, and health-related quality of life (Hsieh et al., 2012, Walker et al., 2006). Further intensive research focusing on the therapeutic effects of ultrasound, interferential current and infrared radiation on patients with knee OA is required (Fitzcharles et al., 2010, Hancock and Riegger-Krugh, 2008, Hsieh et al., 2012). To the best of our knowledge, to date, there have been no reports that evaluated the effects of combination therapy and infrared radiation on pain, functional activity and the HRQoL of older patients with knee OA. We hypothesized that there would be significant difference in HRQoL, pain and functional activity in patients with knee osteoarthritis following administration of combination therapy and infrared radiation. This

study, therefore, is aimed at investigating the differences between the combined application of therapeutic ultrasound and interferential current therapy (Combination therapy) and infrared radiation on pain, functional activity and HRQoL of elderly patients with knee osteoarthritis.

METHODS

Participants

Sixty outpatients with knee OA, diagnosed according to the American College of Rheumatology criteria were recruited (Singh et al., 2014). Patients were excluded from the study if they had any knee diseases other than OA. Patients with serious concomitant systemic diseases, patients who had taken corticosteroid or hyaluronic acid injection in the month before recruitment, and patients with a previous history of any electrotherapy contraindications were excluded from the study. Subsequently, patients were made to understand the research protocols, before they were randomly allocated into two groups (combination therapy group (CTG) and infrared radiation group (IRG)).

Design

A prospective randomized controlled clinical trial.

Randomization

Patients were allocated to CTG or IRG. The principle of block randomization was used to assign patients to the groups, with a block size of 4. Participants were allocated to their groups with sealed envelopes containing their group assignments, which they opened after they were recruited into the study. One physiotherapist enrolled all participants, and the other physiotherapist generated the allocation sequence and assigned participants to their groups as shown in the flow chart in Figure 1.

Measurement

Pain

Pain intensity was assessed on full weight bearing using VAS. Participants were asked to indicate the level of their pain between 0 (no pain) and 10 (severe pain), and were instructed not to under- or overestimate it. The VAS is a single-item numerical scale normally in a straight horizontal or vertical line of fixed length, usually 10-cm (i.e. 100mm), (Hawker et al., 2011). The ends are defined as the extreme limits of the parameter to be measured with anchor points 0 (no pain) and 10 (maximum pain). It is a highly reliable instrument for measuring pain (Bijur et al., 2001), with high psychometric values (Todd et al., 1996, Gallagher et al., 2001, Phan et al., 2012, Pedersen et al., 2016).

Functional Ability

The Western Ontario and McMaster University Osteoarthritis Index (WOMAC) was used to evaluate the functional ability of the participants at baseline and after 12 weeks of treatment. The instrument is an OA specific outcome measure and self-administered questionnaire with 3 domains consisting of 24 items. The Likert scale version of the WOMAC was used for the purpose of this study. This scale allows patients to indicate their responses on a five-point scale (0 = none, 1 = mild, 2 = moderate, 3 = severe, 4 = extreme). The higher the response indicated, the lower the level of perceived health and physical function. Studies have shown high psychometric value for the WOMAC questionnaire. The instrument has been shown to be reliable, valid, and sensitive to changes in the clinical symptoms of individuals with knee and hip OA (Bellamy, 2008, McConnell et al., 2001).

Health-related Quality of Life

Participants' health-related quality of life was assessed and recorded using the 36-item Short Form Health Survey (SF-36) questionnaire both at baseline and post-treatment. This is a generic health-related quality of life (HRQoL) measurement tool, self-administered and user-friendly, which has been reported as valid and reliable with high internal and external consistency (Zhou et al., 2013).

Procedures

The study was conducted at the outpatient units of the Physiotherapy departments of Rasheed Shekoni Specialist Hospital and the Federal Medical Centre, Birnin Kudu, Jigawa State Nigeria. The study was approved by the Biomedical Research and Ethics Committee (BREC) of the University of KwaZulu-Natal, Durban, South Africa and the Ethical Research Committee of the Ministry of Health, Jigawa State, Nigeria. Patients were briefed on the study protocol and signed informed consent to participate in the study, which commenced on 1st June, 2015 and ended on 31st May 2016.

Participants' height and weight were measured and recorded. Body mass index (BMI) was calculated by dividing weight (kg) by height (m) and recorded. All assessments were conducted at baseline and at the end of 12 weeks of treatment. The primary outcome measures used to assess patients' response to the treatment were the Western Ontario and McMaster University Osteoarthritis Index **(**WOMAC**)**, 36-item Short Form Health Survey (SF-36) questionnaire and Visual Analogue Scale (VAS).

