ORIGINAL ARTICLE

Study on the Effect of Local Hypertonic Dextrose Injection in Osteoarthritis Knee – A Cohort Study

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ABSTRACT

Background: Knee osteoarthritis is a prevalent condition among the elderly, causing disability and reduced quality of life. Prolotherapy, using hypertonic dextrose therapy, emerges as a promising non-surgical option for managing knee osteoarthritis.

Objective: To assess the effect of hypertonic dextrose injection given locally in knee osteoarthritis.

Methods: A cohort study was conducted among 125 patients with knee osteoarthritis. In various stages participants received intra-articular and extra-articular injections of 12.5% dextrose solution at weeks 1, 5, and 9. Follow-up evaluations were conducted at weeks 5, 9, and 12, using WOMAC and VAS scores.

Results: The mean age of participants was 56.36 years (±10.68 years) (Table 1). The mean WOMAC score decreased significantly from 58.76 (SD 6.89) at pre-treatment to 46.52 (SD 7.51), 38.96 (SD 8.21), and 32.54 (SD 9.85) at the first, second, and third follow-up visits, respectively. Similarly, the mean VAS score decreased significantly from 7.84 (SD 0.91) at pre-treatment to 6.62 (SD 0.96), 5.24 (SD 1.32), and 4.45 (SD 1.24) at the first, second, and third follow-up visits, respectively. Temporarily pain at injection site was noted in 8.33% cases as the solo complication.

Conclusion: Hypertonic dextrose injection significantly improves WOMAC and VAS scores in patients with knee osteoarthritis, indicating its potential as a non-surgical treatment option. However, further research is needed to explore its long-term efficacy and safety profile.

Keywords: Knee osteoarthritis; Hypertonic dextrose injection; Prolotherapy; WOMAC score; VAS score; non-surgical treatment

INTRODUCTION

Knee osteoarthritis presents a formidable challenge in healthcare, particularly for the aging population, as it is characterized by chronic progression and debilitating joint dysfunction. This condition's prevalence underscores its significant impact on public health, with studies indicating that over 80% of individuals aged 55 and above suffer from osteoarthritis in at least one joint, with the knee being a common site of affliction.[1] Pain and disability are hallmark features of knee osteoarthritis, emanating from a complex interplay of intra-articular and extra-articular structures. Intra-articular factors involve the deterioration of cartilage, inflammation of the synovium, and the formation of osteophytes within the joint, while extra-articular sources of pain may include ligamentous strains, muscle imbalances, and periarticular bursitis.[2]

Table 1: Age and gender distribution of study participants (n=125)

Age and Gender wise distribution		Frequency	Percentage (%)	Mean ±SD
Age	≤40 years	5	4.0	56.36 ± 10.68
	41-50 Years	20	16.0	
	51-60 Years	35	28.0	
	61-70 Years	58	46.4	
	>70 Years	7	5.6	
Gender	Male	53	42.0	–
	Female	72	58.0	–

Knee osteoarthritis is a prevalent condition among the elderly, causing disability and reduced quality of life. Despite its prevalence, there's a lack of universally accepted treatment guidelines.[3] Prolotherapy, using hypertonic dextrose therapy, emerges as a promising non-surgical option for managing knee osteoarthritis, offering an effective

and relatively affordable treatment avenue.[4] However, the current research on hypertonic dextrose therapy is limited and lacks statistical analysis. Further exploration is needed to understand its efficacy, safety profile, and optimal treatment protocols. Enhanced understanding derived from robust research will refine clinical practice and offer hope to patients by expanding treatment options. The principle behind prolotherapy is the injection of small volumes of an irritant solution at multiple painful ligament and tendon insertion sites, as well as adjacent joint spaces, across several treatment sessions.[5] While its exact mechanism of action remains unclear, contemporary theories suggest that prolotherapy stimulates local healing processes within chronically injured tissues. Early literature reported positive outcomes with prolotherapy, ranging from the 1930s to the early 2000s, the methodological rigor of these studies varied. Despite this, a single randomized controlled trial (RCT) and an open-label study demonstrated improvements in outcomes following prolotherapy, albeit with methodological limitations.[6]

