

# PAIN AND FUNCTIONAL OUTCOME WITH SINGLE DOSE 25% DEXTROSE INTRA-ARTICULAR INJECTION IN PATIENTS WITH PRIMARY OSTEOARTHRITIS OF THE KNEE

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## Abstract

**Introduction:** Osteoarthritis (OA) is the most prevalent chronic joint disorder worldwide and is associated with significant pain and disability. The introduction of 25% Dextrose injection has been viewed as an advance in the management of OA knee.

**Methods:** A prospective, randomized clinical trial was conducted with 84 cases in the Physical Medicine and Rehabilitation (PMR) department of BSMMU. Group A, 42 patients received single dose 25% Dextrose injection intra articular 8ml, exercise and ADL; Group B, 42 patients received exercise and ADL. Outcomes were measured by OA specific translated and validated Bengali instrument- Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire and visual analogue scale (VAS 0-10). They were followed up for 6 months.

**Result:** At the initial stage and in week 4, there was no statistical difference between two groups regarding VAS score (as p value was >0.05). But in week 12 and 24, there was highly significant statistical difference regarding VAS score between two groups as the p value was <0.001. Again at the initial stage and week 4, there was no statistical difference between two groups regarding stiffness and physical function score. But in week 12 and 24, there was significant statistical difference regarding stiffness and physical function score between two groups as the p value was less than 0.05.

**Conclusion:** Intra-articular injection of 25% dextrose administered to patients with OA knee has significant effects in pain reduction and functional improvement.

**Key words:** Osteoarthritis, Dextrose, VAS score, WOMAC

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## Introduction

The prevalence of osteoarthritis increases indefinitely with age, because the condition is not reversible and it is the most prevalent form of arthritis and it is the principal cause of disability in the elderly.<sup>1</sup> Pain on walking, stiffness of the joint and difficulty with steps and stairs are the major symptoms.<sup>2</sup> Prevalence of osteoarthritis (OA) knee is 7.5% rural, 9.2% urban slum, 10.6% urban affluent community in Bangladesh perspectives.<sup>3</sup>

The primary objectives in OA treatment focus on pain reduction, joint mobility improvement, and functional impairment limitation. Furthermore, secondary goals are centered on the reduction of disease progression and improvement of muscular strength, in order to preserve patients' independence and quality of life.<sup>4</sup> Current treatments aim at alleviating these symptoms by several different methods: Non-pharmacological treatments (for example, education, exercise, lifestyle changes), Pharmacological treatments (for example, paracetamol, NSAIDs, topical treatments) and Invasive interventions (for example, intra-articular injections, lavage, arthroplasty).<sup>5</sup> However most currently used treatments have limited tolerability and their efficacy is limited to relieving pain.<sup>6</sup>

Several reports have revealed the effects of dextrose injection in treating refractory musculoskeletal disorders such as low back pain, tendonitis, lateral epicondylitis, and ligament damage.<sup>7-9</sup> Though intra-articular dextrose injection has been used for knee OA for many decades, only recently has the efficacy of the results been studied.<sup>10,11</sup> Intra-articular dextrose might be a viable alternative to NSAIDs for knee OA, especially for older patients at greater risk for systemic adverse events.<sup>12</sup>

The prevalence of OA knee in Bangladesh seems to be higher due to poor working conditions, heavy physical labor and occupational injuries which increase in future. This will ultimately create higher clinical and socioeconomic burden to the population and national economy. IA injections of Dextrose in patients with OA knee will be generally well tolerated, provide sustain relief of pain and improve patient's function,

and effective with fewer adverse reactions as continuous treatment with NSAIDs. IA dextrose injection may represent an attractive alternative to the current treatment regimen offering potential comfort and safety benefits to patients. But in fact, there was no published data about the effectiveness in the management of knee OA with dextrose intra-articular injection in Bangladesh. So this research will be helpful to provide evidence based information to the physician as well as patient groups about the efficacy of intra-articular dextrose injection in the management of knee OA both for pain reduction and functional improvement.

