



Short-Term Evaluation of Hypertonic Dextrose Prolotherapy Intra-Articular Injection on Femoral Cartilage Thickness Among Knee Osteoarthritis Patients with Obesity

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ABSTRACT

Introduction: Obesity significantly contributes to higher morbidity rates and increases the risk of knee osteoarthritis (KOA).

Objective: This study evaluated the short-term effect of intra-articular hypertonic dextrose prolotherapy (HDP) injections on femoral cartilage (FC) thickness in obese patients with KOA.

Methods: This quasi-experimental clinical trial included KOA patients with obesity. The intervention group received HDP injections, while the control group received normal saline (NS) injections. FC thickness was measured using musculoskeletal ultrasound (US) before the intervention, 2 weeks, and 6 weeks after the intervention. Mean differences within and between groups were analyzed, with significance at $P < 0.05$.

Results: A total of 38 participants diagnosed with KOA and obesity were included. In the HDP group, FC thickness increased from pre-intervention to 6 weeks post-intervention: in the medial condyle (MC) from 1.33 ± 0.61 mm to 1.48 ± 0.56 mm, in the intercondylar (IC) region from 1.38 ± 0.65 mm to 1.57 ± 0.61 mm, and in the lateral condyle (LC) from 1.57 ± 0.70 mm to 1.78 ± 0.66 mm. Repeated measures of ANOVA revealed significant improvements in FC thickness at all sites (MC, IC, and LC) in the HDP group ($P < 0.05$). No significant changes in FC thickness were observed in the NS group.

Conclusions: HDP injections have a beneficial short-term effect on increasing FC thickness in obese patients with KOA.

Introduction

Obesity is a significant public health issue worldwide, including in Indonesia, where its prevalence continues to rise. Data from the Indonesian Family Life Survey

(IFLS) from 1993 to 2014 showed an increase in the prevalence of overweight and obesity among adults from 17.1% to 33.0%. The study concluded that one-third of Indonesians were overweight in 2014.

The 2018 Indonesian Basic Health Survey revealed a rise in obesity prevalence, with a body mass index (BMI) over 27 kg/m², increasing from 10.5% in 2007 to 21.8% in 2018. Obesity has a significant impact on morbidity and mortality rates, increasing the risk of conditions such as diabetes mellitus, hypertension, stroke, coronary heart disease, dyslipidemia, and knee osteoarthritis (KOA) (Ayuningtyas et al., 2022; Azam et al., 2023; Oddo et al., 2019; Rachmi et al., 2017; Tham et al., 2023).

Obesity is linked to adverse effects on cartilage thickness and joint loading. Evaluating femoral cartilage (FC) thickness using ultrasound (US) scanning may be useful in assessing FC in obese patients at high risk for KOA onset and progression. Obese patients have higher FC echo intensity compared to non-obese individuals, and a high body fat percentage is associated with increased cartilage echo intensity (Pamukoff et al., 2020).

Previous studies have demonstrated that the correlation between joint loads and femoral cartilage (FC) thickness is influenced by body mass index (BMI). Reduced cartilage thickness is associated with both obesity and aging (Blazek et al., 2014). In Indonesia, studies have evaluated FC thickness in patients with knee osteoarthritis (KOA) compared to those without KOA. The KOA group showed thinner FC than the non-KOA group. A

significant difference was observed in medial condyle (MC) thickness on both sides, though no significant difference was found in the intercondylar (IC) or lateral condyle (LC) (Pane et al., 2023). Interestingly, the mean MC thickness was significantly higher in the KOA group compared to the non-KOA group. Another study using a quantitative tridimensional approach showed that the posterior MC was considerably thicker in KOA patients (Omoumi et al., 2018).

