

A Research Protocol: Comparison of Ultrasound therapy with Zingiber Cassumunar Roxb based Phonophoresis and conventional gel in patients with knee Osteoarthritis- Randomized Control Trial

ABSTRACT

Background:

Knee Osteoarthritis is considered as the leading cause of the disability in almost all over the world after age of 40. Almost about 54 percent people will **end up** in knee osteoarthritis in old age. Awareness of non-pharmacological treatment for knee osteoarthritis is more in practice in European as well as in Asian countries. Physical therapy, Ultrasound therapy, Otago exercises etc. are the treatments that are available for conservative management as well as preventive measure of knee Osteoarthritis.

Methodology:

Subjects with knee osteoarthritis with grade II to III on Kallgren and Lawrence classification will be included in the study N = 52. Two groups each of 26 will be allocated randomly as group A who will receive ultrasound treatment with Otago exercises control group and group B who will receive ultrasound treatment with zingiber Cassumunar based gel and Otago exercises as experimental group. The Western Ontario and McMaster University Osteoarthritis Index (WOMAC), VAS, star excursion balance test will be performed before and after the treatment after 2 weeks with single blind procedure.

Objective:

This research will examine the effect of treatment with Zingiber Cassumunar based gel applied by means of phonophoresis with ultrasound therapy in knee osteoarthritis patients with Randomized control trial.

Keywords:

Phonophoresis, Knee Osteoarthritis, Ultrasound, Otago Exercises.

INTRODUCTION:

Knee complex is a combination of patellofemoral and tibiofemoral articulations, that together gives three degrees of freedom to the knee and forms a synovial hinged joint. The medial and lateral menisci along with ligaments and muscles in and around the knee complex are responsible for the static and dynamic stability of the knee complex (1).

Knee joint complex is a major lower limb weight bearing joint which is constantly subjected to high pressure and is therefore susceptible to injuries (2). These injuries if untreated later lead to degenerative changes in the bones that articulate to form the knee complex (3). These degenerative changes lead to the condition termed as Osteoarthritis of knee which contributes to one of the most disabling conditions in the world. Since the condition is associated with forces and weight to which the joint is subjected to(3) , increase in the overall prevalence of obese individuals in population lead to the and increase in the prevalence of people suffering from Knee Osteoarthritis (KOA) (4).

Limited range of motion and stiffness due to pain, joint effusion and bony enlargements is the major manifestation of the condition (5). As a result of these symptoms functional independence of the individual reduces. Surgical treatment for grade 4 of KOA or pain leading to severe functional dependency along with pharmacological treatment have long term side effects (6). Researches have focused upon alternative approach for the long-term treatment of KOA. Exercises, rehabilitation and modifications of lifestyle are the most effective form of intervention according to the recent evidences (7). Rehabilitation of KOA includes strength training of the lower limbs, proprioception training along with other stability exercises (8). The condition generally affects the individuals in the geriatric age where the risk of injuries due to fall is also higher. Inclusion of exercises focusing on stability both static and dynamic in the rehabilitation is important to address the problem of fall which is a associated risk along with high dependency in KOA (9).

Otago Exercise programme is a set of exercises that include stretching, strengthening and balance exercises. Initially developed for the geriatric population to reduce the risk of fall, these when performed regularly are helpful in all the domains of rehabilitation of KOA (10).

Rehabilitation begins with reducing pain by application of therapeutic ultrasound by the physical therapist. The piezo electric effect generated by the high frequency of ultrasound results in an increase in the flow of blood thereby facilitating tissue recovery and reduction in inflammation and pain (11).

Natural Ayurvedic agents have anti-inflammatory effect and reduces pain in patients with Osteoarthritis of knee by its topical application. These Ayurvedic medicines do not generally have any side effects and are as well cost effect with high availability. No previous study has been done with the use of Zingiber Cassumunar Roxb in gel form (12). There is lack of evidence on effectiveness of Zingiber Cassumunar Roxb as a coupling medium adjunct to routinely used aquasonic in phonophoresis. We use Zingiber Cassumunar Roxb. (dry Ginger) as the Ayurvedic herb with anti-inflammatory properties in the form of the gel. We therefore aim to study the effectiveness of this Zinger Cassumunar Roxb phonophoresis as a non-invasive alternative treatment for development of more effective modality with minimal side effects and lower costs (13).