## Materials and Methods

It is a Randomized Clinical trial study which was done in the department of Physical Medicine and Rehabilitation, BSMMU, Dhaka and patients with Knee osteoarthritis from all corner of the country attended BSMMU for comprehensive management. For the study 84 patients (irrespective of sexes) were selected. After taking informed consent, detail history and physical examination of each patient were performed and recorded and treated (and a pretest data form was filled for every patient). The patients were diagnosed according to the criteria developed by the American College of Rheumatology Radiologic and Clinical Criteria for Osteoarthritis (ACR).<sup>13</sup> Sample was collected during the period of September'17 to August'18

## Randomization and Grouping technique:

Participants were randomized in two groups named as group A and group B by lottery. Following the screening period, patients were randomized in a non-blind fashion. Total 84 patients were included and divided into two groups. 84 cards were taken for 84 patients, 42 were tagged with intra-articular 25% dextrose injection which was group A and 42 were tagged with exercise which was group B. All cards were put in a box and each participant was asked to pick up a card and it over to principle investigator. The picked up marking was patient's group. Patients were informed of the design of the study and that they received I/A 25% dextrose or exercise and ADL instruction only during study.

**Details of Treatment:**

## Group A:

1. Single dose of 25% dextrose 10 ml was injected in to the patient's knee with aseptic technique which was adopted with skin disinfection and draping. The injection was administered through a direct parapatellar approach. Preadministration of anesthetic skin spray or subcutaneous local anesthetics were permitted. If there was effusion present in the knee, then aspirated and send to laboratory for synovial fluid analysis. Aspiration was performed by using a separate sterile syringe before injection of the dextrose. After injection patients were allowed to resume normal activities, but advice against vigorous exercise for 2 to 3 days. Ice therapy was recommended in case of transient increase in pain and swelling.
2. All patients were requested to be 24 hours analgesia free before baseline measurement.
3. Quadriceps strengthening exercise in the form of extension of knees 10 repetition 2 times daily.
4. Instruction for activity of daily living (ADLs) were prescribed for all patients.

## Group B:

1. Quadriceps strengthening exercise in the form of extension of knees 10 repetition 2 times daily.
2. Instruction for activity of daily living (ADLs) were prescribed for all patients.

Both group were advised to avoid non-steroidal anti-inflammatory drugs (NAISDs) for six months. Paracetamol was allowed for break-thru pain < 2000mg/day.

**Data collection and Outcome Measures:**

After the treatment of the patients as per schedule, the patients were followed up at 4<sup>th</sup> weeks, 12<sup>th</sup> weeks and 24<sup>th</sup> weeks and outcome were measured by OA specific translated and validated Bengali instrument- Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) questionnaire.<sup>14</sup> Pain score was done on visual analogue scale (VAS1-10).

**Data processing and analysis:**

All the data were compiled and sorted properly and the numerical data were analyzed statistically by using computer software Statistical Package for Social Sciences (SPSS-23). The results were expressed as percentage and mean  $\pm$  SD and  $p < 0.05$  were considered as the level of significant. Comparison of continuous variables between the two groups were made with two sample t-tests as appropriate. Comparison of proportions between the groups were made with chi-square tests.

**Ethical implication**

Ethical clearance was taken from Institutional Review Board (IRB) of BSMMU. Informed and understood written consent was taken from every patient before enrollment.

**Results**

A total number of 84 cases were enrolled, then 42 cases were selected for Group A and 42 cases were selected for Group B by purposive sampling technique. During follow up among respondent of group A, two patients did not come at 24<sup>th</sup> week for follow up. In group B, 4 participants dropped out from the study due to personal issues. So finally 40 cases for Group A and 38 cases for Group B were studied. There was no significant statistical difference at the baseline between the groups regarding age, sex, grading of OA knee, side involvement, mean duration of disease. In Group A male were 12(28.6%) and female were 30(71.4%). In group B male were 19(45.2%) and female were 23(54.8%). Age in Group A and Group B were  $48.00 \pm 8.12$  and  $47.26 \pm 4.94$  respectively.

The comparison of VAS score between two groups; at the initial stage and in week 4, there was no statistical difference between two groups regarding VAS score (as  $p$  value was  $> 0.05$ ). But in week 12 and 24, there was highly significant statistical difference regarding VAS score between two groups as the  $p$  value was  $< 0.001$  (obtained by t-test) (Table 1).