Intervention

Combination therapy group (CTG)

Participants in the combination group underwent electro-diagnosis of the most painful knee area with continuous US ((1 MHz; 0.5W/cm$^{2)}$ and IFC (AMF-100 Hz) at tactile threshold intensity. Treatments were conducted at the intensity of continuous US (1 MHz; 1.5W/cm^2) applied with a 5 cm transducer for 10 minutes using a Sonicator Plus 920® (Mettler Electronics, California, USA). Participants were asked to lie supine with a pillow under the treated knee. Ultrasound transmission gel (Aqueous gel®) was used as contact medium. Two adhesive electrodes (6×6 cm) were placed in opposition to each other (medial and lateral) for deeper penetration. The US was first turned on, then followed by IFC parameters as mentioned above. Participants were informed that they would experience tingling sensations which should not be unpleasant. Treatment was administered for 10 minutes, 3 times a week for 12 weeks.

Infrared radiation group (IRG)

Participants in this group were treated with luminous infrared lamps (IRR, Infraphil ® 150W; Philips Electronics, Amsterdam, Netherland). The source of the radiation was placed 60cm from the patient's skin for the 15 minutes of the treatment session. The treatment took place three times a week for 12 weeks. Participants were positioned suppine with knee flexed at 20^0-30^0 and the knee supported with a pillow. Participants were informed that they were expected to feel a comfortable 'mild warmth' and to tell the researcher if the treatment got too hot as too much heat could lead to skin burns.

All participants received quadriceps isometric exercises of both knees for 10 minutes, and were asked to refrain from taking non-steroidal anti-inflammatory drugs (NSAIDS) and anti-depressants throughout the study period. However, they were advised to take acetaminophen in case of unbearable pain and other comorbid medications throughout the study period.

Statistical Analysis

Statistical analyses were conducted with version 21.0 Statistical Package for the Social Sciences (SPSS Inc., Chicago, IL, USA). The effect size for the sample size calculation was obtained from the previous studies conducted on knee osteoarthritis (Hsieh et al., 2012, Yu et al., 2016). Based on the data from these studies, it was estimated that a sample size of 30 patients in each study group would achieve a power of 80% to detect an effect size of 0.8 in

the outcome measures of interest, assuming a type I error of 0.05. Quantitative data were expressed as mean ± SD (standard deviation). The independent sample *t*-test was used to compare differences between groups at baseline and at follow-up, while the paired sample *t*-test was used to compare findings before and after treatment within each group. A P value equal to or less than 0.05 was considered statistically significant. Furthermore, standardized effect sizes (Cohen's *d*) with 95% confidence interval (CI) were included.

Results

A total of 63 patients with knee osteoarthritis participated in the study and were randomized into two groups: CTG and IRG. During the study, 3 patients (1 from CTG and 2 from IRG group) were lost to follow-up and were not included in the analyses (Figure 1). Of the 60 participants who completed the study, 42 (70%) were female and 18 (30%) were male, with a mean age of 66.3 ± 8.91 years. Table 1 shows participants' demographic characteristics at baseline. There were no statistically significant differences in gender, age, and BMI between the CTG and the IRG at baseline ($p > 0.05$).

Pain and functional activity scores

Table 2 shows pre- and post-treatment comparisons in each group. There were no statistically significant differences ($p>0.05$) in the VAS and WOMAC subscales in the two groups before the treatment. A post-treatment comparison was made between the two groups (Table 2) and a statistically significant difference was demonstrated ($p<0.05$) in the VAS and total WOMAC scores in the CTG compared to the IRG. Between-group comparison at follow-up indicated significant differences between the CTG and IRG (Table 3). Thus, patients in the CTG had better improvement in pain and physical function than patients in IRG.

Health-related quality of life

Table 2 compares the pre- and post-treatment HRQoL of the patients in each group. There were statistically significant differences in all the domains from baseline to post-treatment in the CTG ($p<0.05$). In the IRG, emotional well-being and physical component summary domain scores deteriorated significantly, whereas scores from social functioning did not change significantly from baseline to post-treatment (Table 3). Between-group comparison at follow-up showed significant differences on all the domains between the two groups. However, no statistically significant differences ($p>0.05$) were found in the energy/fatigue and mental summary component of SF-36 domains. Between-group comparison at follow-up

showed significant differences in all the domains between the two groups. Participants in the CTG had their QoL improved compared to the IRG following the 12-week intervention.

Discussion

This was a randomized controlled trial, aimed at evaluating the efficacy of CTG when compared with IRG on pain severity, functional activity, and HRQoL in patients with knee osteoarthritis. According to study findings, patients with knee OA treated with CTG had better improvement in pain, physical function, and HRQoL compared to patients in the IRG, over a period of 12 weeks. The study has clearly indicated that combination therapy is an electrotherapeutic modality that reduces pain and improves functional activity and HRQoL of elderly people with knee osteoarthritis.