METHODOLOGY

Study design

This study will be carried out in the OPD setting of Ravi Nair Physiotherapy College and AVBRH, Sawangi (Meghe), Wardha, The Research Protocol was approved by Institutional Ethical Committee. We have **Registered** with the Clinical Trial Registry of India (CTRI) with ref. no. REF NO. 2021/04/043216. All participants will be educated about the details of the intervention, research and data confidentiality prior to the start of the study. Those participants who will satisfy the inclusion criterion will have to sign an informed consent before participation. Those (n = 52) who full fill the inclusion criteria will then be included in the study for a duration of 2 weeks.

TRIAL DESIG

In this single blinded controlled trial subjects in group A and group B were randomized by simple random sampling through envelope technique. Conventional therapy will be given to group A while group B will be experimental.

PARTICIPANTS

Inclusion Criteria

Participants aged between 40-60 years of all genders with unilateral knee Osteoarthritis having Stiffness < 30mins will be used as a reference population. The grade of osteoarthritis should be between 1-3 of OA of knee diagnosed in X-ray according to Kallgren and Lawrence classification.

Exclusion Criteria

Patients with Grade of OA 4 according to Kallgren and Lawrence classification having with or without any superficial and deep sensory impairments will not be chosen. Patients who have undergone total hip joint replacement (THR) or with clinically diagnosed neurological disorders like stroke, Parkinsonism and those with current participation in another OA intervention study will also be excluded. Those with severe physical disabilities (i.e., unable to walk even with a walking aid) or who are unable to comprehend are also not included in the study.

RECRUITMENT PROCEDURE

Patients who come to the OPD of RNPC and AVBRH who will meet the eligibility requirements according to the inclusion criteria and willing to participate will be engaged in the RCT.

SAMPLE SIZE CONSIDERATION

The prevalence was referred from the research conducted by Venkatachalam J et al (12). In power calculation, we calculated the total sample size required as 52 with number of participants within each group to be 26 with 95% confidence interval, and 0.10 desired error of margin.

RANDOMIZATION

Participants after base line evaluation , who fulfill the inclusion criteria will then randomised into either of the group.A computer-generated randomisation schedule in randomized permuted blocks will be prepared by an independent statistician, to ensure the number of subjects undergoing the two treatments within each group are closely balanced and the allocation numbers will be placed in invisible sealed envelopes. These envelopes will be made available to the player after signing the consent form.

INTERVENTION DESIGN

Participants will receive the protocol 5 times a week for 2 weeks. An Assessment form is filled prior to administration of the intervention which includes the demographic data and the pre- treatment values of our outcome measures for assessing pain, range of motion, functional disability and balance.

Group A (Control group)

The carefully monitored physiotherapy program will include 8 mins of continuous mode Ultrasound therapy of 1 MHz frequency with routine aqua sonic gel and at intensity of 0.8- 2.5 w/cm². This is then followed by Otago exercise program (14).

Group B (Experimental Group)

The carefully monitored physiotherapy program will include 8 mins of continuous mode Ultrasound therapy of 1 MHz frequency with Zingiber Cassumunar Roxb phonophoresis and an intensity of 0.8- 2.5 w/cm². This is then followed by Otago exercise program (15).

