ORIGINAL ARTICLE

IJPHY

Glucosamine Sulphate Iontophoresis Versus Ultrasound on Functional Outcome in Subjects with Patellofemoral Osteoarthritis

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ABSTRACT

Background: Patellofemoral osteoarthritis (PFOA) is a progressive joint condition commonly affecting middle-aged and elderly individuals. Given the substantial physical and financial burden it imposes, evaluating the effectiveness of conservative treatment methods is crucial. This study aimed to compare the functional outcomes of glucosamine sulphate iontophoresis and therapeutic ultrasound in individuals diagnosed with PFOA.

Method: Thirty individuals diagnosed with knee osteoarthritis were randomly divided into two groups of fifteen participants each. Group A was treated with a combination of ultrasound therapy and strengthening exercises targeting the Vastus Medialis Oblique (VMO). In contrast, Group B received glucosamine sulphate iontophoresis alongside the same exercise protocol. Functional outcomes were measured using the WOMAC and 6-MWT over a 10-day intervention period.

Results: Group A showed a significant improvement in WOMAC scores from 42.89 to 29.22 ($p < 0.001$) and 6MWT scores from 15.26 to 20.14 ($p < 0.001$). In Group B, the WOMAC scores changed from 50.22 to 48.09 ($p < 0.001$), and 6MWT scores slightly improved from 16.93 to 17.23 ($p < 0.001$). Inter-group comparisons indicated that Group A exhibited statistically superior functional gains.

Conclusion: The combination of VMO exercise and ultrasound therapy proved to be more effective in improving functional outcomes in individuals with PFOA than the combination of VMO exercise and glucosamine sulphate iontophoresis.

Keywords: Patellofemoral osteoarthritis, glucosamine sulphate iontophoresis, ultrasound, Vastus Medialis Oblique exercise, WOMAC, 6-Minute Walk Test.

Received 18th April 2025, accepted 22nd July 2025, published 09th September 2025

www.ijphy.com

10.15621/ijphy/2025/v12i3/1864

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INTRODUCTION

Patellofemoral osteoarthritis (PFOA) refers to degenerative changes in the knee joint, specifically involving the articular cartilage of the femur, patella, and tibia. The condition often results from cartilage degradation between the patella and the trochlear groove, leading to anterior knee pain. This discomfort may be felt medially, anteriorly, or posteriorly.

Research suggests that knee osteoarthritis is prevalent in ageing populations, with its incidence highest among individuals in their 60s and 70s [1,2].

In India, osteoarthritis ranks as the second most prevalent rheumatologic disorder, affecting between 22% and 39% of the population [3]. Multiple factors contribute to the onset of arthritis, including mechanical wear and tear, autoimmune conditions like rheumatoid arthritis, infections, and post-traumatic damage.

Abnormal patellar mechanics often underlie PFOA, with conditions such as trochlear dysplasia observed in a significant percentage of isolated PFOA cases [4-6]. Factors such as patella alta, an increased Q-angle, weakened vastus medialis, and insufficient medial patellofemoral ligament function can contribute to joint degeneration. Other risk factors include joint instability, systemic inflammatory diseases, obesity, and genetic predispositions [7]. Clinically, patients often present with anterior knee pain [8], patellar crepitus during movement, peripatellar tenderness, and restricted patellar mobility. Positive findings on Clarke's test —pain elicited during knee extension with patellar compression —are common diagnostic indicators [9]. Medical management involves Pain Relievers, nonsteroidal anti-inflammatory drugs (NSAIDs), Acetaminophen (Tylenol), Disease-Modifying Antirheumatic Drugs (DMARDs), Corticosteroids, Hyaluronic Acid Therapy (Viscosupplementation), Antidepressants, and Gout Treatments [10].

Several studies have investigated the use of glucosamine sulphate iontophoresis in the management of osteoarthritis (OA). These studies suggest that glucosamine may be particularly effective in alleviating symptoms in patients with knee OA who have a lower body mass index (BMI), the presence of osteophytes, and reduced functional self-efficacy. Both chondroitin sulphate and glucosamine are commonly recommended as chondroprotective agents in such treatments. The standard daily dosage of glucosamine salts typically ranges from 340 mg to 1,500 mg; however, a significant portion is metabolised in the liver, resulting in limited amounts reaching the cartilage [11].