In patients with OA, pain is the primary and most important and frequent clinical symptom that leads to limited functional activity and poor quality of life (Rutjes et al., 2010, Zhang and Jordan, 2010). The primary goal of OA management is to alleviate the pain, improve functional activity and the quality of life of the individuals (Zhang et al., 2009).

In the current study, the significant pain improvement reported by the combination therapy group could be attributed to the combined effects of the electro-analgesia of IFC (Gundog et al., 2012) and the thermal analgesic effects of continuous US (Yeğin et al., 2017). Several studies have shown that CT is an effective modality in the management of musculoskeletal disorders (Almeida et al., 2003, Çıtak-Karakaya et al., 2006).

Our findings were also supported by a study conducted by S̆ varcova et al. (1988), who studied the combined effects of therapeutic ultrasound, galvanic current and shortwave diathermy in patients with knee osteoarthritis. They reported significant improvement in pain levels.

In spite of the fact that the mechanisms by which combination therapy (CT) relieves pain has not been properly understood, studies have shown that IFC achieves its electro-analgesic effects through the activation of large diameter afferent nerve fibers that inhibit the nociceptive impulses into the posterior horn of the spinal cord through smaller diameter nerves that carry pain impulses (Samuel and Maiya, 2015, Gundog et al., 2012). OA pain is believed to originate from both nociceptive, neuropathic impulses as well as from unusual excitability in the nociceptive pathways of both the peripheral and the central nervous system (Dray and Read, 2007). The pain is proven to be associated with central sensitization as a

result of continued nociceptive activities from the affected knee that lead to prolonged hyperexcitability of pain in the CNS (Woolf, 2011, Mease et al., 2011). IFC may limit this prolonged abnormal hyperexcitation associated with pain observed in patients with knee OA. IFC also achieves its electro-analgesic effects by blockng nociceptive impulses as explained by Melzack and Wall (1967).

Studies have shown that the application of continuous US therapy produces thermal effects (Ulus et al., 2012, Johns, 2002b). Thermal therapies are physiologically known to produce an increase in tissue metabolism, collagen elasticity, improved capillary blood flow and reduce muscle spasm (Baker et al., 2001, Benjaboonyanupap et al., 2015).

Yeğin et al. (2017) reported that US is an effective treatment modality that reduces pain and improves physical function in the short term. In another study, Zeng et al. (2014) reported that continuous US could be used as an effective pain relief in the management of knee osteoarthritis. Studies have shown that US is an effective modality for reducing pain and improving functional activity and quality of life in patients with knee OA (Loyola-Sánchez et al., 2010, Jia et al., 2016).

Unlike our study and the above-reported findings however, Welch et al. (2001), in a systematic review conducted to study the effectiveness of US therapy for (Ulus et al., 2012) patients with knee OA, reported US therapy to have no beneficial effects on pain and function in patients with osteoarthritis when compared with a placebo and shortwave diathermy. In addition, some controlled clinical studies have reported that US had no benefits in improving pain and functional activity in the management of knee osteoarthritis (Cakir et al., 2014, Ulus et al., 2012).

There is no literature that reports that CT is unsafe. In all the available clinical studies on the use of CT on musculoskeletal disorders, no single study reported side effects, neither in the CTG nor the IRG (Almeida et al., 2003, Moretti et al., 2012, Çıtak-Karakaya et al., 2006). Likewise, in the current study, no side effects occurred during or after the CT treatment. Thus, the use of combination therapy was not associated with any negative or adverse effects in the management of knee OA.

The present study shows good improvement in pain relief, functional activity and the quality of life of patients treated with US and IFC concurrently. The findings of this study have added to the clinical evidence with regard to the use of CT in patients with knee OA.

Conclusion

Combination therapy (CT) was found to be an effective electrotherapeutic modality that can be used to relieve pain, improve functional activity and HRQoL in patients with knee osteoarthritis.

Acknowledgment

The authors wish to thank all the patients who participated in this study and the members of staff of the physiotherapy outpatient clinic in the two hospitals for assistance rendered before and during the course of the study.

Tables and Figures

Table 1: Patients' Demographic features between the CT Group and the Infrared Group

Variables	Combination Therapy Group n=30 M(±SD)	Infrared Group n-30 M(±SD)	P-value
Age(years)	65.8(± 9.21)	66.8(±8.61)	0.153
Weight (Kg)	69.29(±10.88)	70.04(±9.66)	0.985
Height (M)	1.66(± 0.08)	1.67(±0.76)	0.780
BMI(Kg/M^2)	25.43(±3.8)	25.54(± 3.20)	0.621
Gender M/F, n (%)	20/80%	40/60%	ND
Gender Ratio	4:1	1.5:1	ND

BMI: Body Mass Index; M: Male; F: female; M: Mean; SD: Standard Deviation. * p>0.05; ND: No Data

Table 2: Baseline to post-intervention changes in VAS and WOMAC scores following 12 weeks of intervention in CTG and infrared groups