The rationale behind conducting a study on the effect of hypertonic dextrose injection in knee osteoarthritis lies in the need to explore alternative treatment options for this prevalent and debilitating condition. Knee osteoarthritis poses a significant burden on individuals, often leading to pain, functional impairment, and reduced quality of life. While various treatment modalities exist, including pharmacological interventions, physical therapy, and surgical options like joint replacement, many patients continue to experience inadequate relief or are ineligible for certain treatments due to factors such as contraindications or financial constraints. Hypertonic dextrose injection, known as prolotherapy, has gained attention as a potential non-surgical intervention for knee osteoarthritis, offering the possibility of symptom alleviation and functional improvement. However, despite its use in clinical practice, there remains a lack of comprehensive evidence regarding its efficacy, safety, and optimal administration protocols. Therefore, conducting a cohort study to investigate the effects of hypertonic dextrose injection in knee osteoarthritis is warranted to provide valuable insights into its therapeutic potential, inform clinical decision-making, and improve patient outcomes in the management of this challenging condition. Thus, the present study was carried out with the aim of assessing the effect of hypertonic dextrose solution in osteoarthritis of knee.

MATERIALS AND METHOD

The present cohort study was conducted among 125 patients with knee osteoarthritis at the Department of Orthopaedic Surgery, Rohilkhand Medical College and Hospital, Bareilly, over a period of one year from 1st November 2022 to 31st October 2023.

The inclusion criteria for the study are: patients aged 18 years or above, patients willing to take the injection, patients with a diagnosis of knee osteoarthritis based on clinical criteria, and patients with radiographic evidence of knee osteoarthritis. The exclusion criteria are: patients with a BMI greater than 40, pregnant women, uncontrolled diabetes, history of total knee replacement, any knee injection in the past 3 months, inflammatory or post-infectious knee arthritis, daily use of opioid medication, comorbidity severe enough to prevent participation in the study, patients with a local skin condition at the injection site, and allergy or history of allergy to dextrose solution or lignocaine.

For the preparation for the injections, for the intra-articular injection, 5 mL of 25% dextrose was mixed with 5ml of 2% lidocaine in a 10 mL syringe, resulting in an effective concentration of 12.5% dextrose solution. A total of 6ml of this solution was then injected into the knee joint. For the extra-articular injection, 10 mL of 25% dextrose was mixed with 10 mL of 2% lidocaine in a 20 mL syringe, again resulting in an effective concentration of 12.5% dextrose solution. 2.5 mL of this solution was then injected at specific extra-articular sites, including the femoral and tibial attachments of the medial and lateral collateral ligaments, coronary ligaments, patellar tendon, and quadriceps tendon, near their bony attachments.

The patient was positioned supine with the knee joint painted and draped using all aseptic precautions to ensure a sterile environment. Next, 2.5 mL of extra-articular injections were administered at the major tender tendon and ligament insertions, as previously identified. Following this, 6 mL of intra-articular solution was delivered into the knee joint.

After the intervention, participants were advised to relatively rest their knee for 2-3 days, with a gradual resumption of routine activities over the course of 1 month. Additionally, participants were instructed to avoid taking non-steroidal anti-inflammatory drugs, unless absolutely necessary, and were allowed to take tramadol only as needed for pain control.

The schedule of injections for the participants consisted of extra articular and intra articular injections of 12.5% dextrose solution, administered at weeks 1, 5, and 9.

Follow-up evaluations were conducted at weeks 5, 9, and 12, during which participants completed the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and Visual Analog Scale (VAS) assessments to track their progress and response to the treatment.

Chi-square and Wilcoxon signed-rank tests were used for statistical analysis with p value <0.05 considered as significant value.

RESULTS

The mean age of participants is 56.36 years (±10.68 years). The age distribution shows a majority (46.4%) in the 61-70 years range, followed by 51-60 years (28.0%), 41-50 years (16.0%), over 70 years (5.6%), and under 40 years (4.0%). The study participants consist of 72 females (58.0%) and 53 males (42.0%).

The table 2 presents the distribution of KL (Kellgren-Lawrence) grades among the study participants, indicating the frequency and percentage of individuals with each grade within the sample. Among the study participants, the most prevalent KL grade is Grade 3, with 80 individuals affected, representing 64.0% of the total sample. Grade 2 is the second most common KL grade, with 31 participants affected, accounting for 24.8% of the total sample. Grade 4 is observed in 14 participants, constituting 11.2% of the total sample.