Surgical treatment options for osteoarthritis include arthroscopy, joint replacement (arthroplasty), joint fusion, and osteotomy, though these are typically considered in the advanced stages of the condition. Physiotherapy plays a crucial role in early management. It includes interventions such as a range of motion exercises, muscle strengthening, manual therapy, bracing, and electrotherapy techniques, including ultrasound, transcutaneous electrical nerve stimulation (TENS), and interferential therapy. Exercise is a key component in managing osteoarthritis, as it aids in pain reduction, enhances joint stability, reduces effusion, and improves blood circulation to joint tissues. Physical activity also stimulates the release of endogenous opioids, which help relieve pain and enhance muscle strength. In cases of knee osteoarthritis, patients often experience joint pain that limits movement, eventually leading to muscle wasting. The vastus medialis oblique (VMO) is typically the first muscle to undergo atrophy [12].

The vastus medialis is one of the four muscles that make up the quadriceps group located at the front of the thigh. A distinct portion of this muscle, known as the vastus medialis oblique (VMO), has fibers that run at a more oblique angle compared to the rest of the vastus medialis. This specific orientation makes the VMO particularly crucial in addressing patellofemoral (kneecap) issues.

The VMO plays a vital role in stabilizing the patella within its groove and ensuring proper alignment or "tracking" of the kneecap during knee flexion and extension. Weakness or improper activation of the VMO can result in poor patellar tracking, leading to damage to surrounding tissues and persistent pain. Addressing this issue requires both improving the timing of VMO activation and ensuring its strength is balanced with the rest of the quadriceps muscles [13].

A study was conducted to evaluate whether the vastus medialis oblique (VMO) muscle exhibits higher electrical activity than the vastus lateralis (VL) during exercises involving hip adduction and medial tibial rotation. Findings indicated that VMO showed significantly greater electromyographic activity than VL during hip adduction exercises, suggesting that these exercises can selectively activate the VMO, making them beneficial in rehabilitation [14].

In another study focused on osteoarthritis, patients received transcutaneous electrical stimulation for four weeks. Participants reported an approximate two-point reduction in pain on a scale from 0 (no pain) to 10 (severe pain) [15].

Further research examined the effects of phonophoresis using piroxicam compared to traditional ultrasound therapy in individuals with symptomatic knee osteoarthritis. The results demonstrated that phonophoresis was notably more effective in alleviating pain and showed a trend toward improved knee function [16].

To avoid the gastrointestinal side effects linked with oral administration, several topical formulations such as glucosamine sulphate creams have been developed. These topical agents also provide the added benefit of faster pain and inflammation relief.

Studies have shown that transdermal glucosamine delivery is more efficient than oral administration in delivering the compound to the synovial fluid, particularly when applied near the joint. Since articular cartilage lacks direct blood, nerve, or lymphatic supply, it relies entirely on synovial fluid to receive nutrients, such as glucose and glucosamine, from surrounding blood vessels. Notably, the concentration of glucosamine in the synovial fluid can

be significantly higher than in the bloodstream following topical application.

Ultrasound therapy contributes to soft tissue repair by reducing inflammation, increasing blood flow and metabolic activity, and alleviating pain. Animal studies also suggest that ultrasound may promote cartilage regeneration [17]. While glucosamine aids in cartilage repair, ultrasound facilitates its healing. This indicates a need to assess the combined therapeutic effects of glucosamine iontophoresis and ultrasound in patients with patellofemoral osteoarthritis.

Therefore, the primary objective of the study was to compare the effectiveness of glucosamine sulphate iontophoresis versus ultrasound therapy on functional outcomes in individuals with patellofemoral osteoarthritis.

METHOD

The study was conducted at Padmashree Physiotherapy Clinic, ESI Hospital, and Padmashree Diagnostics, Bangalore. Ethical approval was obtained from the Institutional Ethical Committee of Padmashree Institute of Physiotherapy in accordance with the Indian Council of Medical Research (ICMR) 2000 guidelines for biomedical research involving human subjects.

This was a pre-post interventional study involving 30 individuals diagnosed with patellofemoral osteoarthritis. Participants were aged between 18 and 55 years and included both males and females. Eligibility was confirmed through orthopedic clinical diagnosis, radiographic evidence of Grade 2 knee osteoarthritis, symptom duration of more than three months, and unilateral knee pain.

The exclusion criteria for the study included individuals with allergic reactions to transdermal medications, systemic conditions such as fever, cardiovascular or neurological diseases, other knee pathologies like tendinitis or bursitis, recent knee surgery or arthroscopy within the past three months, severe deformities that limited ambulation, intra-articular corticosteroid injection within the last six months, open wounds or ischemic conditions around the knee, and recent use of NSAIDs, corticosteroids, or glucosamine supplements within the previous six months. All participants provided informed consent before enrollment and were thoroughly briefed on the study protocol.