Variables	Combination Therapy Group			Infrared Group		
	Pre-treatment M(±SD)	Post-treatment M(±SD)	P-Values	Pre-treatment M(±SD)	Post-treatment M(±SD)	P-Values
VAS	7.07(±1.74)	2.23±4.34	<0.05	7.00(±1.33)	6.24±3.12	<0.05
WOMAC						
Pain	18.77(±2.78)	16.97±(3.38)	<0.05	18.800(±2.38)	20.17(±13.38)	<0.05
Stiffness	5.77(±1.00)	7.13(±2.06)	<0.05	10.33(±0.80)	5.13(±2.06)	>0.005
PF	56.10(±7.35)	45.79(±9.08)	0.023	56.60(±5.73)	14.83(±16.22)	<0.05

WOMAC:Western Ontario and McMaster Universities Arthritis Index; M, Mean; SD, Standard Deviation; * Denotes significance p<0.05. P values are for parametric test; Independent sample *t*-test*)* for comparison groups *indicates statistical significance.

Table 3: Post-treatment changes between CTG and Infrared radiation groups following 12 weeks of treatment

Variables	Combination Therapy Group (n=30) M(±SD)	infrared Group (n=30) M(±SD)	P-Value
VAS	2.23(±4.34)	6.24(±3.12)	<0.05
WOMAC (%)			
Pain	16.97±(3.38)	20.17(±13.38)	<0.05
Stiffness	7.13(±2.06)	10.33(±0.80)	<0.05
PF	45.79(±9.08)	14.83(±16.22)	<0.05

WOMAC:Western Ontario and McMaster Universities Arthritis Index; M, Mean; SD, Standard Deviation; * Denotes significance p<0.05. P values are for parametric test Independent sample *t*-test*)* for comparison groups *indicates significance.

Table 4: Baseline to post-intervention changes in SF-36 domains following 12 weeks of intervention in CTG and Infrared radiation groups

	Combination Therapy Group			Infrared Radiation Group		
Variables	**Pre-treatment**	**Post-treatment**	**P-Values**	**Pre-treatment**	**Post-treatment**	**P-Values**
	M(±SD)	**M(±SD)**		**M(±SD)**	**M(±SD)**	
PF	54.57(±4.76)	80.07(±07)	<0.05	52.70(±4.88)	55.52(±52)	<0.05
RLPH	52.38(±5.62)	79.82(±7.87)	<0.05	52.42(±7.35)	54.05(±8.13)	<0.05
RLEP	67.09(±10.11)	83.70(±12.66)	0.012	66.76(±5.57)	68.60(±5.99)	0.001
E/F	60.98(±7.64)	65.14(±16.37)	0.004	62.64(±6.70)	69.93(±9.05)	0.017
EWB	65.67(±10.93)	78.37(±11.68)	0.011	65.55(±6.52)	65.63(±11.46)	0.678
SF	57.65(8.57)	75.24(±10.40)	< 0.05	57.95(±5.71)	58.18(±10.25)	0.912
Pain	51.54(±7.67)	72.42(±8.88)	<0.05	50.92(± 5.49)	53.33(±6.49)	<0.05
GH	50.82(±6.94)	80.13(±11.69)	<0.05	51.57(±4.17)	52.70(±11.69)	<0.05
PCS	52.37(±1.66)	78.27(±4.93)	<0.05	51.62(±2.56)	55.49(±3.49)	0.034
MCS	63.10(±2.42)	72.90(±14.08)	<0.05	63.29(±1.62)	68.96(±5.60)	0.023

***PCS**, Physical Component Summary; **MCS**, Mental Component Summary; **PF**, physical function; **RLPH**, role of limitation due to physical health; **RLEP**, role of limitation due to emotional problems; **E/F**, energy/fatigue; **EWB**, emotional well-being; **SF**, social functioning ;**GH**, general health; WOMAC, Western Ontario and McMaster Universities Arthritis Index; CI, confidence interval; **M**, Mean; **SD**, Standard Deviation; *Denotes significance p<0.05.The P values are for parametric test, paired t-test) for comparison groups *indicates statistical significance.*

Table 4: Post treatment Changes in QoL between the two groups (CTG and IRG)

Variables	Combination Therapy Group	infrared Group	P-Values
	M±(SD)	M±(SD)	
PF	80.07(±07)	55.52(±52)	0.001
RLPH	79.82(±7.87)	54.05(±8.13)	0.002
RLEP	83.70(±12.66)	68.60(±5.99)	0.011
E/F	65.14(±16.37)	63.93(±9.05)	<0.05
WB	78.37(±11.68)	65.63(±11.46)	<0.05
SF	75.24(±10.40)	58.18(±10.25)	<0.05
Pain	72.42(±8.88)	53.33(±6.49)	0.001
GH	80.13(±11.69)	52.70(±11.69)	0.002
PCS	78.27(±4.93)	55.49(±3.49)	<.0.05
MCS	72.90(±14.08)	68.96(±5.60)	<0.05

