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Comparing the effects of dextrose prolotherapy and extracorporeal shockwave therapy on dynamic balance in knee osteoarthritis patients

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ABSTRACT

Background: Osteoarthritis (OA) is an age-related degenerative disease affecting the subchondral tissue of articular and bone cartilage, leading to biomechanical changes that cause pain, stiffness, and balance impairment, which increases fall risk and its severe consequences, including fractures, joint dislocations, loss of independence, and even death. Dynamic balance function can be assessed using the four square step test (FSST), a recommended functional test for knee OA patients. Knee OA management continues to develop, introducing regenerative therapies such as dextrose prolotherapy and extracorporeal shock wave therapy (ESWT). Therefore, this study aims to analyze the effects of dextrose prolotherapy and ESWT on dynamic balance outcomes.

Methods: Twenty-one subjects with unilateral knee osteoarthritis (grade II-III) were randomly assigned to either the dextrose prolotherapy or ESWT therapy group. The dextrose prolotherapy group received three injections, with a 3-week interval between each. The ESWT group underwent six sessions of therapy spaced one week apart. FSST was assessed before and after the intervention.

Results: Significant improvements in dynamic balance function, as measured by the FSST ($p < 0.05$), were observed within each group when comparing pre-and post-intervention results. However, no significant difference ($p > 0.05$) was found in FSST outcomes between the two groups. No severe adverse effects were reported in patients from either group.

Conclusion: This study demonstrates a positive impact of dextrose prolotherapy and ESWT therapy on the dynamic balance function of patients with knee OA. Both interventions were equally effective in improving dynamic balance function.

Keywords: Osteoarthritis, Dextrose prolotherapy, ESWT, FSST, Rehabilitation.
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INTRODUCTION

Patients with knee osteoarthritis (OA) tend to have impaired balance.[1] This reduced balance function is associated with an increased risk of falls, leading to consequences such as fractures, joint dislocations, soft tissue injuries, loss of independence, and even death.[2] Patients with knee OA have significantly poorer dynamic balance than healthy individuals, leading to a higher risk of falls, with over 50% reporting at least one fall in the past year. The underlying mechanisms of falls in individuals with knee OA are still unclear despite the increased incidence of falls.[3]

Balance is a complex function that requires the integration of sensory information regarding body position and the ability to make appropriate motor responses to body movements. It depends on sensory input from the somatosensory system (proprioception), the visual and vestibular systems, and muscle responses. Loss of balance and falls most often occur during activities such as walking and are less common during static activities. Patients with knee OA experience proprioceptive disturbances, which can affect postural stability and the risk of falling. Postural stability can be defined as the control over body position related to orientation and balance goals. It is important for patients to maintain postural stability (static and dynamic balance) during daily activities and ambulation.[4]

Currently, the management of knee OA includes surgical and non-surgical therapies such as intra-articular injections, medications, and physical exercises. Despite ongoing challenges in repairing and restoring joint structural damage, finding an ideal management approach that alleviates pain, enhances function, and slows disease progression remains clinically crucial.[5] Regenerative therapies, including dextrose prolotherapy and Extracorporeal Shock Wave Therapy (ESWT), are proposed for OA due to their ability to aid tissue regeneration, improve clinical manifestations, and repair damaged tissue structures.[6] ESWT uses transient single-impulse acoustic waves induced by pneumatic, electrohydraulic, electromagnetic, or piezoelectric generators focused on the treated area.[7] ESWT has shown effects on the development of articular cartilage and subchondral bone, neovascularization,

tissue regeneration, and inflammatory responses in several animal studies.[8] ESWT significantly improves the physical function and mobility of knee OA patients, showing superior effectiveness compared to ultrasound treatment.[9,10] When administered weekly, ESWT substantially reduces pain and enhances functional outcomes, including mobility and daily activities.[10] Recent studies have given Increasing attention to the use of ESWT for knee OA due to its non-invasive nature, low complication rates, and lower costs compared to surgical or other conservative management.[11]

Prolotherapy is a non-surgical regenerative injection technique in which a small amount of irritant solution is applied to painful areas and attachments of tendons, joints, ligaments, and degenerative joint spaces over several therapy sessions to encourage the growth of normal cells and tissue.[12] The most used prolotherapy agent is dextrose, with concentrations ranging from 12.5% to 25%. The mechanism of action of prolotherapy is still not fully understood. Current theories suggest that the injected proliferant mimics the body's natural healing process by initiating a local inflammatory cascade. This occurs when induced cytokines become mediators of chemo modulation, leading to the proliferation and strengthening of new connective tissue, improvement of joint stability, and reduced dysfunction and pain.[13,14] Dextrose prolotherapy can be administered at intervals of at least 3 weeks. Pain and isometric strength improvements can be seen after the first therapy session, although most patients do not feel the effects until after the second therapy session.[15]

There has been no research analyzing the effects of these two therapies on the balance of patients with knee OA, nor which therapy is superior. Thus, this research aims to analyze and compare the effectiveness of dextrose prolotherapy and ESWT therapy on the dynamic balance of patients with knee OA.