The materials used in this study comprised a direct current electrical stimulator (Electrostim DT), glucosamine sulphate cream (3 mL, 8% w/w), an ultrasound machine operating at 3 MHz, aquasonic gel, 70% alcohol solution for skin preparation, terry towels, water bowls, lint pads, and equipment required for Vastus Medialis Oblique (VMO) strengthening exercises.

Outcome measures included the WOMAC index, which was used to evaluate pain, stiffness, and functional limitations, and the 6-Minute Walk Test (6MWT), which assessed functional exercise capacity over time.

Participants were randomized into two equal groups. Group A (n = 15) received ultrasound therapy along with VMO exercises. Ultrasound treatment was applied to the most painful knee region in continuous mode at 1.5 W/cm² for eight minutes, five days per week, over two weeks. VMO exercises were initiated after the first week and included straight leg raises (SLR) with hip adduction, SLR with external hip rotation, and terminal knee extension performed over a towel roll. Group B (n = 15) received glucosamine sulphate iontophoresis combined with the same VMO exercise regimen. For iontophoresis, after cleaning the skin with 70% alcohol, glucosamine cream was applied under the positive electrode (active site), which was placed medially on the knee. In contrast, the negative electrode was positioned laterally. A direct current was delivered and gradually increased to the participant's pain threshold and maintained for 15 minutes. This procedure was carried out five days per week over two weeks, followed by the same VMO exercise protocol as Group A, initiated after the first five sessions.

Statistical analysis was performed using SPSS software (version unspecified), with a significance threshold set at $p < 0.05$. Descriptive statistics such as mean, standard deviation, and range were used to summarize demographic and outcome variables. The Chi-square test was applied to assess differences in gender distribution and knee dominance between groups, while independent t-tests compared group means for continuous variables such as age and baseline 6MWT scores. The Mann-Whitney U test was employed to compare non-parametric variables, including WOMAC scores, between groups. Within-group changes in 6MWT scores were analyzed using paired t-tests, and within-group changes in WOMAC scores were evaluated with the Wilcoxon signed-rank test.

RESULTS

Table 1 presents the baseline characteristics of the 30 participants across both groups. Chi-square test results showed no significant differences in gender distribution or knee dominance between the groups ($p > 0.05$), indicating similar demographic profiles. Additionally, the mean age of participants in Group A (45.06 ± 9.48 years) and Group B (46.00 ± 6.01 years) did not differ significantly, further confirming demographic homogeneity between the two groups.

Table 1: Baseline data

Variable	Group A	Group B	P- Value
Age	45.06± 9.48	46.00± 6.01	0.750
Gender (M/F)	9/6	8/7	0.720
Onset & Duration	6.93± 2.86	5.26± 1.83	0.680

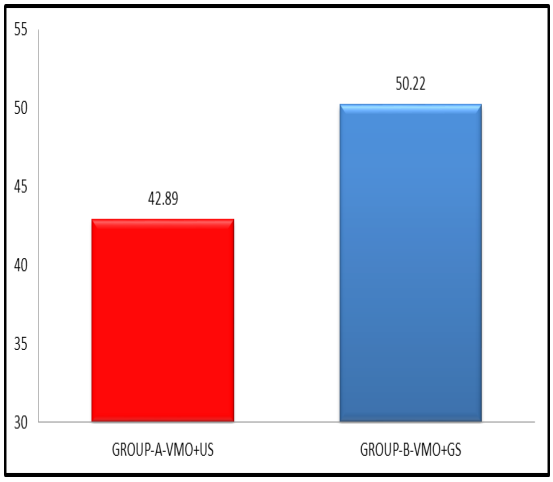
Within-Group Analysis

The Wilcoxon signed-rank test was employed to compare the pre- and post-treatment scores within each group. Group A showed significant improvement in both the WOMAC score and the 6MWT. The mean WOMAC score decreased from 42.89 ± 16.03 to 29.22 ± 9.78 ($p = 0.001$), and the 6MWT distance improved from 15.26 ± 2.05 to 20.14 ± 1.35 ($p< 0.001$). Group B also demonstrated statistically significant changes, although to a lesser extent.