***PCS**, Physical Component Summary; **MCS**, Mental Component Summary; **PF**, physical function; **RLPH**, role of limitation due to physical health; **RLEP**, role of limitation due to emotional problems; **E/F**, energy/fatigue; **EWB**, emotional well-being; **SF**, social functioning ;**GH**, general health; WOMAC, Western Ontario and McMaster Universities Arthritis Index; CI, confidence interval; **M**, Mean; **SD**, Standard Deviation; *Denotes significance p<0.05.The P values are for parametric test, Independent t-test) for comparison groups *indicates statistical significance.*

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APPENDIX L: PUBLICATION 2 (MANUSCRIPT)

Original Research

Physical therapy rehabilitation combining exercises with electro-analgesia for pain, functional activity and quality of life in patients with osteoarthritis of the knee

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Abstract

Background: Individuals with osteoarthritis (OA) of the knee often have pain and reduced mobility which affects their activities of daily living. Often these individuals are referred for physical therapy and rehabilitation. Various modalities are used for therapy such as interferential current (IFC), infra-red radiation (IRR) and exercises, but the effectiveness of these modalities or their combinations is unknown. This study explored a rehabilitation program with these modalities for pain, functional activity and quality of life (QoL) in patients with OA of the knee.

Materials and Methods*:* This randomized pre-test, post-test study allocated patients equally into two groups receiving a rehabilitation program of either infrared radiation (IRR) or interferential current (IFC) with exercises and counseling for gait and ambulation. Pain was assessed with the Visual Analogue Scale (VAS), functional activity with the Western Ontario and McMasters Universities Osteoarthritis Index (WOMAC), and QoL with the Short-form Health Questionnaire (SF-36).

ResultsEighty-three patients completed the study with 60% (n=50) female and 40% (n=33) male; mean age 63.10±6.91 years; BMI of 26.06 ± 4.13 (kg/m^2). Post-intervention, there was significant improvement ($p<0.05$) in VAS and WOMAC scores in both groups. The IFC group showed significant ($p<0.05$) improvement for all domains of QoL but only pain $p=0.043$, physical function $p=0.038$ and physical component summary $p=0.020$ improved for the IRR group. Thus, the IFC group showed better overall scores compared to IRR.

Conclusion This study supports a rehabilitation program with IFC or IRR for patients with OA of the knee and could be a beneficial intermediate non-surgical intervention. The reduced intake of analgesics and non-steroidal anti-inflammatory drugs could minimize the use, cost and adverse effects of these drugs.

Keywords: Quality of life; Interferential current; knee osteoarthritis; infra-red radiation.

Introduction

Osteoarthritis (OA) is a chronic degenerative articular disease disease of the joint, cartilage and bone, with discomfort and disability leading to physical and psychological burden and a poor quality of life.[1-4] Radiological evidence shows loss of joint space, bone sclerosis or marginal osteophytes.[4] Osteoarthritis is progressive with predisposing factors spanning genetic, metabolic or mechanical disturbances and although any joint can be affected, weight-bearing joints are more prevalent with pain, joint crepitus, stiffness and limited range of movement.[5] Pain on ambulation has a negative impact on the patients' social interactions, mental functioning and quality of sleep thereby exacerbating the disability.[6, 7] Pain and functional impairment restrict and limit activities of daily living and the resulting inactivity and sedentary lifestyle augments a vicious cycle of further deconditioning and poor QoL.[8,9] Thus by monitoring QoL scores it is possible to determine the physical, social, and emotional impact of therapies that contribute to reduce pain and functional impairment and improve the QoL of affected individuals.[10] The American College of Rheumatology recommends pharmacological and non-pharmacological management of arthritis, with surgery generally being the last option.[11] Often, the pharmacological management of arthritis, especially in elderly patients, could lead to risks of side effects and comorbidity as these individuals, if they take other medications, run the risk of the different drugs interacting and reducing their pharmaceutical benefits.[12] Based on this, non-pharmacological and alternate therapies are becoming increasingly useful for managing pain, minimizing functional disability and improving activities of daily living. These techniques focus on maintaining, restoring and enhancing QoL which may be a good indicator of successful rehabilitation.[13]

Often patients with OA of the knee are managed conservatively with anti-inflammatory drugs and analgesics and referred for rehabilitation to alleviate pain, improve joint care and function. Although rehabilitation protocols vary, the common goals are to maintain or improve functional activity using exercises, electrotherapy modalities or other physical means. Traditionally, the most used modality for the management of pain in resource-

constrained practices is therapeutic heating with infrared radiation (IRR) using an infra-red lamp. This modality has wavelengths ranging from 750nm to 100μm, a frequency range of 400HTz-3HTz and an energy range between 12.4meV-1.7eV on the electromagnetic spectrum.[14] Infrared wavelengths nearer to visible light referred to as near infrared, could cause thermal effects penetrating about 5-10mm into soft tissue.[15]

