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The Iontophoresis versus ultrasound in treatment of knee Osteoarthritis

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Abstract
Background: Knee osteoarthritis (KOA) is a very common disorder affecting many people during the aging process which finally results in painful symptoms that disturb their lives.
Purpose: This study was conducted to compare the effects of iontophoresis versus ultrasound (US) on knee osteoarthritis.
Methods: Seventy-two subjects diagnosed with KOA according to the American college of rheumatology (grade 2 and 3) participated in this study. Their age ranged from 45 to 60 years old while their BMI ranged from 19 to 30 kg/m^2. They were allocated into three equal groups; Group A (experimental group 1) received Iontophoresis and traditional treatment. Group B, (experimental group 2), received US and traditional treatment. Group C, (control group), received only traditional treatment. All patients received 3 sessions per week for four weeks. Pain intensity, knee ROM, and functional disability, were assessed using the VAS score, the electronic digital goniometer, and the WOMAC index – Arabic version respectively.
Results: There was a significant decrease in VAS and pain, stiffness and function scores of WOMAC of group A compared with that of group B ($p < 0.05$) and group C ($p < 0.001$), There was a significant increase in flexion and extension ROM of group A compared with that of group B and group C ($p < 0.001$).
Conclusions: application of Iontophoresis in conjunction with traditional treatment for patients with KOA was more effective in pain relief and improvement of knee joint ROM and functional ability than ultrasound in conjunction with traditional treatment and traditional treatment alone.

Keywords: Iontophoresis, knee osteoarthritis, ultrasound

Introduction

Osteoarthritis (OA) is a progressive degenerative disease, the incidence of which keeps rising with the growth of the ageing population in many societies, The main complaints of knee OA include: pain during body moving or weight bearing, stiffness, swelling, deformity and decreased walking time and distance. Therefore, the relevant therapies generally aim to relieve pain, improve functionality and mitigate disability for enhancing the quality of life (Zenge *et al*., 2014). It is a common and often debilitating chronic joint disease and is one of the leading causes of pain and disability in worldwide. Symptoms can become increasingly debilitating over time and can greatly affect quality of life, contributing to feelings of dependence and loss of autonomy in older people. As a result of an aging population, combined with increasing obesity rates, the disease burden associated with knee OA is forecast to increase substantially over the coming decade. However, improvements in pain, knee ROM, physical function, and quality of life have been demonstrated with exercise-based interventions. Thus, clinical guidelines consistently emphasize education, exercise, weight loss (if required), and support for self-management to alleviate knee OA symptoms before using surgical or pharmacological interventions (Jones *et al*., 2021) [24].

The OA increases with age. Researches revealed that more than 75% of the population over 65 years old are affected by OA to some extent. More than 186 billion dollars were the cost to treat patients with OA annually as estimated by the World Health Organization (Zhou *et al*., 2018) [50].

The disease may involve progressive symptomatic and structural deterioration over time (Paterson *et al*., 2018) [37].

Iontophoresis (IP) is a physical therapy intervention used to administer anti-inflammatory medications for decreasing pain and inflammation in conditions of the musculoskeletal system. Iontophoresis is a noninvasive drug-delivery intervention that uses an electrical current to transdermally deliver aqueous ionic solutions, via bipolar electrodes. The aqueous ionic solutions are electrically charged mediums that migrate through the skin to promote healing and decrease inflammation in superficial localized areas (Peplinski and Irwin, 2010) [38]. It increases the penetration of ionized compounds into the skin, in the presence of an electric field. The ionized material is also introduced into the tissue by electrical shock and electro-osmosis. This method has the potential to control drug penetration by varying the density and time of the applied current. Because of its easy application, non-invasiveness, and increased drug penetration into target tissues, it has been used to deliver macromolecules, such as proteins and peptide dendrimer (Bok *et al*., 2020) [7].