	Strengthening	Balance retraining	Walking
Exercises	Low limb strengthening exercises up to 4 levels of difficulty		Advice about walking
Intensity	Moderate	Moderate	Walking aid (if using) should be used while walking.
Assessment	Start with 1.5 kgs weight.	Each exercise is set at a level that the person can safely perform unsupervised.	Present walking activities are taken a note of.
Progression	Increase	With support to without support exercises	
Frequency	Thrice a week	Thrice a week	Minimum 2 times / week
Duration	30-40 mins for completion starting from warm up till balance exercise		30 minutes (Break into 10 minutes of walk thrice in the entire day)

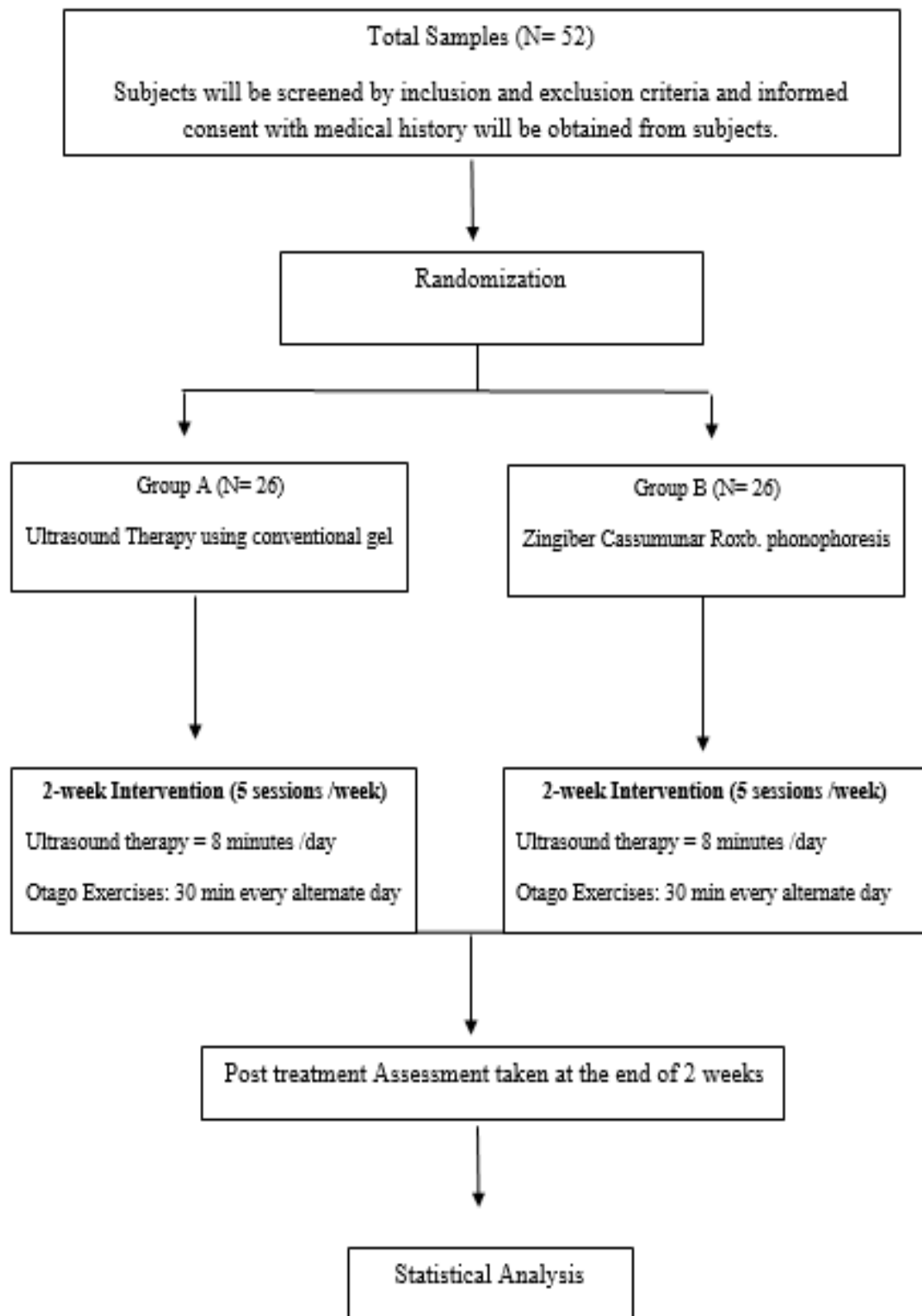
TABLE 1: Domains of Otago Exercise

OUTCOME MEASURES

The primary outcome measure is Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) for assessing functions. Visual Analogue Scale for pain (15,16), Universal goniometer to measure ranges and star excursion balance test (SEBT) a dynamic balance test, are secondary outcome requires flexibility strength and proprioception. SEBT is performed on eight lines taped to the ground, each of them at a 45-degree angle to on another leading to formation of a Star. The distance is marked in centimetres on the tape to determine the reach

distance. The participant stands in the centre of this star and with the opposite leg are asked to reach as far as possible in the specified direction(17).