Electro-analgesia using medium frequency interferential current (IFC) has also gained recognition for being effective for the treatment of acute and chronic musculoskeletal conditions.[16.17] The theory of IFC is based on an *'amplitude modulated frequency'* (AMF) or 'beat frequency' where two currents of 4000 Hz and 4100 Hz interact, resulting in a medium-frequency current of 4050Hz, which is amplitude-modulated at a frequency of 100Hz. This medium frequency current penetrates deeper into soft tissue and muscles by overcoming skin resistance and stimulating nerves and tissues.[18] Another benefit of IFC is the physiological mechanism of '*pain gate control theory'* as postulated by Melzack and Wall,[19] where pain transmitting nerve pathways are blocked thereby reducing pain, and together with an increase in circulation, results in positive benefits for the individual.[20] Clinical studies show that IFC[21.22.23] and IRR [24.25.26] reduce pain and improve function in patients with osteoarthritis. It is also widely supported that exercises and physical activities are an integral component of rehabilitation for cardiorespiratory fitness, improving functional activity, self-confidence, mental relaxation which improve or have a positive impact on QoL.[27]

In the setting for this study which has resource constraints, patients with OA of the knee or those waiting for surgical intervention are referred for pain management and joint rehabilitation. The rehabilitation protocols usually combine exercises and electrotherapy modalities. However, there are limited studies, inadequate and anecdotal evidence of the effects of specific combinations of therapy for OA of the knee.[23,28] There are also no studies comparing exercises with therapeutic heating by IRR or the electro-analgesic effects of IFC on pain, physical function and QoL of these patients. This preliminary study was therefore designed to assess and compare the effects of a rehabilitation program of IFC and IRR, lower limb exercises and counseling on pain, functional activity and QoL for patients with OA of the knee.

Methods and Materials

This randomized pretest-post test prospective study recruited outpatients presenting with OA of the knee, attending Rasheed Shekoni Specialist Hospital in Nigeria. The study was approved by the Biomedical Research and Ethics Committee (BREC) of the University of KwaZulu-Natal, Durban, South Africa and the Ethical Research Committee of the Ministry of Health, Jigawa State, Nigeria. Patients were briefed on the study protocol and signed informed consent to participate in the study which was from January to December 2015.

Procedure

Patients who satisfied the inclusion criteria were randomized equally into two groups using the STAT Computer software (Version 9.0 SAS Inc. NC) for the rehabilitation program which was IRR or IFC for pain, lower limb exercises and counselling for gait and ambulation. The inclusion criteria were unilateral, mild or moderate OA of the knee for at least 6 months based on the American College of Rheumatology criteria and radiologic grade I to III on the Kellgren-Lawrence scale, self-ambulation without walking aids, no contra-indications for electrotherapy and an ability to participate in a lower-limb exercise program. Patients with a cardiac pacemaker, systemic diseases, impaired skin sensation or receiving corticosteroid or hyaluronic acid injections or poor general health status which would affect functional activity during assessment were excluded. Ninety-eight outpatients were referred for rehabilitation for OA of the knee during the period of this study with the flow of patients as shown in Figure 1. All interventions were conducted in a temperature-controlled gymnasium as prescribed for the use of electrotherapy modalities. Prior to participation in the rehabilitation program, anthropometric measurements of weight (kg), height (meters), body mass index (kg/m^2), age (years), and gender were recorded [Table 1]. Patients were evaluated for pain on weight bearing on the affected limb using the visual analogue scale (VAS); for functional activity with the Western Ontario and McMasters Universities Osteoarthritis Index (WOMAC) and quality of life (QoL) by means of the Short-Form Health Questionnaire (SF-36). All data were recorded as mean pre-intervention (pre-test) values [Table 2].

Pain intensity was assessed on full weight bearing using an 11-point VAS with 0 =no pain and 10=severe pain as described by Huskisson [29] which is often used in clinical studies. [30]

Functional outcomes were assessed with WOMAC, which is a multi-dimensional, self-administered health status measure, valid and reliable for assessing OA. [10, 31] The questionnaire has 24-items with 3 subscales measuring pain (5 items); stiffness (2 items); physical function (17 items). Responses were scored on a 5-point Likert scale with none = 0,

slight = 1, moderate = 2, severe = 3 and extreme = 4. Total scores range from 0 to 96 with higher scores indicating greater functional impairment.