Iontophoresis is a transdermal drug-delivery method used to apply anti-inflammatory and anesthetic drugs directly to an area. Iontophoresis uses a mild direct current to repel positive or negative drug ions through the stratum corneum of the epidermis and into the underlying tissues. Iontophoresis has several advantages over other drug-

delivery methods; for example, it does not carry the risk of pain or infection of needle injections, nor does it involve the loss of drug potency during first-pass metabolism as in oral ingestion (Rigby *et al*., 2015) [40].

Therapeutic ultrasound (US) is a well-established deep-heating modality that converts mechanical energy into a form of sound waves. Ultrasound is used to treat many musculoskeletal diseases and is also reputed to relieve pain, increase ROM t, reduce edema and accelerate tissue repair. It is one of several physical therapy modalities suggested for the management of pain and loss of function due to OA and can be used as part of an overall rehabilitation program. US may be administered in either a continuous or a pulsed mode. Pulsed US produces non-thermal effects and is used to aid in the reduction of inflammation, whereas continuous US generates thermal effects. Both modes are often used in the management of painful musculoskeletal disorders (Ulus *et al*., 2012) [45].

Ultrasound can be used a good pain relieving tool in such patients. It is non-invasive, can be repeated easily and has no side effects. The mechanism of ultrasound therapy of knee joint is described as application of high frequency sound waves cause mechanical and thermal effects which in turn result in increase in blood flow and metabolic activity, decreased inflammatory response and decreased pain. Ultrasound therapy is proven to improve the hyaline cartilage repair and it soften the dense fibrous tissue which results in pain free movement and improvement in KOA (Mumtaz and Shah, 2018) [32].

Glucosamine, the main ingredient needed to produce glycosaminoglycans, is naturally produced by our body, but the body loses its capacity to produce sufficient glucosamine with age and causes thinning of the cartilage, leading to joint degeneration (Kong *et al*., 2019) [27]. Glucosamine sulfate (GS) is the precursor of *O*-linked and *N*-linked glycosaminoglycans which form the building block matrix of all connective tissues including cartilage proteoglycan and hyaluronic. It has also been reported that this natural compound can reduce the symptoms of OA, influence cartilage metabolism, promote the synthesis of articular cartilage matrix, and reduce inflammation (Chattopadhyay *et al*., 2020) [12].

Materials and Methods

The current study was conducted at the Outpatient Clinics, Faculty of Physical Therapy Cairo University from February to July, 2023 to compare between glucosamine, sulphate Iontophoresis and US on Knee osteoarthritis

Sample Size Calculation

It was done using G-Power software program. F-test MANOVA within and between interaction effects was selected. Considering a power of 0.80, an α level of 0.05 and effect size of 0.4; three groups and two measurements, generated a sample size of at least 64 participants. Adding 7 subjects (10% as drop out), so the total sample size was 72 subjects (Twenty-four in each group). The subjects were randomly assigned into three groups:

Group (A), (experimental group 1) received Iontophoresis and traditional treatment.

Group (B) (experimental group 2), received US and traditional treatment.

Group(C), (control group), received only traditional treatment.

All groups received treatment for 3 sessions per week for four weeks

Inclusion Criteria

The patients were included in this study according to the following criteria

1. Their age ranged from 45 to 60 years old while their BMI ranged from 19 to 30 kg/m^2.
2. Participant diagnosed with KOA according to the American college of rheumatology (grade 2 and 3).
3. An average pain intensity of ≥ 3 on the 10-cm VAS (Yang *et al*., 2011) [46].
4. For those patients with bilateral KOA, the most painful knee was assessed (Zhang *et al*., 2022) [49].

Exclusion Criteria

The patients were excluded from this study according to the following criteria:

1. Patients with a previous knee surgery (Ip, 2015).
2. Patients with contraindicated cases to the application of US (e. g. cancer, uncontrolled diabetes mellitus, hypertension, etc.) (Teslim *et al*., 2014) [43].
3. Patients with neurological disorders (Teslim *et al*., 2014) [43].
4. Patients with insensitive skin to the used substance GA (Zhang *et al*., 2022) [49].