STUDY PROCEDURE FLOW CHART



DATA MANAGEMENT

Data of the study will be stored in a safe, secured store room with limited access for later review by a biostatistician, a researcher in charge.

STATISTICAL ANALYSIS

Statistical analysis will be done by using descriptive and inferential statistics using chi-square and t-test for the difference between two means. The software used in analysis will be SPSS 24.0 V and Graphed Prism 7.0 v with $p < 0.05$ considered as level of significance.

CONCLUSION

The conclusion will be drawn from the analysis of the values obtained for the outcome measures post data collection.

DISCUSSION

This research protocol is based on evaluation of pain, available movements, functions and dynamic balance post application of therapeutic modality and a regular exercise regime at the end of 10 treatment sessions in subjects with osteoarthritis of knee (KOA) (18). Therapeutic ultrasound is a modality proven to show positive outcomes in arthritic knee pain and swelling. This therefore remains as a conventional treatment approach in this single blinded randomized control trial for the control group (17).

Abdalbary et al in 2016 gave results of the study Ultrasound with mineral water or aqua gel to reduce pain and improve the WOMAC of knee osteoarthritis, which revealed effectiveness of both the groups to be equal (19). A study conducted by Decha et al concluded that phonophoresis with Phyllanthus Amarus nanoparticle gel for osteoarthritic patients is an effective treatment method. 6-MWT has been used as an outcome measure to check the functional capacity of the patients (20). Newberry et al concluded that treatment modalities like TENS, whole body vibration are also an effective treatment approach with an optimal improvement in pain scores and functional ability of patients (12).

Phonophoresis, a technique to provide more effective therapeutic ultrasound have shown to decrease pain and improve functions significantly with the usage of drugs lidocaine (21). Phonophoresis of Zingiber Cassumunar (Ginger) an easily available non pharmacological agent, a study previously not done in patients with KOA, will be carried out to assess its

effectiveness supplemented with Otago Exercise programmes that have proven to be effective for strengthening of lower limbs as well as in enhancing balance in elderly adults.

RESEARCH ETHICS APPROVAL

The trial will be performed in accordance with the Declaration of Helsinki.

DISSEMINATION AND PROTOCOL AMENDMENTS

The primary RCT findings will be sent to a foreign peer-reviewed journal for publication, regardless of whether the findings are positive, negative or inconclusive about the research hypothesis.

CONFIDENTIALITY

Specific Subject information will be kept separate from the central dataset, and will not be exchanged. All personal data will be stored securely before, during and after to preserve the confidentiality.

PATIENT CONSENT

An informed consent will be obtained from the patient on a printed form with the signatures and will be given the proof of confidentiality.

REFERENCES

1. Flandry F, Hommel G. Normal anatomy and biomechanics of the knee. *Sports Med Arthrosc Rev.* 2011 Jun;19(2):82–92.
2. O'Malley MP, Pareek A, Reardon PJ, Stuart MJ, Krych AJ. Distal Femoral Osteotomy: Lateral Opening Wedge Technique. *Arthrosc Tech.* 2016 Aug;5(4):e725.
3. Ghordadekar D, Naqvi WM, Sahu A. A case report on impact of physiotherapy rehabilitation on post coronary artery bypass graft. 2020;6.
4. Paradowski PT. Osteoarthritis of the Knee: Assessing the Disease. *Health Care Curr Rev.* 2014;2(2):4.
5. Mangine GT, Hoffman JR, Gonzalez AM, Townsend JR, Wells AJ, Jajtner AR, et al. The effect of training volume and intensity on improvements in muscular strength and size in resistance-trained men. *Physiol Rep [Internet].* 2015 Aug 13 [cited 2021 Jan 10];3(8). Available from: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4562558/>