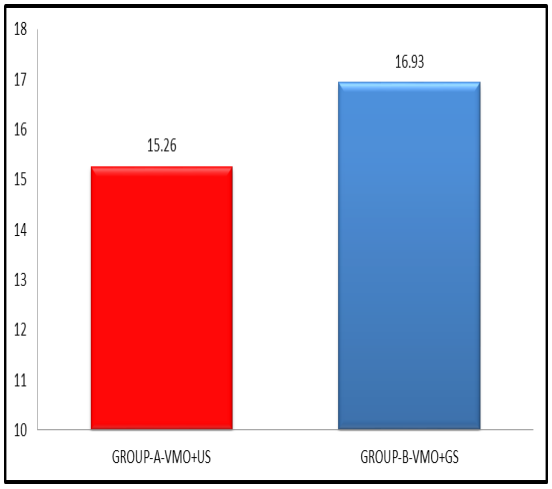
The mean WOMAC score declined from 50.22 ± 5.78 to 48.09 ± 4.57 (p = 0.015), while the 6MWT improved modestly from 16.93 ± 2.21 to 17.23 ± 2.20 (p = 0.436), which was not statistically significant.

Table 2: Pre- and post-difference within the group

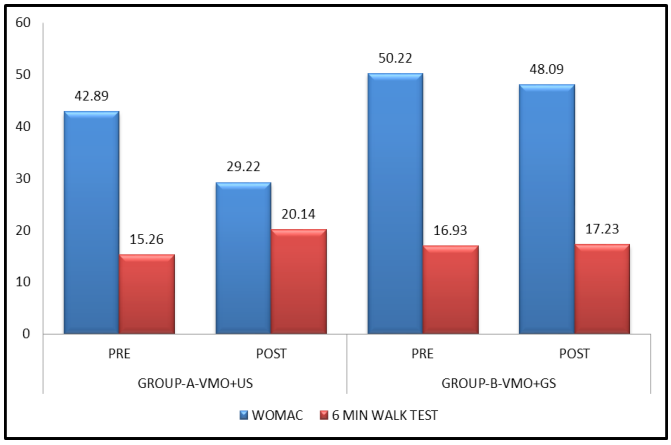
Variables	Group-A-VMO+US			Group-B-VMO+GS		
	Pre	Post	P-Value	Pre	Post	P-Value
WOMAC	42.89± 16.03	29.22± 9.78	0.001	50.22± 5.78	48.09± 4.57	0.015
6MWT	15.26± 2.05	20.14± 1.35	0.000	16.93± 2.21	17.23± 2.20	0.436



GRAPH 1- WOMAC



GRAPH 2- 6 MIN. WALK TEST



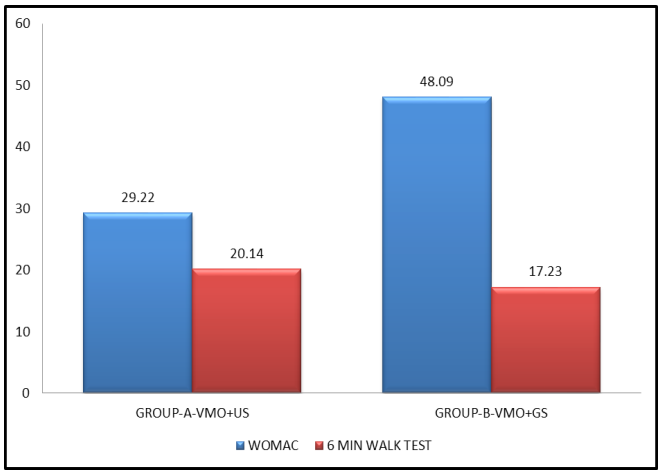
GRAPH 3-WOMAC and 6-minute walk test score for Pre-Post differences within Group

Between-Group Comparison

When post-treatment scores were compared between the two groups using the Mann-Whitney U test, statistically significant differences were observed: Group A had significantly lower post-intervention WOMAC scores compared to Group B (p< 0.0001). Similarly, the post-treatment 6MWT performance was significantly better in Group A than in Group B (p< 0.0001), indicating superior functional improvement in the group receiving ultrasound and VMO exercises.

Table 3: WOMAC and 6-minute walk test difference between the groups

VARIABLE	GROUP-A-VMO+US	GROUP-B-VMO+GS	P-Value
WOMAC	29.22±9.78	48.09±4.57	<0.0001
6 MIN WALK TEST	20.14±1.35	17.23±2.20	<0.0001



Graph 4: WOMAC and 6-minute walk test score difference between the groups

These findings support that ultrasound combined with VMO exercises significantly enhances functional outcomes in individuals with patellofemoral osteoarthritis compared to glucosamine sulphate iontophoresis combined with the same exercise protocol.

DISCUSSION

This study aimed to assess and compare the effectiveness of glucosamine sulphate iontophoresis versus ultrasound therapy on functional outcomes in individuals with patellofemoral osteoarthritis (PFOA).