In case of comparison of WOMAC pain score between two groups, at the initial stage and in week 4, there was no statistical difference between two groups regarding pain score. But

in week 12 and 24, there was highly significant statistical difference regarding pain score between two groups as the p value was less than 0.05 (obtained by t-test) (Table 2). The comparison of stiffness score between two group; at the initial stage and at week 4, there was no statistical difference between two groups regarding stiffness score. But in week 12 and 24, there was highly significant statistical difference regarding stiffness score between two groups as the p value was less than 0.05 (obtained by t-test) (table 3). The comparison of physical function score between two groups, at the initial stage and week 4, there was no statistical difference between two groups regarding physical function score. But in week 12 and 24, there was significant statistical

difference regarding physical function score between two groups as the p value was less than 0.05 (obtained by t-test) (Table 4). In case of total WOMAC score between two groups. There was no significant statistical difference regarding total WOMAC score at week 0 between two groups as the p value was 0.163. But in week 4, significant statistical difference regarding total WOMAC score between two groups as the p value was 0.023. At week 12 and week 24, highly significant statistical difference was found between two groups as  $p < 0.001$  (Table 5).

In group A. Among the 40 respondents, 7 (17.5%) respondents had localized pain and 2 (4.76%) respondents developed redness around the joint in the 24 weeks of treatment.

**Table 1**  
*Comparison of VAS score between two groups*

VAS score	Group A Mean±SD	Group B Mean±SD	P value
Week 0	6.74±0.45 (n=42)	6.74±0.45 (n=42)	1.000
Week 4	5.88±0.39 (n=42)	5.79±0.47 (n=42)	0.318
Week 12	4.48 ±0.51 (n=42)	4.97 ±0.66 (n=41)	<0.001
Week 24	4.33±0.57 (n=40)	5.43±0.63 (n=38)	<0.001

**Table-II**  
*Comparison of pain score between two groups*

Pain score	Group A Mean±SD	Group B Mean±SD	P value
Week 0	306.31±12.69 (n=42)	308.21±13.19 (n=42)	0.502
Week 4	277.26±23.84 (n=42)	282.86±16.27 (n=42)	0.213
Week 12	239.17±22.95 (n=42)	258.15±15.78 (n=41)	<0.001
Week 24	229.13±27.82 (n=40)	268.42±18.16 (n=38)	<0.001

**Table-III**  
*Comparison of stiffness score between two groups*

Stiffness score	Group A Mean±SD	Group B Mean±SD	P value
Week 0	110.71±10.16 (n=42)	112.62±8.43 (n=42)	0.352
Week 4	93.81±11.52 (n=42)	96.79±9.23 (n=42)	0.195
Week 12	76.42±13.12 (n=42)	90.00±10.12 (n=41)	<0.001
Week 24	72.50±12.51 (n=40)	91.58±9.73 (n=38)	<0.001

**Table-IV**  
*Comparison of physical function score between two groups*

Physical function score	Group A Mean±SD	Group B Mean±SD	P value
Week 0	1027.02±53.35 (n=42)	1038.09±41.38 (n=42)	0.291
Week 4	880.52±40.60 (n=42)	902.59±68.71 (n=42)	0.077
Week 12	724.76±60.05 (n=42)	810.61±63.93 (n=41)	<0.001
Week 24	694.13±103.42 (n=40)	862.76±92.88 (n=38)	<0.001

**Table-V**  
*Comparison of total WOMAC score between two groups*

Total WOMAC score	Group A Mean±SD	Group B Mean±SD	P value
Week 0	1444.05±54.74(n=42)	1458.93±41.19(n=42)	0.163
Week 4	1251.59±54.06(n=42)	1282.24±66.14(n=42)	0.023
Week 12	1040.36±81.42(n=42)	1158.76±66.68(n=41)	<0.001
Week 24	995.75±124.98(n=40)	1222.76±95.26(n=38)	<0.001

## Discussion

Nonsurgical treatment of Osteoarthritis is a multidimensional approach, which includes oral analgesia, physical therapy, multiple kinds of injections, etc.<sup>15</sup> Prolotherapy is an alternative therapy that was first used in 1950.<sup>16</sup> Hypertonic dextrose is a usual substance in prolotherapy.<sup>17</sup> The present randomized clinical trial was conducted to assess the effects of intra-articular 25% dextrose injection in the management of knee OA both for pain reduction and functional improvement.

The mean ages of participants were 48.00(±8.12) years and 47.26(±4.94) years in group A and in group B respectively. Other study showed that onset of OA was found after age 40.<sup>18</sup> (Bosomworth, 2009).