Current KOA management generally includes non-steroidal anti-inflammatory drugs (NSAIDs) and physical rehabilitation therapy. However, many patients report recurrent knee pain once the drug effects wear off. Intra-articular injection is an alternative method for KOA management. High-density platelet (HDP) therapy has been proposed as an alternative therapy that may aid tissue regeneration, improve clinical symptoms, and restore damaged tissue structures—pathological issues associated with KOA. A systematic review of 12 studies showed that HDP was more effective in improving functional outcomes compared to other treatments (Waluyo et al., 2023). Although the mechanism of HDP in reducing KOA pain is not fully understood, recent studies suggest a rapid and medium-term analgesic effect after intra-articular HDP injection, accompanied by beneficial changes in synovial fluid

neuro cytokines such as substance P (SP) and neuropeptide Y (NPY) (Topol et al., 2022). The objective of this study was to evaluate the short-term effect of intra-articular HDP injection on FC thickness in obese patients with KOA.

Methods

This quasi-experimental clinical trial evaluated femoral cartilage (FC) thickness using musculoskeletal ultrasound (US) measurements. Participants were KOA patients with obesity, recruited from the Department of Physical Medicine and Rehabilitation (PM&R) at Hajj Regional General Hospital of East Java Province (RSUD Haji Provinsi Jawa Timur), Surabaya, Indonesia. These patients received treatment at the outpatient clinic between May and August 2023.

Inclusion and exclusion criteria

The inclusion criteria were KOA patients with obesity, diagnosed based on clinical and radiological assessments, including grades I-IV of the Kellgren-Lawrence criteria. Grade I shows possible osteophytes and questionable joint space narrowing. Grade II shows definite osteophytes and joint space narrowing. Grade III presents multiple moderate osteophytes, definite joint space narrowing, and possible bone contour deformity. Grade IV shows large osteophytes, definite

joint space narrowing, and bone contour deformity. Obesity was defined using the World Health Organization (WHO) Asia-Pacific standards: underweight ($<18.5 \text{ kg/m}^2$), normal ($18.5 - 22.9 \text{ kg/m}^2$), overweight ($23 - 24.9 \text{ kg/m}^2$), and obese ($\geq 25 \text{ kg/m}^2$). Patients with a history of knee surgery, knee injury, or prior knee intra-articular injection were excluded. Eligible participants were allocated into two groups: the intervention group and the control group.

Intervention

The intervention group received high-density platelet (HDP) injections, while the control group received normal saline (NS) injections. The intervention group was given an intra-articular injection of 25% dextrose (4 ml) at the first visit (week 0) and the second visit (week 2). The control group received a single injection of normal saline and 1% lidocaine, with the volume adjusted for each patient, at the first visit (week 0). Injections for both groups were administered under musculoskeletal US guidance.

Measurements

Basic data such as age, gender, weight, height, BMI, and Kellgren-Lawrence stage were recorded at the initial appointment. The primary outcome was FC thickness, measured three times: before the

intervention, 2 weeks after the intervention, and 6 weeks after the intervention. FC thickness was measured in millimeters using the musculoskeletal US on the knee diagnosed with KOA. Measurements were taken at three sites: the medial condyle (MC), intercondylar (IC) region, and lateral condyle (LC). A Canon Xario 100, a 2D musculoskeletal US device with a 7.2-14 MHz linear transducer (type 18L7; Canon Medical Systems USA, Inc., Tustin, Calif, USA), was used. The evaluation was performed by a certified physiatrist with over five years of experience in musculoskeletal US scanning.

Data analysis

Age, gender, BMI, Kellgren-Lawrence grade, KOA side, and pre-intervention FC thickness were analyzed descriptively, with data presented as mean \pm SD or number (%). Initially, the normality of the primary data, FC thickness, was tested. As the data were normally distributed, a parametric test was used. Between-group analysis was performed using the Mann-Whitney test to compare the mean difference between the two groups, while within-group analysis was conducted using repeated measures analysis of variance (ANOVA) to assess changes in mean FC thickness from pre-intervention to week 6 in each group. A significance level of $p < 0.05$ was considered statistically significant. Data

were collected using Microsoft Excel 365 (Microsoft Corp., Redmond, Washington, USA), and data analysis was performed using IBM SPSS Statistics version 26.0 for Mac (IBM Corp., Armonk, NY, USA).