The baseline demographic characteristics were comparable between the two groups. The average age in Group A was 45.06 years, while in Group B it was 46.00 years. Group A consisted of nine males and six females, whereas Group B comprised eight males and seven females. Symptom duration ranged from 3 to 12 months in Group A and from 3 to 9 months in Group B. Baseline values for the outcome variables were also similar across both groups.

Significant improvements were observed in the WOMAC pain sub-score and the 6-minute walk test in both groups. In Group A, the WOMAC score improved from 42.89 to 29.22, and the 6-minute walk test increased from 15.26 laps to 20.14. These improvements can be attributed to the therapeutic benefits of ultrasound, which is commonly

used in combination with exercise to manage chronic musculoskeletal conditions such as knee osteoarthritis [18]. Ultrasound therapy helps alleviate pain, enhances physical function, improves patient perception of disease severity, and promotes cartilage repair. It delivers deep heat to tissues, increasing temperature, circulation, and metabolic activity while reducing pain [19]. Additionally, non-thermal effects of ultrasound include stimulation of cellular activity, acceleration of the inflammatory process, and efficient removal of waste products [20].

The greater improvements in pain scores in Group A compared to Group B may be due to the combination of ultrasound and vastus medialis oblique (VMO) strengthening exercises. These exercises are believed to activate joint mechanoreceptors more effectively, potentially overriding pain signals.

Statistically, Group A showed a notable improvement in WOMAC scores (42.89 to 29.22) and the 6-minute walk test (15.26 to 20.14 laps). This supports previous studies indicating that exercise programs based on mechanical diagnosis yield better outcomes than passive treatment or waitlist control [21]. VMO-targeted exercises enhance joint proprioception, postural control, and quadriceps strength, all contributing to better physical function in OA patients.

Other research comparing VMO strengthening and orthotic use for patellofemoral pain concluded that increasing VMO strength produced more consistent reductions in joint loading than orthotic devices. Another study involving 60 knee OA patients found that strengthening exercises significantly improved their functional capacity [22].

Additionally, a study evaluating the preventive role of diet, exercise, and glucosamine sulphate in knee OA showed that glucosamine sulphate may help lower the risk of disease development [17]. Glucosamine has also demonstrated benefits in reducing symptoms, improving joint function, and modifying cartilage metabolism in patellofemoral OA.

The WOMAC index, widely recognized for its reliability and validity, was used to assess outcomes. A comparative clinical and biochemical study found that topical glucosamine/chondroitin sulphate provided more symptomatic relief (pain, stiffness, function) than oral administration, though it may not significantly restore cartilage.

Iontophoresis is known to deliver medications to depths of 5–20 mm (sometimes up to 1.7 cm), achieving higher local concentrations than oral routes, although still less than those achieved with injections. In the current study, Group B, which received glucosamine iontophoresis, showed modest improvements, as evidenced by a decrease in the WOMAC score (from 50.22 to 48.09) and an increase in the 6-minute walk test (from 16.93 to 17.23 laps). These limited gains reflect the ongoing debate about glucosamine's efficacy for managing PFOA. Although earlier studies support its benefits, a recent Cochrane review of high-quality trials concluded that glucosamine offers no significant advantage over placebo for pain relief [15].

However, evidence does suggest that transdermal glucosamine is more effective than oral forms in delivering the compound to synovial fluid, especially when applied near the joint. While animal studies show promising results for joint repair, more research is needed to confirm similar effects in humans.

The 6-minute walk test proved to be a reliable measure for assessing improvements in functional capacity following intervention. Participants in the ultrasound group showed significant increases in walking distance post-treatment. All treatment approaches in the study were effective to some extent in reducing pain and improving WOMAC scores [23].

In conclusion, the study found that the combination of ultrasound therapy and VMO-specific exercises was more effective in improving functional outcomes than glucosamine sulphate iontophoresis in patients with patellofemoral osteoarthritis.

CONCLUSION

The study compared two intervention combinations for individuals with patellofemoral osteoarthritis (PFOA). Participants who underwent vastus medialis oblique (VMO) strengthening exercises with ultrasound therapy showed significantly greater improvements in pain reduction, mobility, and overall knee function.

Ultrasound likely enhances local circulation and tissue healing, complementing the effects of targeted muscle strengthening. In contrast, VMO exercise with glucosamine sulphate iontophoresis showed lesser improvement, suggesting limited clinical impact of iontophoresis in this context. Thus, combining VMO training with ultrasound therapy may provide a superior evidence-based approach to managing PFOA.

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