In group A, initially, VAS score was 6.74±0.45. VAS score gradually decreased in week 4 (5.88±0.39) and week 12 (4.48 ±0.51). In week 24, VAS score did not decrease significantly (4.33±0.57). This result was consistent with other study which determined the therapeutic efficacy of dextrose prolotherapy on pain, range of motion, and function in patients with knee osteoarthritis.<sup>19</sup> In group B, VAS score significantly decreased in week 4 and week 12. But from week 12, it gradually increased. By the end of 24 week, the VAS score was 5.43.

Difference in VAS score from baseline to week 24 was 1.32±0.66. Isometric exercise training of the quadriceps alone also reduced knee pain towards the end of the treatment period.<sup>20</sup>

The outcome of the interventions was also assessed by WOMAC questionnaire. In group A, at the beginning of treatment, the mean pain score of the respondents was 306.31. The pain score gradually decreased in week 4 and week 12. In group B, the pain score also decreased parallel with group A. Similar result was found that pain score had improved significantly in week 4 and week 8.<sup>21</sup>

Regarding stiffness score, at week 4, there was no statistical difference between two groups regarding stiffness score. But in week 12 and 24, there was highly significant statistical difference regarding stiffness score between two groups.

In group A, like pain and stiffness score, physical function score also gradually decreased in week 4 and week 12. In week 24, it slightly decreased comparing to week 12. In adults with moderate to severe KOA, dextrose prolotherapy may result in safe, significant, sustained improvement of knee pain, function, and stiffness scores.<sup>22</sup> In group B, physical function score significantly decreased in week 4 and week 12. Land based therapeutic exercise was shown



to reduce pain and improve physical function for people with OA of the knee.<sup>23</sup> In week 12 and 24, there was significant statistical difference regarding physical function score between two groups as the p value was less than 0.05. In the meta-analysis of two eligible studies, prolotherapy is superior to exercise on the WOMAC function subscale scores.<sup>24</sup>

Among the 40 respondents in group A, 7 (17.5%) respondents had localized pain and 2 (4.76%) respondents developed redness around the joint in the 24 weeks of treatment. For localized pain participants were advised to use ice pack on the affected area. If pain worsen, they were advised to take Paracetamol 500 mg but not to take more than 2gm in a day.

### Conclusion

The results from this study showed that intra-articular injection of 25% dextrose administered to patients with OA knee had significant effects in pain reduction and functional improvement. Although both treatment offered significant effectiveness but Intra articular 25% dextrose provided sustain pain reduction and improve physical function.

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### Conflict of interest

None

### References

- Shakoor MA, Taslim MA, Ahmed MS, Hasan SA. Clinical profile of patients with Osteoarthritis of the knee: A study of 162 cases. *Indian Journal of Physical Medicine and Rehabilitation*. 2009;20(2):44-7.
- Shakoor MA, Huq MN, Khan AA, Moyeenuzzaman M. Presentation of patients with Osteoarthritis of knee joint-A study of 54 cases. *The Healer*. 2003;10(1):20-5.
- Haq SA, Darmawan J, Islam MN, Uddin MZ, Das BB, Rahman F, et al. Prevalence of rheumatic diseases and associated outcomes in rural and urban communities in Bangladesh: a COPCORD study. *The Journal of rheumatology*. 2005 Feb 1;32(2):348-53.
- Snibbe JC, Gambardella RA. Treatment options for osteoarthritis. *Orthopedics*. 2005 Feb 1;28(2):S215-20.
- Jordan KM, Arden NK, Doherty M, Bannwarth B, Bijlsma JW, Dieppe P, et al. EULAR Recommendations 2003: an evidence based approach to the management of knee osteoarthritis: Report of a Task Force of the Standing Committee for International Clinical Studies Including Therapeutic Trials (ESCISIT). *Annals of the rheumatic diseases*. 2003 Dec 1;62(12):1145-55.
- Bjordal JM, Ljunggren AE, Klovning A, Slørdal L. Non-steroidal anti-inflammatory drugs, including cyclooxygenase-2 inhibitors, in osteoarthritic knee pain: meta-analysis of randomised placebo controlled trials. *Bmj*. 2004 Dec 2;329(7478):1317.
- Rabago D, Best TM, Beamsley M, Patterson J. A systematic review of prolotherapy for chronic musculoskeletal pain. *Clinical Journal of Sport Medicine*. 2005 Sep 1;15(5):E376.
- Yelland MJ, Glasziou PP, Bogduk N, Schluter PJ, McKernon M. Prolotherapy injections, saline injections, and exercises for chronic low-back pain: a randomized trial. *Spine*. 2004 Jan 1;29(1):9-16.
- Klein RG, Eek BC, DeLong WB, Mooney V. A randomized double-blind trial of dextrose-glycerine-phenol injections for chronic, low back pain. *Journal of Spinal Disorders*. 1993 Feb;6(1):23-33.
- Hauser RA, Hauser MA. *Prolo your pain away!: curing chronic pain with prolotherapy*. Beulah Land Press; 2007.
- Rabago D, Zgierska A, Fortney L, Kijowski R, Mundt M, Ryan M, Grettie J, Patterson JJ. Hypertonic dextrose injections (prolotherapy) for knee osteoarthritis: results of a single-arm uncontrolled study with 1-year follow-up. *The Journal of Alternative and Complementary Medicine*. 2012 Apr 1;18(4):408-14.
- Bannuru RR, Schmid CH, Kent DM, Vaysbrot EE, Wong JB, McAlindon TE. Comparative effectiveness of pharmacologic interventions for knee osteoarthritis: a systematic review and network meta-analysis. *Annals of internal medicine*. 2015 Jan 6;162(1):46-54.
- Nelson AE, Jordan JM. Clinical features of osteoarthritis. Dalam: Firestein GS, Budd RC, Gabriel SE, et al.(eds.) *Kelley's textbook of rheumatology*. Ed. ke-9.
- Rabbani MG, Haq SA, Bellamy N, Islam MN, Choudhury MR, Naheed A, Ahmed S, Shahin A. Development, linguistic and clinimetric validation of the WOMAC® VA3. 01 Bangla for Bangladesh Index. *Rheumatology international*. 2015 Jun 1;35(6):997-1003.