6. Zade R, Deshmukh M. A Comparative Study Based On Two Stretching Protocol for Piriformis Tightness: A Research Protocol. *J Crit Rev.* 2019;6(6):911–4.
7. Dhankar² NTS. Correlation of Physical Activity with Fear of Fall in Patients with Total Knee Replacement - A Research Protocol. *Indian J Forensic Med Toxicol.* 2021;15(1):1835–9.
8. Bais¹ A, Phansopkar² P. Impact of Pilates Training versus Progressive Muscle Relaxation Technique on Quality of Life in Menopausal Women- A Comparative Study. *Indian J Forensic Med Toxicol.* 2021;15(1):7–11.
9. Kohn MD, Sassoon AA, Fernando ND. Classifications in Brief: Kellgren-Lawrence Classification of Osteoarthritis. *Clin Orthop.* 2016 Aug;474(8):1886.
10. Farr II J, Miller LE, Block JE. Quality of Life in Patients with Knee Osteoarthritis: A Commentary on Nonsurgical and Surgical Treatments. *Open Orthop J.* 2013 Nov 13;7:619–23.
11. Focus on pain. *Nat Neurosci.* 2014 Feb;17(2):145–145.
12. Venkatachalam J, Natesan M, Eswaran M, Johnson AKS, Bharath V, Singh Z. Prevalence of osteoarthritis of knee joint among adult population in a rural area of Kanchipuram District, Tamil Nadu. *Indian J Public Health.* 2018 Apr 1;62(2):117.
13. Almarzouki R, Bains G, Lohman E, Bradley B, Nelson T, Alqabbani S, et al. Improved balance in middle-aged adults after 8 weeks of a modified version of Otago Exercise Program: A randomized controlled trial. *PLOS ONE.* 2020 Jul 15;15(7):e0235734.
14. Martins AC, Santos C, Silva C, Baltazar D, Moreira J, Tavares N. Does modified Otago Exercise Program improves balance in older people? A systematic review. *Prev Med Rep.* 2018 Sep;11:231.
15. Heller GZ, Manuguerra M, Chow R. How to analyze the Visual Analogue Scale: Myths, truths and clinical relevance. *Scand J Pain.* 2016 Oct;13:67–75.
16. Alghadir AH, Anwer S, Iqbal A, Iqbal ZA. Test–retest reliability, validity, and minimum detectable change of visual analog, numerical rating, and verbal rating scales for measurement of osteoarthritic knee pain. *J Pain Res.* 2018 Apr 26;11:851–6.
17. Stockert B, Barakatt E. TEST-RETEST RELIABILITY OF THE STAR EXCURSION BALANCE TEST IN A GERIATRIC POPULATION. *J Geriatr Phys Ther.* 2005 Dec;28(3):116.
18. Darware M, Naqvi WM. A case report on Physiotherapy rehabilitation accelerating the recovery of older patient with anterior cruciate ligament reconstruction. 2020;6.
19. Abdalbary SA. Ultrasound with mineral water or aqua gel to reduce pain and improve the WOMAC of knee osteoarthritis. *Future Sci OA.* 2016 Mar;2(1):FSO110.
20. Pinkaew D, Kiattisin K, Wonglangka K, Awoot P. Phonophoresis of Phyllanthus amarus nanoparticle gel improves functional capacity in individuals with knee osteoarthritis: A randomized controlled trial. *J Bodyw Mov Ther.* 2020 Jan 1;24(1):15–8.

21. Bhandakkar¹ P, Patil² D, Kapoor³ A. A Study Protocol for a Randomized Trial on Effect of Safe Patient Handling (SPH) program on Rehabilitation Outcomes and on Safety of Physical Therapists in Rural Hospital. Indian J Forensic Med Toxicol. 2021;15(1):154–8.

UNDER PEER REVIEW