METHODS

The research method employed in this study was a prospective comparative study conducted at the Rehabilitation Outpatient Clinic of Dr. Soetomo General Academic Hospital. The study period spanned from December 2023 to October 2024. The subjects were knee osteoarthritis (OA) patients who visited the clinic from April to September 2024. The sample size was determined using a statistical formula that considered combined variance, significance level, and research power. Eligible participants were randomly allocated to either the dextrose prolotherapy group or the extracorporeal shock wave therapy (ESWT) group. Randomization was performed using sealed envelopes that were opened sequentially as participants were enrolled. Sampling was conducted through consecutive sampling.

Inclusion criteria included patients with unilateral knee OA graded as Kellgren-Lawrence (KL) grade II-III knee OA confirmed from radiological examination. Patients must be 40-59 years old, have undergone a standard rehabilitation program for one month, can walk independently, and be willing to participate in the study by signing a consent form. Meanwhile, exclusion criteria included various medical conditions such as a body mass index (BMI) $\geq$ 35 kg/m^2, a history of knee injection therapy in the past year, having undergone ESWT therapy before, acute arthritis, rupture of knee tendons and ligaments, malignancy, clotting disorders, pregnant woman, history of trauma to the lower limbs, deformities and restricted range of motion in the lower limbs, autoimmune diseases, uncontrolled type 2 diabetes mellitus, and neuromuscular diseases that could affect the study results. The independent variables in this study were dextrose prolotherapy and ESWT therapy, while the dependent variable was the dynamic balance function measured using the Four Square Step Test (FSST). Confounding variables considered were age, gender, BMI, and comorbidities such as diabetes mellitus and hypertension.

The instruments used in this study include Richard Wolf's focused-ESWT Piezo Shockwave device and ultrasound equipment for additional examination. The dextrose prolotherapy group underwent a treatment regimen of three injections spaced three weeks apart.[16] The dextrose concentration for intra-articular injections was 25% (4 ml), while for extra-articular injections was 15% (1 ml). The extra-articular injections were administered to the medial collateral ligament, lateral collateral ligament, pes anserine attachment, tibial tuberosity, coronary ligaments, and patellar tendon. The injections were guided by ultrasonography (USG) and administered by a physiatrist board-certified in Interventional Pain Management. The ESWT group received six therapy sessions, each one week apart[17], using focused-ESWT with energy settings of F10/G4, an intensity of 0.27 mJ/mm^2, a frequency of 4 Hz, and a total of 2000 shocks per session. Both groups were educated on knee joint conservation for daily activities. Dynamic balance function measurements were conducted using the FSST, which measures the time to step quickly in four directions. Data analysis was performed using SPSS software version 27.0. Statistical tests were used for descriptive analysis of subject characteristics, normality tests to determine data distribution, comparative tests to compare the dependent variable before and after treatment, and the two groups. The change in scores for each group was calculated using a paired T-test. The independent two-sample T-test was used to analyze the difference between the two treatment groups. Statistical significance is defined as $p < 0.05$.

The ethical feasibility of this research has been approved by the Health Research Ethics Committee of Dr. Soetomo General Academic Hospital with number 0964/KEPK/IV/2024. Each subject was asked to sign a written informed consent form after receiving an explanation regarding the purpose, procedures, and potential risks that may occur during the study.

RESULTS

Table 1 shows the characteristics of the study subjects; patients with OA in this study were predominantly female, with eight individuals (88.9%) in the dextrose prolotherapy group and 11 individuals (91.7%) in the ESWT therapy group. The age range of OA patients in this study was between 41 and 59 years, with an average age of 52.33 ± 3.841 years in the dextrose prolotherapy group and 53.92 ± 4.870 years in the ESWT therapy group.