The Short-Form Health Questionnaire (SF-36) is valid and reliable to evaluate QoL.[32,33] It has 36 items with 8 scales: Physical Functioning (PF), Role Limitation-Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role Limitation-Emotional (RE), and Mental Health (MH). Total scores range from 0-100, with a mean of 50 and standard deviation of 10 being norm-based for the general population. [34] Scores from the eight domains can be computed into two measures, the physical component summary (PCS) and mental component summary (MCS), which provide greater accuracy and remove the floor and ceiling effects of many of the domains.[35] Higher scores indicate improved health status and a better QoL.

The rehabilitation program was for 30 minutes commencing with either IRR or IFC for 15 minutes for pain. The IRR group received radiation from a Luminous IRR (Philips IRR, Infraphil ® 150W) placed 60 cm from the center of the knee with the joint receiving equal radiation. Patients were warned that the sensation should be *"mild warmth"* and were asked to indicate if heat became too much, as too much heat can result in a burn or damage to the skin. IFC was generated by a combination therapy unit (Sonicator Plus 920®, California, USA) with the current set at carrier frequency of 4 kHz; beat frequency of 100 Hz; sweep frequency of 150 Hz using a dipole vector field of 6:6 sweep as prescribed by Eftekharsadat.[22] Four 4×6 cm self-adhesive electrodes transmitting two currents were applied to the anterior-posterior and medio-lateral aspects of the knee so that each current ran diagonally, converged in the center and covered the entire joint. All the equipments were calibrated by a technician prior to use.

Patients were instructed to inform the therapists if they perceived any uncomfortable or unpleasant sensation during the application of IRR or IFC. Both modalities were applied for 15 minutes, three times a week for four weeks. Following IRR or IFC, patients engaged in an exercise program to strengthen the lower limbs for 10 minutes, during which they did 10 quadriceps static muscle contractions, 10 straight leg raises between 30-45 degrees in supine lying position with two pillows under the head and 10 sit-to-stand exercises from a chair. Although there are more complex exercises for strengthening the lower limbs, these basic exercises were used due to resource constraints and the age of the patients. After the exercises, patients were assessed and counseled on posture, balance and gait while walking in

a 15m² room. After each session of the program, relevant data were recorded as mean post-intervention (post-test) values by a senior therapist blinded to the treatment modality or group allocation. Patients were requested to discontinue analgesic and nonsteroidal anti-inflammatory drugs during participation in the study, except in instances where it was not possible to notify the therapist.

Statistical Analysis

Statistical analyses were done with SPSS (Version 21.0, SPSS Inc., and Chicago, IL, USA) and quantitative data shown as mean ± standard deviation (SD) with significance defined at $p<0.05$. Independent *t-test* and paired sample *t-test* were used to compare data between groups, pre- and post-intervention respectively.

Results

A total of 98 outpatients were referred for rehabilitation following diagnosis of OA of the knee. Five did not meet the inclusion criteria, three did not consent to participate, and after group allocation, three from the IFC and four from the IRR group were lost to follow-up, resulting in 83 patients for data analysis [Figure 1]. The gender distribution of the study was female 60% (n=50) and male 40% (n=33); mean age was 63.10±6.91 years and BMI 26.06±4.13 (kg/m^2) with no significant differences between groups [Table 1]. VAS and WOMAC scores for both groups showed significance ($p<0.05$) for all values post-intervention [Table 2]. Values for QoL for the IFC group showed significance ($P<0.05$) for all sub-scales while IRR showed significant only for PF ($p=0.038$); SF ($p=0.023$); GH ($p=0.034$); PCS ($p=0.044$) and MCS ($p= 0.046$) [Table 3]. Eight patients from the IFC group and 6 from the IRR group reported taking their analgesics and non-steroidal anti-inflammatory medication during participation in the study.

Discussion

This is the first documented randomized clinical study comparing the effects of a rehabilitation program with IRR or IFC. The findings of this study show that both modalities were beneficial with lower VAS, improved WOMAC and QoL scores and no adverse reactions after the interventions. Importantly, in this study, functional impairment was assessed by WOMAC which is specific for OA outcomes and evaluates the impact of therapeutic modalities for this condition.[36] Interestingly, the results show that IFC was more effective than IRR in reducing pain, improving mobility and physical function and the QoL

