Original Article

Comparison of intra-articular injection of platelet-rich plasma with combination of bupivacaine and corticosteroid in osteoarthritis knee

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Abstract

Background and Aims: The use of intra-articular injection has been widely accepted as a therapy for pain due to osteoarthritis of the knee. We aimed to compare the efficacy of intra-articular injection of platelet-rich plasma (PRP) with a combination of bupivacaine and corticosteroid in osteoarthritis of the knee.

Material and Methods: Fifty patients (aged more than 50 years) with pain pattern consistent with osteoarthritis of the knee who did not respond to conservative treatment were included in the study. They were randomly divided into two groups of 25 each: group I ($n = 25$) patients were administered fluoroscope-guided intra-articular knee injection of bupivacaine and steroid, and group II ($n = 25$) patients were administered intra-articular knee injection of PRP. In group I, patients were administered 9 ml of drug solution comprising 8 ml of 0.5% bupivacaine and 1 ml of triamcinolone (40 mg). In group II, patients were administered 6 ml of PRP. Pain, patient satisfaction, and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) were assessed at different time intervals before and after the procedure for up to 12 months.

Results: Pain score and WOMAC were both clinically and statistically better at 2 weeks and 1 month after injection in group I ($P < 0.05$). But results were better clinically in group II compared to group I at 2, 3, 6, and 12 months after the procedure. More than 50% of patients in both groups had excellent satisfaction.

Conclusions: Both techniques were effective in providing good analgesia. Pain relief and improvement in disability were clinically higher with PRP for longer duration.

Keywords: Intra-articular injection, osteoarthritis of the knee, PRP

Introduction

Osteoarthritis (OA) is the most common form of chronic arthritis. It causes chronic pain and affects the functioning of the patient adversely. The use of intra-articular injection has been widely accepted as a therapy for pain due to OA of the knee. Intra-articular corticosteroid injection is a frequently used method to relieve symptoms of arthritis. Steroid absorbed from the synovial cavity leads to improvement in indices of generalized joint inflammation. Intra-articular knee injections can be administered using superomedial patellar, medial mid-patellar, superolateral patellar, and lateral mid-patellar techniques.[1-4]

The clinical interest in autologous growth factor treatment, such as the use of platelet-rich plasma (PRP), has been increasing nowadays. PRP is an autologous concentration of human platelets in a small volume of plasma, where the platelet

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concentration is higher (typically up to four times higher) than the normal platelet concentration in a healthy person's blood. Platelet-derived growth factors (PDGFs) stored in the alpha granules of platelets regulate biological processes of tissue repair. Therapeutic PRP should have platelet concentrations 4–6 times higher than that of whole blood. Emerging evidences suggest that in addition to the role platelets play in hemostasis, PRP has the potential to have a regenerative effect on body tissues.[5-8]

We conducted this prospective study with the primary objective of comparing the efficacy of intra-articular injection of PRP with a combination of bupivacaine and corticosteroid in OA knee, in terms of producing pain relief and improvement in disability. The secondary objectives were to determine ease of administration of the block and side effects, if any.

Material and Methods

This prospective, randomized study was conducted at the Pain Management Center of a postgraduate teaching institute after institutional ethical committee approval was obtained. Fifty patients of either gender and of age more than 50 years attending the pain clinic and fulfilling the following three criteria were included in the study: (i) history, physical examination, and pain pattern consistent with OA of the knee; (ii) X-ray of the knee joint findings corresponding with the patient's clinical symptoms; and (iii) failure to respond to 6 weeks of conservative treatment. Patients with history of uncontrolled diabetes mellitus, infection, or active wound in the knee area, history of treatment with anticoagulants and antiplatelet drugs 10 days before injection, or history of adverse reactions to local anesthetics and steroids were excluded from the study.

In the pain center, a detailed clinical history was elicited, the patients were examined, and imaging studies were reviewed. The procedure was explained to patients in detail, and written informed consent was obtained. Patients were divided randomly into two groups of 25 each by a computer-generated randomization number table. Group I ($n = 25$) patients were administered fluoroscope-guided intra-articular knee injection of bupivacaine and steroid, and group II ($n = 25$) patients were administered fluoroscope-guided intra-articular knee injection of PRP.