Table 2: KL grading of study participants (n=125)

KL Grade	Frequency	Percentage (%)
Grade 2	31	24.8
Grade 3	80	64.0
Grade 4	14	11.2

The table 3 provides the frequency and percentage of symptoms reported by the study participants at different follow-up visits, including pre-treatment and three subsequent follow-up visits. Swelling was the most commonly reported symptom, with 85 participants (68.0%) experiencing it during the pre-treatment phase. The frequency of swelling decreased over the follow-up visits but remained relatively high, with 76 participants (60.8%) reporting it during the first follow-up, 43 participants (34.4%) during the second follow-up, and 29 participants (23.2%) during the third follow-up. Tenderness was reported by a majority of participants at all stages, with 119 participants (95.2%) experiencing it during the pre-treatment phase. The frequency of tenderness decreased slightly over the follow-up visits, with 116 participants (90.6%) reporting it during the first follow-up, 108 participants (86.4%) during the second follow-up, and 95 participants (76.0%) during the third follow-up. Crepitus was consistently reported by a high proportion of participants at all stages, with 125 participants (100.0%) experiencing it during the pre-treatment phase, and 125 participants (100.0%) reporting it during all subsequent follow-up visits.

The table 4 presents the results of chi-square (χ^2) tests conducted to assess the association between the presence of symptoms and different follow-up visits among the study participants. The p-values indicate the level of significance of the association.

Table 3: Symptoms of study participants (n=125) at different visits

Symptoms	Pre-treatment		First follow up		Second follow up		Third Follow up	
	Incidence	Percentage (%)	Incidence	Percentage (%)	Incidence	Percentage (%)	Incidence	Percentage (%)
Swelling	85	68.0	76	60.8	43	34.4	29	23.2
Tenderness	119	95.2	116	90.6	108	86.4	95	76.0
Crepitus	125	100.0	125	100.0	125	100.0	125	100.0

Table 4: Change in Pre-treatment Symptoms of Study Population (n=125)

Symptoms	First follow up		Second follow up		Third Follow up	
	χ^2	p	χ^2	p	χ^2	p
Swelling	0.214	0.68	6.235	0.004	13.632	<0.001
Tenderness	1.546	0.54	13.256	0.003	12.965	0.001
Crepitus	1.845	0.15	1.845	0.18	1.945	0.178

There is no significant association between swelling and the first follow-up, as indicated by a chi-square value of 0.214 and a p-value of 0.68. However, at the second follow-up, the chi-square value increases to 6.235 with a p-value of 0.004, indicating a significant association between swelling and the second follow-up. At the third follow- up, the association becomes even more significant, with a chi-square value of 13.632 and a p-value of less than 0.001. There is no significant association between tenderness and the first follow-up (chi-square = 1.546, p = 0.54). However, both the second follow-up (chi-square = 13.256, p = 0.003) and the third follow-up (chi-square = 12.965, p = 0.001) show significant associations between tenderness and the respective follow-up visits.

There are no significant associations between crepitus with any of the follow- up visits, as indicated by the relatively low chi-square values and non-significant p- values across all follow-up periods.

The WOMAC and VAS scores were measured at pre-treatment and three follow-up visits (table 5). The WOMAC score decreased from 58.76 (SD 6.89) at pre-treatment to 46.52 (SD 7.51), 38.96 (SD 8.21), and 32.54 (SD 9.85) at the first, second, and third follow-up visits, respectively. Similarly, the VAS score decreased from 7.84 (SD 0.91) at pre-treatment to 6.62 (SD 0.96), 5.24 (SD 1.32), and 4.45 (SD 1.24) at the first, second, and third follow-up visits, respectively.

The table 6 presents the mean change, standard deviation (S.D.), percentage change, t-value, and p-value for WOMAC score across different follow-up visits compared to the pre-treatment stage. At the first follow-up visit, there is a mean decrease of 4.61 units in the variable compared to the pre-treatment stage. The standard deviation of this change is 3.45 units. This corresponds to a percentage

change of - 10.21%. The t-value associated with this change is -11.854, indicating a significant difference between the pre-treatment and first follow-up means. The p-value is less than 0.001, suggesting a highly significant difference.