Instrumentations and procedures for evaluation

1. **The VAS:** The Visual Analogue Scale (VAS) is a 100 mm horizontal line with a description of pain limits (0, "no pain" on the left and 10, "worst pain imaginable" on the right) at either end of the scale. By use of a millimeter scale, this score provides 101 levels of pain intensity (Tschoner, 2021.) [44]

2. **The electronic digital goniometer:** (Model: TMT333601), digital angle ruler with high performance. It measures the angle, and it could be able to show the result as digital data, the acquired digital data could be interfaced with the signal condition system (Boobalan *et al*., 2020) [8].

3. **The WOMAC index:** A self-administered or interview-administered questionnaire. It has been validated for use in person, over the telephone, or electronically via a computer or mobile phone**.** It is demonstrated acceptable reliability and validity in patients with hip or KOA (Basaran *et al*., 2010) [4]. The total score for each subscale is the sum of scores for each response to each item, and can be calculated manually or using a computer (Collins *et al*., 2011) [13].

Participants Preparation

1. All the patients were given explanation of the treatment protocol in their understandable language and they participated after signing a written consent form.
2. All the participants' information and data recording were collected in specially well-designed sheets.
3. All participants underwent the same evaluation and recording of all parameters before and after 12 session on alternative days. All the measurements were performed by the same therapist.

Procedures

Ethical committee approval No:P.T.REC/012/004166

1. Assessment of Pain

Patients are asked to report "current pain intensity" or "pain intensity in the last 24 hours" and asked to place a line perpendicular to the VAS line at the point that represents their pain intensity The scale is most commonly determined by "no pain" (score of 0) and "worst imaginable pain" (score of 100 [100-mm scale]) for pain intensity (Shimoji, & Aida.,2021) [41]

2. Assessment of Range of Motion

Patients was placed supine for the measurement of the active knee flexion and extension ROM, with extended knees and the hip in a neutral position and patients were asked to actively flex and extend their knee as far as possible to the maximum. The goniometer was positioned with its center fulcrum over the lateral epicondyle of the femur, the proximal arm was aligned with the lateral midline of the femur, using the greater trochanter for reference, and the distal arm was aligned with the lateral midline of the fibula, using the lateral malleolus and fibular head for reference (Casaña *et al*., 2021) [11]

3. Assessment of Physical Function

The WOMAC scale (Arabic Version): It was used to evaluate how well patients with OA of the knee performed functionally. It has 24 criteria that describe the existence and intensity of pain throughout various daily activities**.** (Abd El Bakk *et al* 2023) [2]

Instrumentations and procedures for Treatment

1. Iontophoresis Device: (Model: 5060004-PM850-Phoresor II Auto iontophoretic drug delivery system with tl7 twin lead). An iontophoretic device was used which comprises a power source and two electrode compartments. The drug formulation containing the ionized molecule is placed in the electrode compartment bearing the same charge Glucosamine sulfate (2-amino-2-deoxy-D-glucose) is a sulfate derivative of the natural amino monosaccharide glucosamine (Chattopadhyay *et al*., 2020) [12].

The solution was prepared by dissolved Glucosamine sulphate powder was in water by stirring in a percentage of 14%. The anodal (active) electrode, with topical glucosamine sulphate with 1,5 ml / day dose for each patient were placed on the popliteal fossa, and the nonnative electrode was placed on the gastrocnemius muscles 10 cm distal to the anode A prone line position was used (Büyükşireci *et al*., 2022) [10]., Intensity was set at 1 MA for 5 minute, then was increased to 1.5 M A for another 5minute, and then to 2MA for the last 5 minute.