Patients were placed in supine position with pillow under the knee to flex the leg at the knee joint. The procedure was performed under strict aseptic precautions. Lignocaine 1% was infiltrated subcutaneously. A 21-G, 1½-inch needle was advanced into the knee joint using medial mid-patellar approach under fluoroscopic guidance. In group I, patients were administered 9 ml of the drug solution comprising 5 ml of 0.25% bupivacaine and 1 ml of triamcinolone (40 mg). In group II, patients were administered 6 ml of PRP prepared by collecting 20 ml of patient's blood and running it through a centrifuge for 15 min at 1600 rpm. Then the upper layers of buffy coat and plasma were separately centrifuged for 7 min at 2800 rpm, thus giving 6 ml of PRP. Drug spread was ensured in all three compartments, that is, medial, middle, and lateral compartments of the knee joint.

Sample size was calculated on the basis of a previous study.[5] A sample size of 25 per group was calculated to achieve a power of 80%, with a confidence interval (CI) of 95% and type I error rate of 5%.

Pain relief, improvement in disability, and patient satisfaction were the primary outcomes of the study. The ease of administration of block, the side effects, and complications related to the procedure were the secondary outcomes.

Pain was assessed using NRS (Numeric rating scale) (0–10). Patients were asked to sit on a chair, stand, and walk before rating their pain. NRS was recorded at the following time intervals: half an hour before the procedure, half an hour after the injection, and 2 weeks, 1 month, 2 months, 3 months, 6 months, and 12 months after the procedure.

Patient satisfaction was assessed at 2 weeks, 1 month, 2 months, 3 months, 6 months, and 12 months after the procedure on a four-point scale: "excellent" when the pain was completely gone or reduced by 75% or more; "good" when the pain reduced by 50%–74%; "fair" when the pain reduced by 25%–49%; and "poor" when the pain reduction was less than 25% or there was an increase in pain.

Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) is a tool to evaluate the effectiveness of treatment in OA knees and informs about the health status of a patient over a period of time and the effect of treatment on the health status. In this study, WOMAC was calculated taking into consideration only those parameters which were answered by the patients. WOMAC was calculated half an hour before the injection and 2 weeks, 1 month, 2 months, 3 months, 6 months, and 12 months after the procedure.

Number of attempts and pain during injection were recorded to determine the ease of administration of the technique. All injections were fluoroscope guided, and the needle was advanced under fluoroscopic guidance. Pain was assessed on a four-point scale during administration of the injectate: 1 for no pain, 2 for mild pain, 3 for moderate pain, and 4 for severe pain.

Statistical Package for the Social Sciences (SPSS) version 20 (IBM SPSS Statistics Inc., Chicago, IL, USA) was used for statistical analysis. The unpaired *t*-test (to compare quantitative data of two independent groups) and Friedman test (for quantitative data within two groups) were used for quantitative data comparison of all clinical indicators. Chi-square test was used to compare the qualitative data. The results were considered to be statistically significant if the *P* value was ≤0.05.

Results

The two groups were comparable in age, weight, and gender distribution [Table 1].

Table 1: Distribution of age, gender, and weight in the two groups

Parameter	Group I IAKCS (*n*=25)	Group II IAKPRP (*n*=25)	*P*
Age (in years) Mean±SD	61.50±11.38	63.70±9.10	0.27
Weight (in kg) Mean±SD	64.75±8.65	68.70±9.93	0.88
Male-to-female ratio	20:5 (80%:20%)	22:3 (88%:12%)	0.37

IAKCS=intra-articular knee injection of corticosteroid, IAKPRP=intra-articular knee injection of PRP, PRP=platelet-rich plasma, SD=standard deviation

The variation in pain score in both the groups when compared to baseline at different time intervals was clinically and statistically significant. In group I, the mean pain score (NRS score) half an hour before injection was 8.50 ± 0.88, which decreased to 2.10 ± 1.16 half an hour after injection. The pain score was 2.50 ± 1.98, 2.30 ± 1.21, 2.90 ± 2.24, 2.55 ± 2.13, 4.10 ± 2.10, and 4.90 ± 2.23 at 2 weeks, 1 month, 2 months, 3 months, 6 months, and 12 months after injection, respectively. In group II, the mean pain score (NRS score) half an hour before injection was 8.60 ± 0.88, which decreased to 3.60 ± 1.66 half an hour after injection. The pain score was 4.85 ± 1.92, 3.95 ± 2.18,1.60 ± 1.23, 1.40 ± 1.14, 2.30 ± 1.21, and 2.90 ± 2.24 at 2 weeks, 1 month, 2 months, 3 months, 6 months, and 12 months after injection, respectively [Figure 1]. Patient in group I had lower pain scores at half an hour, 2 weeks, and 1 month after the procedure compared to group II patients ($P < 0.05$). Patients in group II had lower pain scores at 2, 3, 6, and 12 months after the procedure compared to group I patients ($P < 0.05$).