Table 5: WOMAC and Pain (VAS) Scores of study participants (n=125) at different Visits

Visit	WOMAC Scores		Pain (VAS Score)	
	Mean	S.D.	Mean	S.D.
Pre-treatment	58.76	6.89	7.84	0.91
First follow up	46.52	7.51	6.62	0.96
Second follow up	38.96	8.21	5.24	1.32
Third Follow up	32.54	9.85	4.45	1.24

Table 6: Change in Pre-Treatment WOMAC Score at follow up visits (Paired 't' test)

Follow up Visit	Mean Change	S.D.	% change	't'	p-value
First follow up	-4.61	3.45	-10.21	-11.854	<0.001
Second follow up	-8.47	5.31	-18.86	-12.564	<0.001
Third Follow up	-12.68	7.12	-25.34	12.104	<0.001

At the second follow-up visit, the mean change further decreases to -8.47 units compared to the pre-treatment stage. The standard deviation of this change is 5.31 units. This corresponds to a percentage change of -18.86%. The t-value associated with this change is -12.564, indicating a significant difference between the pre-treatment and second follow-up means. The p-value is less than 0.001, again suggesting a highly significant difference.

At the third follow-up visit, the mean change continues to decrease, with a change of -12.68 units compared to the pre-treatment stage. The standard deviation of this change is 7.12 units. This corresponds to a percentage change of -25.34%. The t- value associated with this change is 12.104, indicating a significant difference between the pre-treatment and third follow-up means. The p-value is less than 0.001, indicating a highly significant difference.

The table 7 presents the mean change, standard deviation (S.D.), percentage change, Z-score (Z), and p-value for the VAS score across different follow-up visits compared to the pre-treatment stage. At the first follow-up visit, there is a mean decrease of 1.21 units in the VAS score compared to the pre-treatment stage. The standard deviation of this change is 0.71 units. This corresponds to a percentage change of -17.85%. The Z-score associated with this change is 5.862. The p-value is less than 0.001, suggesting a highly significant difference between the pre-treatment and first follow-up means.

At the second follow-up visit, the mean change further decreases to -2.63 units compared to the pre-treatment stage. The standard deviation of this change is 1.08 units. This corresponds to a percentage change of -34.68%. The Z-score associated with this change is 5.856. The p-value is less than 0.001, indicating a highly significant difference between the pre-treatment and second follow-up means.

Table 7: Change in Pre-Treatment Pain at follow up visits (Wilcoxon Signed Rank Test)

Follow up Visit	Mean Change	S.D.	% change	'Z'	p-value
First follow up	-1.21	0.71	-17.85	5.862	<0.001
Second follow up	-2.63	1.08	-34.68	5.856	<0.001
Third Follow up	-2.34	1.36	-38.16	5.848	<0.001

At the third follow-up visit, the mean change continues to decrease, with a change of -2.34 units compared to the pre-treatment stage. The standard deviation of this change is 1.36 units. This corresponds to a percentage change of -38.16%. The Z- score associated with this change is 5.848. Injection site pain in 8.33% cases was reported as solo complication in present study (table 8).

Table 8: Complications in patients

Complications (Beyond 72Hrs)	Number	Percentage
Injection Site Pain	10	8.33%
Swelling	0	0.00%
Infection	0	0.00%
Bleeding/ Haemarthrosis	0	0.00%
Neurovascular	0	0.00%
Redness/Skin Discoloration	0	0.00%

DISCUSSION

The present study was done to assess the clinical effectiveness of hypertonic dextrose injection in knee osteoarthritis. All the patients affected by a Unilateral or Bilateral knee osteoarthritis, attending the department from November 2022 to October 2023 were invited to participate in the study. Of these 125 patients fulfilling the inclusion criteria and giving their consent for inclusion were enrolled as subjects in the present study.

In our study the mean age of participants is 56.36 years, with a standard deviation of ±10.68 years with a majority proportion falling into the 61-70 years range (46.4%). The concept that aging contributes to, but does not directly cause OA, is consistent with the multifactorial nature of OA and the knowledge that not all older adults develop OA and not all joints in the body are affected to the same degree.[7] While some studies have included patients as young as 18 years old in their investigations, Halpern et al.[8] have observed a patient age profile and average age similar to our findings. Similarly, Kon et al.[9] reported a mean patient age of 56.5 years in their series, which closely resembles the average age of patients in our study.