The US Device: (Model: Gymna electric ultrasonic laser combination combi 200l with touch screen), Manufacture in Belgium

Specifications: Frequency: Multifrequency head (1 and 3 MHz), 4 cm², Mode: Continuous and pulsed mode (10–20–30–40–50-100%) and Mains voltages: 100-240-VAC, 50/60 Hz +/- 10%

Procedures

The pulsed US interventions similarly used a 1 MHz frequency with an intensity of 1 W/cm^2 for 10 min at a pulsed mode (Berteau, 2022). pulsed mode, 20% duty cycle pulsed mode, 20% duty cycle (1:5) pulse ratio ((Loyola-Sánchez *et al*., 2010) [29]. a supine position was used with knee slightly with pillow flexed The treatment area was involved superior medial patella border for 2,5 minute,lateral patellar border 2,5 minutes, medial to patellar tendon for 4,5 minute

All treatments were standardized using a device that placed the participant in a supine position, and the knee was angled at the semiflexion position and supported by a rolled towel (Jia *et al*., 2016) [23].

Traditional treatment

The program emphasized knee strengthening but also involved an aerobic warm-up, and stretching (Kuntz *et al*., 2018) [28]. Subjects in all groups were asked to perform stretching exercises and strengthening.

Each stretch 3 times/session. was sustained for 15-30 seconds, with 10 seconds rest between each stretch. The strength exercise was performed for 3 sets of 10 repetitions/session. Both stretching and strengthening exercises were performed 3 sessions per week for 4 weeks (Ontario, 2015). The patients made warm up 5 - 10 minutes on a treadmill (Øiestad *et al*., 2015) [33]. The treadmill was set to the median speed of 2.20 km/h (Möckel *et al*., 2003) [31]. the patients was performed 5 minutes worm-up in first week and increase gradually to 5 minutes' before and after exercise then 7 minute in third week and 10 minute in a final week

Stretching of the Hamstrings Muscle

With the patient's knee fully extended, support the patient's lower leg with your arm or shoulder. Stabilize the opposite extremity along the anterior aspect of the thigh with your other hand or a belt or with the assistance of another person. With the knee at 0° extensions and the hip in neutral rotation, flex the hip as far as possible (Kisner *et al*., 2018) [26].

Stretching of the Calf Muscle

The therapist was standing beside affected leg and grasped the patient's heel (calcaneus) with one hand, maintain the subtalar joint in a neutral position, and place your forearm along the plantar surface of the foot. Stabilize the anterior aspect of the tibia with your other hand. Dorsiflex the talocrural joint of the ankle by pulling the calcaneus in an inferior direction with your thumb and fingers while gently applying pressure in a superior direction just proximal to the heads of the metatarsals with your forearm (Kisner *et al*., 2018) [26].

Stretching of the Iliotibial Band

The therapist stabilized the pelvis at the iliac crest with the proximal hand. Flex the knee and extend the patient's hip to neutral or into slight hyperextension, if possible. Let the patient's hip adduct with gravity and apply an additional stretch force with your other hand to the lateral aspect of the distal femur to further adduct the hip (Kisner *et al*., 2018) [26].

Isometric Quadriceps Exercise

Patients sitting position. A rolled up towel was put beneath the knee. They were instructed to maximally activate their thigh muscles in order to straighten their knee and hold the contraction for 5 seconds (Anwer and Alghadir, 2014) [1].

Straight Leg Raising Exercise
Patients lay in a supine position. They were instructed to perform a maximum isometric quadriceps contraction prior to the lifting phase of the exercise. Then they were instructed to lift the leg up to above the plinth and hold the contraction during the lifting phase for 10 seconds (Anwer and Alghadir, 2014) [1].

Hip Abductor Strengthening Exercise
The side lying position was used as it has been shown to create the greatest activation of the hip abductors (Palmer *et al*., 2015) [36].

Hip Extensor Strengthening Exercise
Patient lies prone, tightens quadriceps on the affected leg, keeping the knee straight, lifts his heel straight up toward ceiling against weight, keeping toes pointed straight down (Bryan, 2018**)** [9].