Table 1. Characteristics of study subjects

Variable	Dextrose Prolotherapy Group (n=9) Mean ± SD or n (%)	ESWT Therapy Group (n=12) Mean ± SD or n (%)	*P-value*
Gender			
Male	1 (11.1%)	1 (8.3%)	1.0
Female	8 (88.9%)	11 (91.7%)	
Age (years)	52.33 ± 3.841	53.92 ± 4.870	0.431
Weight (kg)	72.78 ± 13.479	67.58 ± 13.049	0.384
Height (cm)	157.22 ± 6.760	154.83 ± 7.602	0.465
BMI (kg/m^2)			
Underweight	0 (0%)	0 (0%)	0.405
Normal	0 (0%)	2 (16.7%)	
Overweight	2 (22.2%)	1 (8.3%)	
Obese grade 1	3 (33.3%)	6 (50%)	
Obese grade 2	4 (44.4%)	3 (25%)	
Side of osteoarthritis			
Right	3 (33.3%)	4 (33.3%)	1.0
Left	6 (66.7%)	8 (66.7%)	
Grade osteoarthritis			
Grade 2	5 (55.6%)	11 (91.7%)	0.941
Grade 3	4 (44.4%)	1 (8.3%)	
Osteoarthritis onset (months)	15.44 ± 6.425	16.83 ± 11.777	0.941
Initial VAS	5.11 ± 0.601	4.92 ± 0.289	0.324

Cm; centimeter; ESWT, extracorporeal shock wave therapy; kg, kilogram; m^2, meter square;

Table 2. Differences in FSST results before and after intervention in the dextrose prolotherapy group

Group	Mean ± SD	Difference FSST	*P*-value
Dextrose Prolotherapy		-2.25 ± 1.552	0.002
Before Intervention	10.75 ± 1.726		
After Intervention	8.50 ± 1.227		

ESWT, extracorporeal shock wave therapy

Table 3. differences in first results before and after intervention in the eswt therapy group

Group	Mean ± SD (seconds)	Δ FSST (seconds)	*P*-value
ESWT Therapy		-1.52 ± 0.876	<0.001
Before Intervention	10.67 ± 1.875		
After Intervention	9.15 ± 1.198		

ESWT, extracorporeal shock wave therapy.

The average body weight in the dextrose prolotherapy group was 72.78 ± 13.479 kg, while in the ESWT therapy group, it was 67.58 ± 13.049 kg. The average height in the dextrose prolotherapy group was 157.22 ± 6.760 cm, and in the ESWT therapy group, it was 154.83 ± 7.602 cm.

Subjects in the dextrose prolotherapy group had a body mass index (BMI) categorized as overweight for two individuals (22.2%), obese grade 1 for three individuals (33.3%), and obese grade 2 for four individuals (44.4%). In the ESWT therapy group, there were two individuals (16.7%) with a normal BMI, one individual (8.3%) who was overweight, six individuals (50%) with obese grade 1, and 3 individuals (25%) with obese grade 2. Knee OA pain in the dextrose prolotherapy and ESWT groups was predominantly felt on the left side, with six individuals (66.7%) and eight individuals (66.7%), respectively. The grade of knee OA in the dextrose prolotherapy and ESWT groups was predominantly grade 2, with five individuals (55.6%) and 11 individuals (91.7%), respectively. The average onset of knee OA in the dextrose prolotherapy group was 15.44 ± 6.425 months, while in the ESWT therapy group, it was 16.83 ± 11.777 months. The average initial Visual Analog Scale (VAS) score in the dextrose prolotherapy group was 5.11 ± 0.601; in the ESWT group, it was 4.92 ± 0.289.

According to the data in Table 2, there was a decrease in the meantime achievement in the dynamic balance function test assessed by FSST in the dextrose prolotherapy group, from 10.75 ± 1.726 seconds before the intervention to 8.50 ± 1.227 seconds after the intervention. After further analysis using the paired T-test comparing FSST results from the two different time points, it was determined based on the p-value that there was a significant difference between the dynamic balance function test results of subjects before and after the intervention in the dextrose prolotherapy group ($p < 0.05$). Based on the data in Table 3, it can be observed that there was a decrease in the meantime achievement in the dynamic balance function test assessed by the Four Square Step Test (FSST) in the ESWT group, from 10.67 ± 1.875 seconds before the intervention to 9.15 ± 1.198 seconds

Table 4. Comparison of difference of FSST between groups

Group	FSST Before Intervention (seconds)	FSST After Intervention (seconds)	Δ FSST (seconds)	P-value
Dextrose Prolotherapy	10.75 ± 1.726	8.50 ± 1.227	-2.25 ± 1.552	0.189
ESWT Therapy	10.67 ± 1.875	9.15 ± 1.198	-1.52 ± 0.876	

FFST, our square step test; ESWT, extracorporeal shock wave therapy.

after the intervention. After further analysis using the paired T-test to compare the FSST results from the two different time points, it was determined based on the p-value that there was a significant difference between the dynamic balance function test results of subjects before and after the intervention in the ESWT group ($p < 0.05$).