We found that among the study participants, there are 72 females, representing 58.0% of the total sample. The number of male participants is 53, accounting for 42.0% of the total sample. This distribution suggests that females are slightly more represented in the study sample compared to males. The incidence of knee, hip, and hand OA is higher in women than men and in women it increases dramatically around the time of menopause.[10] However, various clinical studies investigating the role of hypertonic dextrose injection have shown discrepancies in gender distribution. Wang-Saegusa et al.[11] found only 41.8% women in their study, while Filardo et al.9 had just 37.4%. Conversely, Sanchez et al. reported higher proportions of females at 60% and 66% in their two study groups. In a separate study from India, Dhillon[12] observed that 70.7% of their study population were women, aligning with the predominance of women observed in our current study.

The most prevalent KL grade is Grade 3, with 80 individuals affected, representing 64.0% of the total sample. Grade 2 is the second most common KL grade, with 31 participants affected, accounting for 24.8% of the total sample. Grade 4 is observed in 14 participants, constituting 11.2% of the total sample. In contrast to our findings, Filardo et al.[9] found that 57.9% of their patients were classified in KL grades I-III, with the remaining 42.1% falling into grade IV. Similarly, Wang-Saegusa et al.[11] observed a lower percentage of grade IV cases at 36.9%. However, it's worth noting that certain researchers opted to exclude grade IV patients from their analysis. For instance, Dhillon et al.[12] utilized Ahlback grade rather than KL grade as their criteria, limiting their inclusion to grades 1-3 while excluding more severe cases (grades 4-5). Despite this, considering promising results from previous studies that did include grade 4 cases, our study opted to include these patients in our analysis.

In our study, all patients required minimum three injections. Among the study participants, the most common time for starting active exercise after injection is immediately after injection with 78 individuals, representing 62.4% of the total sample. In our study, the mean value of the WOMAC score among these patients was 58.76, with a standard deviation of 6.89. The mean value decreased to 46.52, with a slightly increased standard deviation of 7.51 compared to the pre-treatment stage. The mean value decreased further to 38.96, with a standard deviation of 8.21. The mean value of the variable continued to decrease to 32.54, with a higher standard deviation of 9.85 compared to the previous follow-up visits. In the research conducted by Rahimzadeh et al.[13] in 2018, a notable trend emerged in the WOMAC scores of both groups over the course of the study. Initially, there was a rapid decline in the overall WOMAC score observed in both groups during the first and second months. Subsequently, by the sixth month, there was a slight increase in the overall WOMAC score, although it remained lower than the score recorded in the first month. Statistical analysis confirmed a significant reduction in the overall WOMAC score across both patient groups over the 6-month period.

In our study, similar to WOMAC score, pain intensity among osteoarthritis (OA) patients was evaluated through a visual analogue scale (VAS), a tool comprising a 10 cm horizontal line. The line was labelled with "no pain" at one end and "worst pain imaginable" at the other. Patients indicated their pain intensity by marking a point along the line that best represented their experience. The mean value of the VAS score among these patients was 7.84, with a standard deviation of 0.91. At the first follow-up visit, mean value of the VAS score decreased to 6.62, The mean value decreased in next follow ups to 4.45 in the last follow up. The results of our study are consistent with the study performed by Serkan Akpancar et al., 2019[14], VAS scores of both comparative groups were significantly improved compared to pretreatment values ($P<0.001$) and there was no significant difference between the groups at the follow-up periods (P1=0.099, 0.914, 0.894, 0.811 for 21-, 90-, 180-, and 360-day follow-up periods, respectively).

This study has several limitations. The small sample size may limit the generalizability of the findings, and the follow-up period may not have been sufficient to capture long-term outcomes and potential complications. Additionally, the study lacked a control group, which would have provided a baseline for comparison. The study relied on self-administered scales, such as VAS and WOMAC, to assess joint pain, which may not have captured the full complexity of the condition. To increase reliability, the study should have controlled for additional variables such as clinical, pathological, and other characteristics. Furthermore, the study lacked morphological assessments of cartilage, soft tissue, and structures in and around the knee joint, which would have provided valuable information on the effects of hypertonic dextrose injection.

CONCLUSION

Hypertonic dextrose injection demonstrated promising clinical effectiveness in managing knee osteoarthritis, as evidenced by improvements in symptoms and health parameters over the follow-up period. These findings support the potential use of hypertonic dextrose injection as a therapeutic intervention for knee osteoarthritis, although further research is warranted to validate these results and explore long-term efficacy and safety.

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