Short Arc Terminal Extension Exercise
Initially, have the patient extend the knee only against the resistance of gravity, Later, combine short-arc terminal knee extension with an isometric hold and/or a SLR when the knee is in full extension. To reduce lateral shear forces at the knee, have the patient invert the foot as he or she extends the knee (Kisner *et al*., 2018) [26].
All exercises started active free then progress to, patients were hold in each exercise for (6-10) second.
-the progression was done when patient was eased to do exercises, weight had been added according to DeLorme Principle for strengthening.

Statistical Analysis
Subject characteristics were compared between groups using the MANOVA test. Chi-squared test was conducted for comparison of sex distribution between groups. Normal distribution of data was checked using the Shapiro-Wilk test. Levene's test for homogeneity of variances was conducted to test the homogeneity between groups. Mixed MANOVA was performed to compare within and between groups effects on WOMAC, VAS and knee ROM. Post-hoc tests using the Bonferroni correction were carried out for subsequent multiple comparison. The level of significance for all statistical tests was set at $p < 0.05$. All statistical analysis was conducted through the statistical package for social studies (SPSS) version 25 for windows (IBM SPSS, Chicago, IL, USA).

Results

General characteristics of the subjects

Subject characteristics
Table (1) shows the subject characteristics of group A, B and C. There was no significant difference between groups in age, BMI and sex distribution ($p > 0.05$).

Table 1: Basic characteristics of participants.

	Group (A)	Group (B)	Group (C)	p-value
	Mean ± SD	Mean ± SD	Mean ± SD	
Age (years)	52.66 ± 4.53	54.75 ± 5.15	53.08 ± 4.20	0.26
BMI (kg/m²)	24.06 ± 1.91	24.08 ± 2.53	23.92 ± 2.04	0.95
Sex, n (%)				
Females	*I*8 (75%)	19 (79%)	21 (87.5%)	0.53
Males	6 (25%)	5 (21%)	3 (12.5%)	

SD, standard deviation; p-value, level of significance

Effect of treatment on pain, ROM, and function on knee
Mixed MANOVA revealed that there was a significant interaction of treatment and time ($F = 8.46$, $p = 0.001$, Partial Eta Squared = 0.44). There was a significant main effect of time ($F = 435.39$, $p = 0.001$, Partial Eta Squared = 0.97). There was a significant main effect of treatment ($F = 4.28$, $p = 0.001$, Partial Eta Squared = 0.28).

Within group comparison
There was a significant decrease in pain in the three groups post treatment compared with that pretreatment ($p < 0.001$). (Table 2),
There was a significant increase in flexion and extension ROM in the three groups post treatment compared with that pretreatment ($p < 0.001$). (Table 3).
There was significant decrease in stiffness and function scores of WOMAC in the three groups post treatment compared with that pretreatment ($p < 0.001$). (Table 4).

Between group comparison
There was a significant decrease in pain, stiffness and function scores of WOMAC and VAS of group(A) compared with that of group(B) ($p < 0.05$) and group(C) ($p < 0.001$). There was a significant decrease in pain, stiffness and function scores of WOMAC and VAS of group (B) compared with that of group(C) post treatment ($p < 0.01$).
There was a significant increase in flexion and extension ROM of group (A) compared with that of group(B) and group(C) ($p < 0.001$) and a significant increase flexion and extension ROM of group (B) compared with that of group (C) ($p < 0.01$). (Table 2-3).

Table 2: Mean VAS pre and post treatment of group A, B and C

	Group (A)	Group (B)	Group (C)	p-value		
	mean ± SD	mean ± SD	mean ± SD	A vs B	A vs C	B vs C
VAS						
Pre treatment	6.89 ± 0.93		7.13 ± 1.12	7.08 ± 1.10	0.73	0.81	0.99
Post treatment	2.75 ± 0.88		3.58 ± 1.21	4.64 ± 1.15	0.02	0.001	0.003
MD (% of change)	4.14 (60.09%)		3.55 (49.79%)	2.44 (34.46%)			
	p = 0.001		p = 0.001	p = 0.001			