Results and Discussion

This study involved a total of 38 participants diagnosed with both KOA and obesity, as shown in Figure 1. The average age of participants in the NS and HDP groups was 62.5 ± 7.78 years and 62.4 ± 8.88 years, respectively, with a predominance of females in both groups. The mean BMI in the NS group was higher compared to the HDP group, while the mean Kellgren-Lawrence grade was higher in the HDP group than in the NS group (Table 1). Before the intervention, the FC thickness at the lateral condyle (LC), intercondylar (IC) region, and medial condyle (MC) were 1.47 ± 0.45 mm, 1.23 ± 0.47 mm, and 1.33 ± 0.49 mm, respectively, in the NS group. In the HDP group, the thickness was 1.57 ± 0.70 mm, 1.38 ± 0.65 mm, and 1.33 ± 0.61 mm at the same locations.

Statistical analysis using the Mann-Whitney test showed no significant differences between the two groups ($P > 0.05$) (Table 2). However, within-group analysis using repeated measures ANOVA from pre-intervention to 6 weeks post-intervention revealed significant

improvements in FC thickness at all sites (LC, IC, and MC) in the HDP group ($P < 0.05$), but no significant changes were observed in the NS group ($P > 0.05$) (Table 3).

Before the intervention, the NS group had thinner FC at the LC and IC sites compared to the HDP group, while the average thickness at the MC site was similar. Among the three sites observed, the MC was the thinnest. This finding supports our earlier study, which evaluated 254 adult knees in non-OA individuals from Indonesia, showing average cartilage thicknesses of 1.76 mm in the MC, 1.89–1.92 mm in the IC, and 1.69–1.71 mm in the LC (Pane et al., 2022). Other studies also suggest that the MC is more affected by weight-bearing, with structural damage such as thinning and cartilage defects occurring in obese individuals due to

increased pressure (Lacy et al., 2016). Increased knee flexion during the early ambulation phase, coupled with the heavier load on the medial condyle, is observed in obese patients. A cadaveric study found that weight-bearing in individuals with a $BMI \geq 30$ increased stress, contributing to MC defects (Chen et al., 2020). Obesity is also known to exacerbate KOA in patients with varus malalignment, though this effect is less pronounced in those with valgus malalignment, as genu valgus helps protect the medial condyle.

In contrast, varus malalignment combined with obesity tends to accelerate disease progression, particularly in the medial tibiofemoral joint, suggesting that correcting malalignment may be a therapeutic target in obesity-related KOA (Rogers et al., 2021).

Table 1. General data

Variables	HDP group (20)	NS group (18)
Age (years)	62.4 ± 8.88	62.5 ± 7.78
Sex (female)	19 (95.0%)	15 (83.3%)
BMI (kg/m ²)	28.66 ± 4.52	30.62 ± 3.87
Kallgren-Lawrence Grade	3.05 ± 0.60	2.77 ± 0.65
KOA Side		
Right	7 (35.0%)	5 (27.7%)
Left	13 (65.0%)	13 (72.3%)
FC Thickness (mm) ^a		
Medial Condyle	1.33 ± 0.61	1.33 ± 0.49
Intercondylar	1.38 ± 0.65	1.23 ± 0.47

Lateral Condyle	1.57 ± 0.70	1.47 ± 0.45
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Note: Data are presented as mean ± SD or number of participants.

^aFemoral Cartilage Thickness before intervention

Abbreviations: HDP = hypertonic dextrose prolotherapy; NS = normal saline; BMI = body mass index; KOA = knee osteoarthritis; FC = femoral cartilage.

Table 2. Between-group analysis of FC thickness.