for patients with OA of the knee. The improvement in VAS and WOMAC scores with IFC in this study is supported by other studies that showed improvements for pain alleviation, stiffness and physical function for knee related OA. [37.23.38] Additionally, there is evidence that IFC reduces pain more effectively than therapies without electro-stimulation as IFC demonstrated pain relief for at least 1 week and up to 6 months in some patients with OA of the knee, reducing the need for intake of paracetamol analgesics. [22. 37.40] This finding is similar to that of this study. In another study by Adedoyin et al.,[41] where IFC and TENS were combined with a program of exercises for OA of the knee, there were significant improvements in functional activity due to diminished pain, a finding supported by the data in this study. Theoretically, it is possible that by overcoming skin resistance and penetrating deeper into tissue, IFC does not elicit the discomfort generally experienced with low frequency currents like trans-cutaneous electric nerve stimulating current which acts superficially on the skin.[23] Additionally, based on the researcher's clinical experience and patients' anecdotal reports, the use of medium frequency current is supported as producing a more "pleasant" sensation and is preferred to low frequency transcutaneous electric nerve stimulating current. But this study was in contrast with the study by Young et al., [42] who reported that IFC was not as effective and served as a placebo effect in reducing pain for the knee. Perhaps the positive benefits of this study may have been elicited by the rehabilitation program which included lower limb strengthening which, together with IFC, improved circulation and modulated nociceptive traffic by stimulating nerve cells and enhancing regional changes by releasing pain-reducing endorphins.[16.19] This contrasts with IRR, which is essentially a heating modality and is therapeutic through its phototherapy effects**,** bringing changes in cell membrane permeability by improving the synthesis of endorphins, **and** increasing nerve cell potential resulting in pain relief.[43] The biological phototherapy effect of this heating improves microcirculation by increasing the diameter of arterioles and blood velocity.[44] Studies show that increased vasodilatation and blood flow improved nitrogen oxide, prostacyclin and endothelial-derived benefits of endothelial cells [45] which enable IRR to reduce pain and improve functional activity for patients with OA of the knee.[24.26] Exposure to IRR radiation also stimulates the production of nitrogen oxide which is a potent endogenous vasodilator.[46] Nitrogen oxide dilates venous, arterioles and lymph vessels, improving circulation and tissue oxygen and nutrients thereby eliminating metabolites and relaxing smooth muscle cells.[47] The effects of IRR are time-dependent to release NO initiated by the intensity of radiation per session, treatment time and duration of therapy. This facilitates biochemical and physiological cascade reactions with monochromic infrared

energy improving function and reducing pain in patients with knee OA, resulting in effective therapy [25.48] which is supported by the results of this study. Although this study is in contrast to a study by Hsieh et al., [49] who noted that short term-radiation therapy had no therapeutic effects in patients with OA of the knee due to inadequate dosage. However, it is possible that in this study the combination of the rehabilitation program incorporating an exercise protocol had adequate dosages of IRR thereby improving the relevant scores.

It is widely accepted that patients with OA of the knee present with poor quality of life due to pain, functional limitations and activities of daily living.[50] In this study, the significant improvements in PCS scores may have been due to the patient's positive engagement and compliance with the rehabilitation program because they perceived less pain, had improved joint mobility and functional activity resulting in higher scores. It must also be noted, that when patients experience pain and physical limitations, there is a vicious cycle of inactivity, but participation in a rehabilitation program reduces pain, improves physical function and QoL.[13] However, this study did not show any significant improvement in MCS scores in both groups which possibly supports similar findings by De Bock et al., [51] where they noted that psychological and depressive symptoms affect areas beyond physical functioning.

In summary, this study compared a rehabilitation program using IFC and IRR for pain, functional activity and QoL. Although the results support both modalities, IFC was more effective than heating with IRR for patients with OA of the knee. Since many of the patients refrained from taking analgesic or non-steroidal anti-inflammatory medication during participation, this shows that the program could also reduce the use, cost and adverse effects often associated with the use of these medications. The results of this study therefore support a rehabilitation program of exercises with IFC or IRR to be beneficial as an intermediate non-surgical intervention or for those awaiting surgery for OA of the knee.

The researchers acknowledge that the study has limitations. First, although patients were requested to notify the therapist if they had taken analgesic or non-steroidal anti-inflammatory drugs during their participation, there may be instances where this was not reported. Secondly, all data were analyzed during the 4 weeks of study, making our follow-up relatively short; so it is unknown how long the improvements were sustained. Finally, although a crossover study may have generated more relevant data, the limited resources, period of study and personal circumstances of the patients were a challenge.

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Conflicts of Interest

None declared.

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APPENDIX M

PAN AFRICAN CLINICAL TRIAL REGISTRATION CERTIFICATE

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21 September 2017

To Whom It May Concern:

RE: Efficacy of Electrotherapy on Health Related Quality of Life of Nigerian Elderly Patients with Knee Osteoarthritis: Randomized Controlled Trial

As project manager for the Pan African Clinical Trial Registry (www.pactr.org) database, it is my pleasure to inform you that your application to our registry has been accepted. Your unique identification number for the registry is **PACTR201709002536342**

Please be advised that you are responsible for updating your trial, or for informing us of changes to your trial.

Additionally, please provide us with copies of your ethical clearance letters as we must have these on file (via email or post) at your earliest convenience if you have not already done so.

Please do not hesitate to contact us at +27 21 938 0835 or email epienaar@mrc.ac.za should you have any questions.

Yours faithfully,

Elizabeth D Pienaar
www.pactr.org Project Manager

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