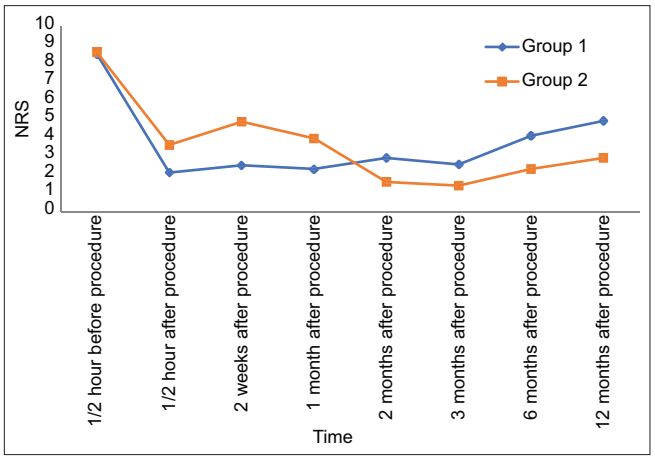

Figure 1: Pain score (NRS) at different time intervals in the two groups

When patient satisfaction was compared between the two groups, it was observed that there was a statistically significant better patient satisfaction in group I compared to group II at 2 weeks and 1 month. However, at 2, 3, 6, and 12 months, patient satisfaction was clinically and statistically better in group II compared to group I.

There was a clinically and statistically significant variation in WOMAC at different intervals of time when compared to WOMAC before injection in both the groups. In group I, the mean WOMAC half an hour before injection was 64.69 ± 16.83, which decreased to 20.60 ± 17.37 2 weeks after injection. WOMAC was 17.61 ± 12.14, 22.19 ± 19.77, 20.07 ± 17.99, 30.61 ± 13.14, and 37.61 ± 14.14 at 1, 2, 3, 6, and 12 months after injection, respectively. In group II, the mean WOMAC half an hour before injection was 72.05 ± 16.81, which decreased to 38.05 ± 18.54 at 2 weeks after injection. WOMAC was 31.84 ± 19.55,13.37 ± 10.08, 11.53 ± 9.02, 15.61 ± 12.24, and 17.41 ± 13.14 at 1, 2, 3, 6, and 12 months after injection, respectively [Figure 2]. It was clinically and statistically significantly better in group I at 2 weeks and 1 month after the procedure compared to group II ($P < 0.05$). However, it was clinically and statistically significantly better in group II at 2, 3, 6, and 12 months after the procedure compared to group I ($P < 0.05$).

When different subscales of WOMAC like pain, stiffness, and physical activity were compared between the two groups, results were clinically and statistically significantly better in group I ($P < 0.05$) at 2 weeks and 1 month after injection. Results were better in group II compared to group I at 2, 3, 6, and 12 months after the procedure.

Both the groups were comparable in ease of administration of the block. Majority of the patients in group I had mild pain and in group II had no pain on injection. Two patients in both the groups reported soreness and swelling after the injection. The soreness was resolved within 2–3 days with the use of cold fomentation. No serious side effects related to the technique or the injectate were observed.

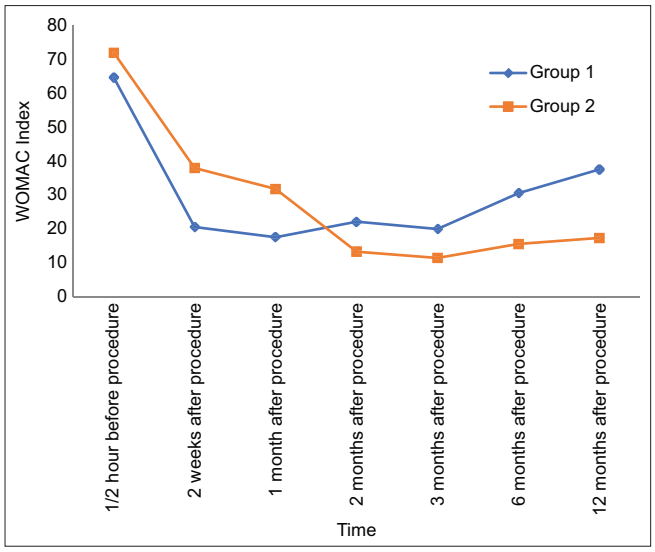

Figure 2: WOMAC at different time intervals in the two groups. WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

Discussion

In the present study, majority of patients in both the groups were in 50–70 years age group. Mean weight was about 65 kg, and 85% of them were females. Female preponderance in our study could be attributed to the social milieu of our region. Females are regularly engaged in domestic work, agricultural work, animal husbandry, and labor activities.