Variable	HDP group	NS group	P-value ^a
Medial Condyle (mm)			
Pre-intervention	1.33 ± 0.61	1.33 ± 0.49	0.961
Week-2	1.39 ± 0.54	1.35 ± 0.46	0.809
Week-6	1.48 ± 0.56	1.34 ± 0.46	0.428
Intercondylar (mm)			
Pre-intervention	1.38 ± 0.65	1.23 ± 0.47	0.421
Week-2	1.45 ± 0.61	1.18 ± 0.48	0.144
Week-6	1.57 ± 0.61	1.22 ± 0.49	0.067
Lateral Condyle (mm)			
Pre-intervention	1.57 ± 0.70	1.47 ± 0.45	0.620
Week-2	1.66 ± 0.67	1.44 ± 0.47	0.258
Week-6	1.78 ± 0.66	1.45 ± 0.46	0.094

Note: Data are presented as mean ± SD.

^aSignificant value was considered P < 0.05

Abbreviations: HDP = hypertonic dextrose prolotherapy; NS = normal saline.

Table 3. Within group analysis of FC thickness.

Variable	Pre-intervention	Week-2	Week-6	P-value ^a
Medial Condyle (mm)				
HDP group	1.33 ± 0.61	1.39 ± 0.54	1.48 ± 0.56	0.015
NS group	1.33 ± 0.49	1.35 ± 0.46	1.34 ± 0.46	0.883
Intercondylar (mm)				
HDP group	1.38 ± 0.65	1.45 ± 0.61	1.57 ± 0.61	0.000
NS group	1.23 ± 0.47	1.18 ± 0.48	1.22 ± 0.49	0.233
Lateral Condyle (mm)				
HDP group	1.57 ± 0.70	1.66 ± 0.67	1.78 ± 0.66	0.000
NS group	1.47 ± 0.45	1.44 ± 0.47	1.45 ± 0.46	0.372

Note: Data are presented as mean ± SD.

^aSignificant value was considered P < 0.05

Abbreviations: HDP = hypertonic dextrose prolotherapy; NS = normal saline.

The evaluation at three-time points—before the intervention, 2 weeks after, and 6 weeks after—revealed that the HDP group

showed significant improvements in FC thickness at all locations (MC, IC, and LC), while the NS group did not show significant

changes. A previous study evaluating HDP injections in KOA patients with musculoskeletal ultrasound over a 12-month follow-up also demonstrated a significant increase in MC and LC thickness compared to baseline (Soliman et al., 2016).

Thinning of femoral cartilage (FC) occurs naturally with aging, and knee osteoarthritis (KOA) accelerates its severity. Throughout life, cartilage undergoes a remodeling process, but in KOA patients, the ability to regenerate is impaired due to the reduced quality of the extracellular matrix and rapid turnover rate (Jeon et al., 2023). FC thickness has become an important biomarker for diagnosing and monitoring KOA progression (Dório et al., 2020). The progressive nature of KOA is associated with gradual cartilage defects and bone degeneration (Keefe et al., 2023). In early-stage KOA, changes in cartilage composition occur before significant cartilage thinning (Küçükakkaş et al., 2022).

FC thickness varies significantly and is influenced by factors such as gender, weight, height, and BMI. A previous study evaluating healthy adults concluded that gender plays a role, with men having thicker FC than women (Pane et al., 2022). Another study involving 100 participants found that men and athletes had significantly thicker FC compared to women and individuals with low physical activity. However, no

significant relationship was found between BMI and articular cartilage (AC) thickness in non-obese adolescents with adequate physical activity (Bedewi, Elsifey, Naguib, Saleh, Nwihadh, et al., 2020; Herrera H et al., 2020). In addition, FC thickness is linked to diabetes mellitus (DM). Previous research indicated that DM affects FC thickness, with ultrasound scans showing that FC in diabetic patients appears thinner and irregular, suggesting cartilage degeneration (Banu Aydın & Köseoğlu, 2023; Bedewi, Elsifey, Naguib, Saleh, Al-Ghamdi, et al., 2020).

Conclusion

In conclusion, HDP injection demonstrated a beneficial effect in increasing femoral cartilage (FC) thickness in obese patients with knee osteoarthritis (KOA) in the short term. The FC thickness was thinnest at the medial condyle (MC) compared to the intercondylar (IC) and lateral condyle (LC) sites. A significant improvement in FC thickness was observed in the HDP group in the within-group analysis.

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