SD, Standard deviation; MD. Mean difference; p-value, Level of significance

Table 3: Mean knee flexion and extension ROM pre and post treatment of group A, B and C

ROM (degrees)	Group (A)	Group (B)	Group (C)	p-value		
	mean ± SD	mean ± SD	mean ± SD	A vs B	A vs C	B vs C
Flexion						
Pre-treatment	118.21 ± 6.53	117.83 ± 5.76	116.75 ± 4.98	*0.97*	0.66	*0.79*
Post treatment	130.79 ± 4.20	126.13 ± 3.54	121.71 ± 4.59	0.001	0.001	0.001
MD (% of change)	-12.58 (10.64%)	-8.3 (7.04%)	-4.96 (4.25%)			
	p = 0.001	*p = 0.001*	*p = 0.001*			
Extension						
Pre-treatment	3.04 ± 1.04	3.14 ± 0.97	3.08 ± 1.02	0.93	0.98	0.97
Post treatment	0.63 ± 0.39	1.16 ± 0.52	1.64 ± 0.47	0.001	0.001	0.002
MD (% of change)	2.41 (79.28%)	1.98 (63.06%)	1.44 (6.75%)			
	p = 0.001	*p = 0.001*	*p = 0.001*			

SD, Standard deviation; MD. Mean difference; p-value, Level of significance

Table 4: Mean WOMAC pre and post treatment of group A, B and C

	Group (A)	Group (B)	Group (C)	p-value		
	mean ± SD	mean ± SD	mean ± SD	A vs B	A vs C	B vs C
WOMAC						
Pain score						
Pre- treatment	9.25 ± 1.96	9.13 ± 1.65	9.62 ± 1.88	0.97	0.76	0.61
Post treatment	3.58 ± 0.83	4.58 ± 1.14	6.04 ± 1.16	0.004	0.001	0.001
MD (% of change)	5.67 (61.30%)	4.55 (49.84%)	3.58 (37.21%)			
	p = 0.001	p = 0.001	p = 0.001			
Stiffness score						
Pre- treatment	4.54 ± 1.44	4.42 ± *1*.02	4.58 ± 1.1	0.93	0.99	0.88
Post treatment	1.50 ± 0.78	2.29 ± 1.04	3.13 ± 1.19	0.02	0.001	0.01
MD (% of change)	3.04 (66.96%)	2.13 (48.19%)	1.45 (31.66%)			
	p = 0.001	p = 0.001	p = 0.001			
Function score						
Pre-treatment	27.58 ± 6.99	26.83 ± 8.77	27.92 ± 8.09	0.94	0.98	0.88
Post treatment	12.33 ± 2.22	14.54 ± 1.96	16.58 ± 3.20	0.009	0.001	0.01
MD (% of change)	15.25 (55.29%)	12.29 (45.81%)	11.34 (40.62%)			

SD, Standard deviation; MD. Mean difference; p-value, Level of significance

Discussion

The study was conducted to compare between the effect Iontophoresis of and ultrasound on knee osteoarthritis

Osteoarthritis (OA) is the most common disease of the musculoskeletal system, leading to impaired performance in daily life, especially among the elderly. According to the WHO, it is one of the most common causes of disability in developed countries. OA can affect any joint, although the knee joints suffer from it most often

The selection of methods and the course of treatment depend on a number of factors, including age, sex, the degree of advancement of degenerative changes, and coexisting diseases. The therapeutic approach should be individually tailored to the needs and physical condition of the patient, and aimed at improving the quality of life and postponing or, if possible, avoiding surgery. Physical procedures with the use of direct current, such as galvanic treatment and iontophoresis, are widely used in the treatment of OA (Dakowicz, *et al*., 2022) [15]

The results of this study revealed that:

-There was a significant decrease in pain, stiffness and function scores of group (A) compared with that of group(B) and group (C). There was a significant decrease in pain, stiffness and function scores of group B compared with that of group (C) post treatment.