Pain scores were significantly less in group I than group II for 1 month after the injection. This could be due to the shorter onset of action of local anesthetic and corticosteroids. It has been postulated that local anesthetics relieve the pain by suppression of nociceptive discharge and the blockade of sympathetic reflex arc, axonal transport, sensitization, and anti-inflammatory effects. The mechanism of therapeutic effect of corticosteroids in OA knee is likely related to its potent anti-inflammatory effect, but their mechanism of action is complex. They interrupt the inflammatory and immune cascade at several levels, and thus reduce vascular permeability and inhibit accumulation of inflammatory cells, phagocytosis, production of neutrophil superoxide, metalloproteases, and metalloprotease activator and prevent the synthesis and secretion of inflammatory mediators like prostaglandins and cytokines.[4]

However, pain scores in group II were significantly less than in group I from 1 month after the procedure. Intra-articular knee PRP injection caused pain relief at 2, 3, 6, and 12 months after the injection. This was due to the onset of action of growth regenerative factors from PRP injection. Platelets in PRP are activated, and this activation causes the release of a large number various types of mediators from the platelet granules, which contain up to 800 different protein components. Majority of these components are not only different types of growth factors like transforming growth factor-beta, vascular endothelial growth factor, hepatocyte growth factor, insulin growth factor, PDGF, connective tissue growth factor, and fibroblast growth factor, but also soluble anti-inflammatory mediators like interleukin (IL) receptor antagonists (IL-1, IL-4, IL-8, IL-10, etc.) that may contribute to therapeutic effects. Preclinical studies have shown that the granule secretions have mainly a homeostatic effect with anabolic and anti-inflammatory impacts on joint tissues and cells.[9-15] Intra-articular injections of PRP are effective for the treatment of knee OA in early stages.

Patient satisfaction was similar to the pain scores trend. Similar results with improvement in pain scores and WOMAC resulting in good patient satisfaction after PRP and corticosteroid injections have been observed in other studies.[5-8,16-19]

In the present study, the injection was given using the same technique as the initial procedure, if pain relief was not adequate (NRS > 4). Ten patients in group I and four patients in group II required second injection during the study period. Some studies have administered repeated PRP injections at weekly or monthly interval, but in the present study, we administered only one injection and observed good pain relief in around 85% of patients at 2, 3, 6, and 12 months after the procedure.

In this study, pain on administration of the injectate was the most common side effect. Majority of the patients in both the groups had mild pain on injection. However, the pain was temporary and was relieved within few minutes of administration of the injectate. Fluoroscopy use involves radiation exposure and contrast medium administration. However, radiation exposure can be minimized by following standard operational principles. We used nonionic contrast medium (0.5–1 ml, omnipaque 350). Spread of contrast medium in all the three compartments, the "Moustache sign," was ensured before injecting the drug [Figure 3]. No side effects due to the use of contrast were observed.

The present study has few limitations. First, the results of the study may have shown the experience of one practitioner, which limits generalizability of the findings. Second, the long-term effects should be evaluated in the future based on the results of the short-term effects. In this study, patients were followed for 12 months, but trials could focus on long-term outcomes up to 2 years after the procedure. Third, this study was not conducted as a double-blinded study because with nontraditional modalities like fluoroscope, it is difficult to conduct a double-blinded, controlled study.

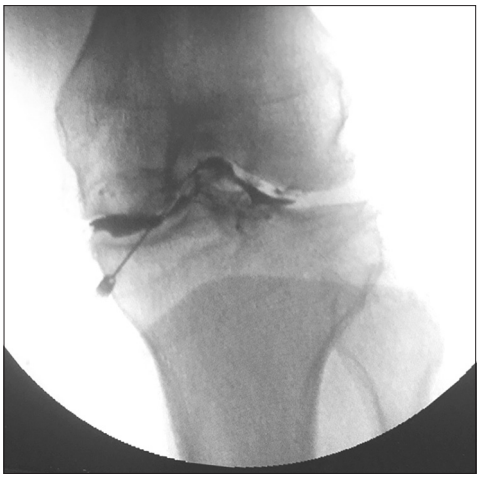

Figure 3: Moustache sign: spread of contrast medium in all three compartments (medial, middle, and lateral) of the knee joint

Conclusions

Both the techniques of injection, that is, fluoroscope-guided intra-articular injection of bupivacaine with corticosteroids and PRP, were effective and provided good pain relief to the patients with symptomatic OA knee. However, pain relief and improvement in disability were better and sustained over a period of 1 year with administration of PRP.

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Conflicts of interest
There are no conflicts of interest.

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