The comparison of changes in dynamic balance function test results, measured by the FSST, between the dextrose prolotherapy group and the ESWT group was analyzed using an independent two-sample T-test. The analysis showed no statistically significant difference between the two groups with the interventions given ($p > 0.05$). However, there was a more significant change in the dextrose prolotherapy group, with a mean change of -2.25 ± 1.552 seconds, compared to the ESWT group, which had a mean change of -1.52 ± 0.876 seconds.

Two participants in the dextrose prolotherapy group experienced pain at the injection site during the first two days following the intervention. The pain was alleviated within 1-2 hours after receiving 500 mg of paracetamol. No additional side effects or adverse events were reported. Likewise, no side effects or adverse events were noted in the ESWT therapy group.

DISCUSSION

The characteristics of the subjects in this study align with established theories regarding risk factors for knee osteoarthritis (OA), where females are more frequently affected than males, particularly in older age and in cases of obesity. Most subjects in both groups were female, with 19 out of 21 participants. The average age of subjects in the dextrose prolotherapy group was 52.33 ± 3.841 years, while in the ESWT therapy group, it was 53.92 ± 4.870 years. These findings are consistent with previous studies, which indicate that being female is a significant risk factor for knee OA, with a higher incidence in females compared to males, both under and over 55 years of age.[18] Middle-aged women (ages 40-60) also have a high prevalence of moderate to severe knee OA.[19]

In this study, excess body weight (ranging from overweight to grade II obesity) was predominant, with 19 out of 21 subjects experiencing this condition. The distribution included three individuals classified as overweight, nine as grade I obese, and seven as grade II obese. This prevalence correlates with a significantly increased risk of developing knee OA, approximately 2.45 times higher in overweight individuals and about 4.55 times higher in those who are obese.[20] Obesity not only increases the mechanical load on weight-bearing joints such as the knees, but also contributes to systemic inflammation and metabolic changes that exacerbate the progression of OA.[21]

Knee OA can significantly alter balance control mechanisms through joint instability, quadriceps weakness, and altered proprioception. Joint instability arises from weakened ligaments and cartilage degradation, leading to uneven weight distribution and increased joint pressure. Quadriceps weakness further exacerbates instability, as the quadriceps muscle is crucial for knee joint support and movement control. Altered proprioception, due to damaged joint receptors, impairs the body's ability to sense joint position and movement, resulting in poorer balance and increased risk of falls. These factors collectively contribute to impaired FSST performance in individuals with knee OA.[22]

The average pain scale (VAS) before the intervention in the dextrose prolotherapy group was 5.11 ± 0.601; in the ESWT therapy group, it was 4.92 ± 0.289. These findings are not far off from the previous research, which found that the average VAS in knee OA with the same grades (grades 2-3) was 5.57 ± 1.19.[23] he higher initial VAS in the dextrose prolotherapy group may be due to more severe symptoms in patients who tend to choose more invasive interventions for faster symptom relief.[24]

Prolotherapy effectively enhances tissue healing at the injection site, targeting articular cartilage, tendons, and ligaments around the knee joint. Among various injection materials, dextrose is the most commonly used due to its ability to create a mild inflammatory response. This response leads to cytokine release, increases growth factor activity, and induces the proliferation of healing cells.[25] A systematic review found hypertonic dextrose to be more effective in reducing pain and improving tissue function than other proliferants.[26] Dextrose prolotherapy, compared to corticosteroids, offers superior and longer-lasting pain reduction for knee OA patients, with benefits extending beyond three months. Its advantages include low cost and easy availability.[27]

In this study, dextrose prolotherapy was administered in three sessions at three-week intervals, consistent with previous research. Concentrations typically range from 10% to 25%, as concentrations above 10% can trigger the necessary inflammatory response for regeneration. This approach results in significant improvements in pain, stiffness, functional status, and quality of life in knee OA patients.[16] While generally safe, minor side effects like pain and mild bleeding may occur but usually resolve on their own. Post-injection pain can be managed with paracetamol.[28] The significant improvement in FSST observed in the dextrose group is attributed to mechanisms like local inflammation stimulating fibroblast proliferation and collagen synthesis, which strengthen ligaments and tendons, enhancing joint stability and balance. Both prolotherapy and ESWT improve balance through pain reduction, neuromuscular improvements, and proprioceptive enhancement, with dextrose prolotherapy specifically

strengthening joint structures crucial for maintaining balance.[29]

