

Original Article

Comparative Study of Intra-articular Steroid Injection *versus* Prolotherapy in Regards to Improvement of Pain in Osteoarthritis of Knee JointSuvadeep Bose¹, Sourav Dhar², Ashish Yadav³, Arupjyoti Kurmi⁴

Abstract

Background : Osteoarthritis of the knee is one of the leading causes of pain, loss of function and decreased quality of life among adult rheumatological diseases. Osteoarthritis (OA) is a clinical syndrome of joint pain characterized by gradual loss of articular cartilage, osteophyte formation, subchondral bone remodelling, and inflammation of the joint¹. When oral analgesic is ineffective, intra-articular (IA) injection (local corticosteroids, visco-supplements, platelet-rich plasma, prolotherapy) is another *non-operative modality* that can be performed^{2,3}.

Aims and Objectives : The present study was performed to assess the therapeutic effects of intra-articular dextrose prolotherapy on knee osteoarthritis and its comparison with intra-articular triamcinolone injection in terms of pain relief (VAS Score) and improvement in quality of life (WOMAC Score).

Materials and Methods : This prospective randomized study was conducted on patients visiting the OPD of NILD, Kolkata from March, 2020 to April, 2021. This study was performed on patients suffering from knee OA as a double-blind randomized clinical trial. One group received Prolotherapy (mixed with a local anesthetic- Lignocaine) and the other group received Intraarticular Steroid (mixed with a local anesthetic). Pre-procedural baseline assessment was done by VAS score and WOMAC score and compared it with the post-procedural improvement at 2nd, 4th and 6th week.

Results : Compared to pretreatment, both interventions caused significant improvement in pain (evaluated by VAS) and WOMAC (all its components) (all with P-value <0.005). At 2nd, 4th and 6th week post-procedure, pain reduction was significantly better in the corticosteroid group.

Conclusion : Both steroids (triamcinolone acetonide) and prolotherapy (25% dextrose) are effective as IA injections in the OA knee joint for providing pain relief, however, steroid is more efficacious than single session of prolotherapy. As both provide analgesia by different modes of action, a multimodal approach can be used to provide more complete analgesia with minimal side effects.

Key words : Osteoarthritis of the Knee, Steroids Injection, Prolotherapy, Local Anaesthetic.

Knee osteoarthritis (OA), also known as degenerative joint disease, is typically the result of wear and tear and progressive loss of articular cartilage. It is most common in elderly women and men. OA knee is a major source of disability worldwide owing to pain and loss of function⁴. It mostly involves weight-bearing joints of the body. Broadly it can be divided into primary and secondary Osteoarthritis. Primary osteoarthritis occurs in previously intact joints

Editor's Comment :

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and is idiopathic. Secondary Osteoarthritis follows birth defects, dislocation, trauma and fracture, deformities and other diseases of joints or some systemic diseases. Synovial inflammation plays a critical role in the symptoms and structural progression of osteoarthritis⁵.

Non-surgical treatment options include patient education, activity modification, physical therapy, weight loss, knee bracing, acetaminophen, NSAIDs, COX 2 inhibitor, corticosteroid injection and prolotherapy⁶.

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Local Corticosteroids have been a mainstay in the treatment of osteoarthritis knee owing to their anti-inflammatory effects and immuno-suppressive effects. Clinically, it causes a decrease in erythema, swelling, heat and tenderness of the inflamed joints. It also leads to an increase in the relative viscosity of the synovial fluid with an increase in Hyaluronic Acid (HA) concentration^{7,8}.

Prolotherapy involves the injection of a small amount of an irritant substance (most commonly, hypertonic solution of dextrose) into synovial space. It is presumed to work by several mechanisms including a direct, osmotic, and inflammatory growth effect⁹. The hypothesized mechanisms for pain relief include stimulation of local healing among chronically injured extra- and intra-articular tissues, reduction of joint instability through the strengthening of stretched or torn ligaments and stimulation of cellular proliferation¹⁰.

The aims and objectives of the study was to find the efficacy in remission of pain and duration of remission for (1) Prolotherapy, (2) Intra-articular steroid injection and (3) Compare between prolotherapy and intra-articular steroid injection.

MATERIALS AND METHODS

Study Design & Population :

This prospective randomized study was done from March, 2020 to April, 2021 at National Institute for Locomotors Disabilities, Kolkata on patients visiting to the Outpatient Department. Total 60 knee joints with knee pain are divided into two groups by Group A and B with 30 knee joints in each group.