15. Shoara R, Hashempur MH, Ashraf A, Salehi A, Dehshahri S, Habibagahi Z. Efficacy and safety of topical *Matricaria chamomilla* L.(chamomile) oil for knee osteoarthritis: a randomized controlled clinical trial. *Complementary therapies in clinical practice*. 2015 Aug 1;21(3):181-7.
16. Rabago D, Mundt M, Zgierska A, Grettie J. Hypertonic dextrose injection (prolotherapy) for knee osteoarthritis: Long term outcomes. *Complementary therapies in medicine*. 2015 Jun 1;23(3):388-95.
17. Hauser RA, Sprague IS. Outcomes of prolotherapy in chondromalacia patella patients: improvements in pain level and function. *Clinical Medicine Insights: Arthritis and Musculoskeletal Disorders*. 2014 Jan;7:CMAMD-S13098.
18. Bosomworth NJ. Exercise and knee osteoarthritis: benefit or hazard?. *Canadian Family Physician*. 2009 Sep 1;55(9):871-8.
19. Eslamian F, Amouzandeh B. Therapeutic effects of prolotherapy with intra-articular dextrose injection in patients with moderate knee osteoarthritis: a single-arm study with 6 months follow up. *Therapeutic advances in musculoskeletal disease*. 2015 Apr;7(2):35-44.
20. Cheing GL, Hui-Chan CW, Chan KM. Does four weeks of TENS and/or isometric exercise produce cumulative reduction of osteoarthritic knee pain?. *Clinical rehabilitation*. 2002 Nov;16(7):749-60.
21. Dumais R, Benoit C, Dumais A, Babin L, Bordage R, de Arcos C, Allard J, Bélanger M. Effect of regenerative injection therapy on function and pain in patients with knee osteoarthritis: a randomized crossover study. *Pain Medicine*. 2012 Aug 1;13(8):990-9.
22. Rabago, D., Slattengren, A. and Zgierska, A.,. Prolotherapy in primary care practice. *Primary Care: Clinics in Office Practice*. 2010;37(1), pp.65-80.
23. Fransen M, McConnell S, Bell M. Therapeutic exercise for people with osteoarthritis of the hip or knee. A systematic review. *The Journal of rheumatology*. 2002 Aug 1;29(8):1737-45.
24. Sit RW, Chung VC, Reeves KD, Rabago D, Chan KK, Chan DC, Wu X, Ho RS, Wong SY. Hypertonic dextrose injections (prolotherapy) in the treatment of symptomatic knee osteoarthritis: a systematic review and meta-analysis. *Scientific reports*. 2016 May 5;6:25247.