Dextrose prolotherapy also reduces pain by inhibiting the vanilloid receptor type 1, reducing pain and inflammation, and has a neurotrophic effect on growth factors that contribute to nerve repair. A previous case showed immediate pain improvement following serial dextrose prolotherapy. Reducing pain allows patients to move more freely, thereby maintaining better balance.[29]

Significant improvement in FSST in the ESWT group also occurs through various mechanisms, including analgesic effects. ESWT works by reducing CGRP in the dorsal root ganglion (DRG) and decreasing substance P in the target tissue and DRG. The reduction of these two neuropeptides affects unmyelinated sensory fibers. Another mechanism is improving muscle strength and reducing inflammation and regenerative processes in articular cartilage through the secretion of growth factors that repair damaged tissue.[30] The duration and dosage of ESWT in this study align with several previous studies suggesting effective variations of ESWT administration between 3-8 weeks, with 1-2 therapy sessions each week.[31]

The results indicate a more significant change in dynamic balance function in the dextrose prolotherapy group, with −2.25 ± 1.552 seconds, compared to the ESWT therapy group, which had −1.52 ± 0.876 seconds. Although the average FSST results after intervention in the dextrose prolotherapy group were relatively better at 8.50 seconds compared to 9.15 seconds in the ESWT therapy group, there was no statistically significant difference in dynamic balance function between the two groups. This study is the first to investigate differences in dynamic balance function outcomes between dextrose prolotherapy and ESWT therapy in knee OA patients.[32]

The more significant improvements in dynamic balance, with 4 out of 9 subjects experiencing FSST improvements of over 3 seconds. This contrasts with the ESWT group, where no significant changes were observed. The variation within the dextrose group ranged from minimal improvements (-0.54 and -0.18 seconds) to substantial gains (-4.73 and -3.94 seconds). Factors such as OA grade, BMI, and baseline FSST times influenced these outcomes.[33] Higher OA grades and elevated BMI were associated with poorer balance, while those with OA grades 1-2 benefited from significant pain relief and better balance stability.[22]

Although the improvements in FSST performance are statistically significant, their clinical relevance warrants further evaluation. Established FSST cut-off values for fall risk reduction in knee OA patients suggest that improvements of 3 seconds or more are clinically meaningful, potentially reducing fall risk. In this study, 4 out of 9 subjects in the dextrose prolotherapy group achieved such improvements, indicating a potentially meaningful impact on fall risk. Variability in treatment response may be attributed to factors such as baseline functional status, OA severity, and individual differences in pain perception and treatment response. Subjects with less severe OA or superior baseline function may achieve greater improvements due to a higher capacity for rehabilitation and adaptation. Regarding the durability of these effects, previous research suggests that the benefits of dextrose prolotherapy may persist beyond 3 months, particularly in terms of pain reduction. Similarly, ESWT has demonstrated lasting benefits in muscle strength and pain reduction in other studies. However, further research is needed to confirm the long-term sustainability of these interventions specifically for dynamic balance improvement in knee OA patients.[34,35]

This study has several limitations, including the difficulty in assessing the intensity of physical activity and nutrition during the follow-up period (7-8 weeks), as these factors may have varied among participants. Nevertheless, this study demonstrates that both interventions can positively affect the dynamic balance function of patients with knee osteoarthritis and can be recommended due to their safety and lack of serious side effects.

CONCLUSION

This study concluded that dynamic balance function in knee OA patients improved following both dextrose prolotherapy and ESWT interventions. Both treatments were equally effective in enhancing dynamic balance function, with dextrose prolotherapy showing a tendency for greater improvement.

ETHICAL CONSIDERATION

This study received approval from the Health Research Ethics Commission for basic/clinical research at Dr. Soetomo General Hospital, Surabaya, under registration number 0964/KEPK/IV/2024. Informed agreement from the respondents to the survey was also provided, which approved the use of sampling.

CONFLICT OF INTEREST

This study has no conflicts of interest.

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AUTHOR CONTRIBUTIONS

FAR prepared study designs, collected data, analyzed data, and wrote manuscripts. NIH, YDP, LA, AJAH and A directed data collection and revised the manuscript.

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