Sample Size :

The formula used for sample size calculation was as follows : —

$$n = 4pq / (L^2)$$

Where, n= required sample size,

p= 0.287 (as per the study by Pal CP, *et al*¹³⁵),

q = 1 – p,

L = Loss % (Loss of information),

Here p= 0.287,

q=1-p = 1- 0.287 =0.713,

4pq = 4 x 0.287 x 0.713 = 0.81852

L² = 0.01364

L = 0.1167

Loss of information percentage = 11.67%

n = 4pq / (L²) = 0.81852/0.01364 = 60.00 = 60

Study Tool:

Numeric pain rating scale as per WOMAC pain score was used.

Study Technique :

Cases were selected as per inclusion and exclusion criteria. The patients who fulfil inclusion and exclusion criteria will be approached with the proposal of the study. The aim of the study and procedure was explained and written informed consent was taken from patients, who agreed to participate. Thorough history and physical examination were done as per Study Performa.

All patients received conservative management, which included oral medications (paracetamol) and physical therapy, for the initial 3 months. Patients who were not cured were divided in two groups, group A and group B. A total of 60 patients with knee OA were randomly assigned into two groups by generating random numbers with MATLAB 2014b software, where even and odd numbers were attributed to corticosteroid injection and dextrose injection, respectively. Group A patients received prolotherapy and group B patients received intra-articular steroid injection.

The patients were assessed at baseline, 2nd, 4th and 6th week after the procedure by a trained assessor (unaware of the injection process) using Visual Analog Scale of pain (VAS) and a Western Ontario and McMaster Universities Arthritis (WOMAC) questionnaire.

Statistical Analysis :

For statistical analysis, data were entered into a Microsoft Excel spreadsheet and then analyzed by SPSS (version 27.0; SPSS Inc, Chicago, IL, USA) and Graph Pad Prism version⁵. Data had been summarized as mean and Standard Deviation for numerical variables and count and percentages for categorical variables. Two-sample t-tests for a difference in mean involved independent samples or unpaired samples. A Chi-squared test (χ^2 test) is any statistical hypothesis test wherein the sampling distribution of the test statistic is a Chi-squared distribution when the null hypothesis is true. Without other qualifications, 'the chi-squared test' often is used as short for Pearson's Chi-squared test. Unpaired proportions were compared by Chi-square test or Fischer's exact test, as appropriate.

Explicit expressions that can be used to carry out various t-tests are given below. In each case, the

formula for a test statistic that either exactly follows or closely approximates a t-distribution under the null hypothesis is given. Also, the appropriate degrees of freedom are given in each case. Each of these statistics can be used to carry out either a one-tailed test or a two-tailed test.

Once a 't' value is determined, a p-value can be found using a table of values from Student's 't' - t-distribution. If the calculated p-value is below the threshold chosen for statistical significance (usually the 0.10, 0.05, or 0.01 level), then the null hypothesis is rejected in favour of the alternative hypothesis.

p-value ≤ 0.05 was considered statistically significant.

ANALYSIS AND RESULT

All continuous variables were presented as mean \pm SD or median (1st Quartile, 3rd Quartile) as appropriate and compared between the groups by independent t-test for normally distributed data and by Mann-Whitney 'U' test for non-normal data. We have checked the normality of continuous data by the Shapiro-Wilk test. All qualitative data were presented as no.s and percentages of patients. The chi-square test or Fisher's exact test was used to see the difference between the groups for qualitative variables. All p-values < 0.05 were considered as statistically significant.

Table 1 — Demographic Details

	Group A	Group B	p-value	Test Used
No of Patients	30	30		
Age (Years)	49.17 \pm 8.52 Median 49 Range (36-65)	52.27 \pm 9.13 Median 54 Range (37-69)	0.18	Independent sample t- test
Sex (Male/Female)	17:13 (56.7%:43.3%)	20:10 (66.7%:33.3%)	0.43	Chi- square test

Table 2 — Age Distribution in Groups

Age Group (Years)	Group A	Group B
<40	6 (20%)	3(10%)
40-50	10 (33.3%)	8 (26.67%)
50-60	10 (33.3%)	13 (43.33%)
60-70	4 (13.33%)	6 (20%)
Total	30	30

Table 3 — Association of Womac Pain scores and groups(pre-treatment)

Womac Score	Group A	Group B	P-value (Chi-square test)
6	6(20%)	7(23.3%)	0.73
7	18(60%)	15(50%)	
8	6(20%)	8(26.7%)	
Total	30	30	

DISCUSSION

This prospective randomized study was conducted on patients visiting to the Outpatient Department of the National Institute for Locomotors Disabilities, Kolkata 700090 from January, 2020 to April, 2021. Total 60 knee joints with knee pain are divided into two groups. Group A and B with 30 knee joints in each group. Prolotherapy has been reported as a useful method in the treatment of chronic musculoskeletal and joint diseases. It is proposed that prolotherapy causes mild inflammation and cell stress in the weakened ligament or tendon area, releases cytokines and growth factors and induces a new healing cascade in that area, which leads to the activation of fibroblasts, generation of collagen precursors, and strengthening of the connective tissue¹³.