-There was a significant increase in flexion ROM of group (A)compared with that of group (B) and group (C) and a significant increase of group (B) compared with that of group (C). There was a significant increase in extension ROM of group (A) compared with that of group (B) and group (C) and a significant increase of group (B) compared with that of group (C).

iontophoresis is chosen as an alternative route through which patients with OA could benefit from such medications thereby preventing the development of unnecessary co-morbid conditions. It is a non-invasive procedure by which high concentration of ionisable substances, mostly medications or bio-active agents, is propelled trans dermally by repulsive electromotive force generated from two electrodes fastened over the overlying skin of the body segment. (Bello *et al*.,2014) [5]

Use iontophoresis technique in clinical trials which will be cost effective, having minimal adverse effects, maximum penetration and strong deeper effect on affected area to decrease pain and swelling and thereby, we can prevent disease progression and improve activities of daily living so that we can decrease the number of osteoarthritic patients (Tonk and Sharma, 2018) [39].

Iontophoresis may be considered as an alternative therapy in knee osteoarthritis that is inexpensive, simple and non-invasiveTransdermal administration via iontophoresis allows for localized delivery, thus bypassing many of the unwanted toxicities and nuisances (Tonk and Sharma, 2018) [39].

The human body depends on glucosamine, an amino sugar, for the synthesis of connective tissue and cartilage. Glucosamine is used as the starting material for tendons and ligaments, mucous membranes in the digestive and respiratory tracts, and synovial fluid in the joints. It also supports healthy mucous secretion of the digestive,

respiratory, and urinary tracts. There is evidence that glucosamine also helps to improve the structure of joints. the glucosamine supplementation could provide some degree of pain relief and improve function in person who experiences regular knee pain, as a result of cartilage injury or osteoarthritis. The study of the penetration of drugs through the skin has become increasingly important in recent years (Ayodele *et al*, 2011) [3].

These result were supported by Mario *et al*., 2018 who investigate efficacy of glucosamine and /or chondroitin sulphate on knee O.A this systematic review and meta-analysis of randomized placebo-controlled trials, 29 trials were selected and included in the systematic review and meta-analysis, result showed Treatments with glucosamine and chondroitin were found to significantly reduce pain in VAS

The findings of this study are in line with Büyükşireci *et al*. (2022) [10] that evaluate the effectiveness of galvanic current and dexamethasone iontophoresis in the treatment of knee osteoarthritis and Baker's cyst, This prospective, randomized, controlled, single-blind study included 37, result show A significant clinical and functional improvement was detected with dexamethasone iontophoresis in the treatment of patients with knee osteoarthritis.

Add to this, Fathy and Abd El Rahman, (2016) [19] compared Dexamethasone 0.4% iontophoresis combined with traditional treatment against the traditional treatment only. They found that Dexamethasone 0.4% iontophoresis is beneficial in improving functional performance in patients with KOA.

This finding was contradicted by finding of Teslim *et al*., 2014 [43] who attempted to compare between the immediate effects of glucosamine sulphate and methyl salicylate cream on pain, flexibility and knee flexion. 41 patients were randomly assigned to receive glucosamine sulphate or methylsalicylate Both group had a baseline intervention in the form of infra-red radiation therapy and bicycle ergometry for 15 minutes each.,patints were evaluated by The modified sit and reach flexibility box. A short armed half circle plastic goniometer, stadiometer, and visual analogue scale was used. concluded that transdermal massage of glucosamine was as effective as methyl salicilate in alleviating pains, improving hamstring flexibility and increasing knee flexion range of motion in a single treatment session among knee OA participants in this study.

Ultrasound (US), which is a frequently used physical therapy agent, has been accepted as an effective treatment agent in knee OA since it has been shown to increase blood flow, metabolic activity and tissue recovery and to reduce pain and inflammation via high-frequency sound waves that generate thermal and mechanic effects in soft tissues. US therapy may have positive effects on reducing knee pain and enhancing knee functionality in knee OA patients.