Group-A (Prolotherapy) :

Solution consisted of 5ml of 25% dextrose with 1 ml of lignocaine 2%.

Group-B (Steroid) :

Solution consisted of 40mg(1ml) triamcinolone acetone, 1 ml of lignocaine 2% and 4 ml sterile water.

It was observed that age and sex ratio (Tables 1 and 2) were comparable in two groups. Respective p-values were 0.18 and 0.43. Age in two groups were 49.17 \pm 8.52 and 52.27 \pm 9.13 respectively. There were 17(56.7%) and 20(66.7%) male patients in two groups respectively. We found that 38(63.3%) patients were under OA grade II and 22(36.7%) patients were under OA grade III.

Eslamian F, *et al*¹¹(2015) found that total WOMAC score and its subcategories showed a continuous improvement trend in all the evaluation sessions, so that at the end of the study, the total score decreased by 30.5 \pm 14.27 points (49.58%)($p < 0.001$). Improvements of all parameters were considerable until week 8 and were maintained throughout the study period.

Erdem Y, *et al*¹² (2020) found that clinical efficacy and pain were evaluated via the Visual Analog Scale (VAS) and the Western Ontario and McMaster Universities Arthritis Index (WOMAC) at pre-treatment and one, three and six-month follow-ups. Intra-group statistical analyses revealed significant improvements in PrT+HA and PrT+DX groups for WOMAC and VAS scores compared with baseline.

Table 4 — Womac pain scores at different period

Womac Score	Group A	Group B	P-value	Test used
Pre-treatment	7±0.64 Median 7(7,7) Range (6-8)	7.03±0.72 Median 7(6.75,8) Range (6-8)	0.84	
2 Weeks	5.03±0.76 Median 5(4,6) Range (4-6)	3.83±0.83 Median 4(3,4.25) Range (2-5)	<0.0001	Mann-Whitney 'U' test
4 Weeks	4.83±0.75 Median 5(4,5) Range (4-6)	3.53±0.9 Median 3(3,4) Range (2-5)	<0.0001	
6 Weeks	5.03±0.76 Median 5(4,6) Range (4-6)	3.8±0.96 Median 4(3,4.25) Range (2-6)	<0.0001	

Fatimah N, *et al*¹³(2016) found that 16.1 % showed 50% or more improvement in WOMAC score at 3 months post IASI therapy, whereas 38.7% of OA patients had more than 50% improvement in VAS score. Out of all factors, range of movement, local knee tenderness and radiographic score of the affected joint are the three parameters which can predict the improvement in WOMAC score after 3 months of IASI therapy (P = 0.013, P = 0.045 and P = 0.000, respectively).

Table 3 showing In Group A, 6(20%),18(60%) and 6(20%) patients had WOMAC pain scores of 6,7 and 8 respectively whereas in Group B, 7(23.3%),15(50%) and 8(26.7%) had those respective scores. There is no significant association between pain scores and groups (p=0.73).

Table 4 shows at 2 weeks after treatment, it was observed that the median WOMAC pain score was 5 and 4 respectively in the groups and there was a statistically significant difference between the groups (P-value <0.0001).

At 4 weeks after treatment, it was observed that the median WOMAC pain score was 5 and 3 respectively in the groups and there was a statistically significant difference between the groups (P-value <0.0001)

At 6 weeks after treatment, it was observed that the median WOMAC pain score was 5 and 4 respectively in the groups and there was a statistically significant difference between the groups (P-value <0.0001).

It was also observed that pain score was significantly reduced in both the groups but it was more reduced in the steroid group (Group B).

CONCLUSION

It was concluded that both steroid (triamcinolone acetonide) and prolotherapy (25% dextrose) are effective as IA injections in OA knee joint for providing pain relief; however, steroid is more efficacious than prolotherapy. As both provide analgesia by different modes of action, a multimodal approach can be used to provide more complete analgesia with minimal side effects.

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Conflict of Interest : None

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