Therapeutic US is used as a complementary treatment in physical therapy regimens focused on managing pain and aiding in the healing of soft tissue injuries.7 The treatment exerts therapeutic effects through thermal (continuous US) and nonthermal (pulsed US) modalities via a variety of application parameters (i.e., intensity, wavelength, duty cycle, and frequency).8 Continuous US achieves the thermal effect and is purported to produce analgesia through temperature elevation, which increases capillary permeability and tissue metabolism, thereby enhancing fibrous tissue extensibility and pain thresholds. Non-thermal effects are achieved by modulating cell membrane permeability, increasing protein synthesis, and activating immune response near the injury site, which may stimulate regeneration of damaged tissue (Dantas *et al*., 2022)

A recent systematic review demonstrated positive benefits of low-intensity pulsed US on some properties of cartilage formation, especially in the increase of type II collagen,which is the principal fiber structure of articular cartilage, and in the reduction of a specific type of metalloproteinase expression, an inflammatory mediator that predisposes to OA (Dantas *et al*., 2022) The result of (Yi Zhou *et al*., 2018) [50] indicated that LIPUS, used to treat knee OA without any adverse effect, had a beneficial effect on pain relief and knee functional recovery

These result were supported by Zeng *et al*., 2014 to investigate the efficacy of continues and pulsed ultrasound (US)in the management of knee osteoarthritis (OA), their finding indicated that pulsed US, with greater probability of being the preferred mode, is more effective in both pain relief and function improvement when compared with the control group. However, continuous US could only be considered as pain relief treatment in the management of knee OA, the findings also confirmed that none of these mode is dangerous.

In patients with knee OA various pathophysiological disorders are present, such as quadriceps weakness, decrease in the joint range of motion (ROM) and joint instability, Pain is by far the most frequent and important complaint. Quadriceps weakness is frequently found in knee OA, even in patients who do not have knee pain or muscle atrophy. (Eyigor, 2004) [18]

As lower limb musculature is the natural brace for the knee joint, potentially important muscle dysfunction may arise from either quadriceps weakness or relative weakness of the hamstrings (Hafez *et al*.,2014) [20]

The American College of Sports Medicine (ACSM) has created a thorough physical activity prescription for seemingly healthy individuals that includes appropriate volume and quality cardiorespiratory, resistance, flexibility, and neuromotor exercise (Guo *et al*.,2022) [49].

The lower extremities have formed a whole kinematic chain, making it impossible for the hip, knee, or ankle joints to work entirely independently. Instead, they may affect each other. For example, hip abductor strengthening exercises can reduce pain and improve overall function in people with KOA. The balance of strength between the quadriceps and hamstrings is critical for reducing the risk of KOA. The latest research study also shows that the performance of the gastrocnemius and Achilles tendon is also altered in KOA patients

To improve joint mobility, stability and physical function, various exercise therapies such as strengthening, ROM and stretching exercises have been performed. A recent systematic review recommended specific muscles that should be stretched for optimal KOA care (Elgendy *et al*., 2002) [17]

Therapeutic exercise is recommended in numerous international guidelines as a nonpharmacologic treatment for knee osteoarthritis. Resistance exercise,defined as use the external resistance load (e.g. body weight, resistance bands, machines) to force skeletal muscles contract may be successful in normalizing muscle firing patterns and joint

biomechanics for knee osteoarthritis.8 Resistance exercise can be performed in a variety of ways, and numerous studies have shown that it can reduce pain, Resistance exercise is beneficial in terms of reducing pain, alleviating stiffness, and improving physical function in patients with knee osteoarthritis (Yanan *et al*., 2015) [47]

Conclusions

Application of Iontophoresis in conjunction with traditional treatment for patients with KOA was more effective in pain relief and improvement of knee joint ROM and functional ability than ultrasound in conjunction with traditional treatment and traditional treatment alone.

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