

# Comparative Study of Post-injection Pain in Superolateral vs. Inferolateral Approach in Platelet-rich Plasma Injection for Osteoarthritis of Knee: A Retrospective Study

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## ABSTRACT

**Background:** Injection site pain is not uncommon after interventional procedures particularly after platelet-rich plasma (PRP) injection. This retrospective study aims to find out the incidence of post-injection pain after injection and any relation of post-injection pain with injection site in PRP injection for osteoarthritis of the knee.

**Methods:** Patients of osteoarthritis of the knee who received PRP injection were grouped into two. Group A received PRP injection at the superolateral approach and group B received PRP injection at the inferolateral approach. Pre-procedure pain score on verbal rating score and post-procedure injection pain were compared in both the group and post-procedure injection pain were compared between the two groups.

**Results:** The sample size was calculated accepting alpha error as 0.05 and power of study 80%. The inferolateral approach was thought to be more painful because of narrowing of injection space and mean pain score was presumed as 6/10 ± 1 on the verbal rating scale (VRS). The superolateral approach was considered as less painful and anticipated pain score on VRS was 5/10. The calculated sample size was 16 in each group. However, in our study sample size were 35 in group A and in group B, it was 34. Demographic profiles were compared using students t-test and Chi-square test and the two groups were found similar in age and sex ratio. Pain score of two groups was compared using the Mann-Whitney U test and was found comparable (6.31 ± 1.1 in group A and 5.76 ± 1.46 in group B). Post-injection pain at 7 days was compared between groups and was also found similar (4.62 ± 1.7 in group A and 4.74 ± 1.4 in group B) without any statistically significant difference between two groups. Pre-procedure pain (6.04 ± 1.31) in both groups compared with post-injection pain (4.68 ± 1.55) of both groups and were found less than pre-injection pain and was found statistically significant ( $p < 0.00001$ ).

**Discussion:** Post-injection pain after 7 days after PRP injection were found to be less than pre-procedure injection and there is no relation pain with the injection site.

**Keywords:** Post-injection pain, Platelet-rich plasma injection, Osteoarthritis of the knee.

**How to cite this article:** Mistry SD, Bhattacharya D, Das S, Das G. Comparative Study of Post-injection Pain in Superolateral vs. Inferolateral Approach in Platelet-rich Plasma Injection for Osteoarthritis of Knee: A Retrospective Study. *J Recent Adv Pain* 2018;4(3):96-99.

**Source of support:** Nil

**Conflict of interest:** None

## INTRODUCTION AND BACKGROUND

Interventional pain management is done to alleviate pain and to avoid major surgeries like knee joint replacements. But most patients fear injection pain and post-injection pain. Most patients posted for procedures are interested to know the likelihood of increased pain after the procedure. We need scientific data regarding the chance of increased pain and any relation with the injection site.

The PRP injection is one of the recent interventions done in osteoarthritis of the knee. It is a safe intervention with very less reported side effects. Functional improvement has been reported at most of the studies. However, injection site pain after any interventional procedures for a few days is a common complaint. This is also true for PRP injection at the knee. But searching literature, we could not find any good publication about the incidence of post-injection pain or any relation about the site of injection and post-procedure pain. With this background, we wish to study the incidence of post-injection pain with its relationship with the injection site if any.

There are four approaches to intra-articular knee injection. Superolateral (beneath the upper lateral margin of patella), superomedial (beneath the upper medial margin of patella), inferolateral or anterolateral (below and lateral to patella) and inferomedial or anteromedial (below and medial to patella). Superolateral (SL) and inferolateral (IL) are two most common sites of intra-articular injection.

## Research Hypothesis

We aim to find out any deference of amount of pain after injection of PRP in osteoarthritis of the knee at inferolateral part of the knee which is more commonly

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done with superolateral injection site assuming that SL injection site will produce less pain as there is no chance of touching damaged cartilage. A secondary objective was to find an increase of post-injection pain after 7 days.

Post-injection pain is a common observation, but unfortunately, there is a scarcity of publications on the site of injection and incidence. This study will help to understand the magnitude of the problem and relation with the injection site.

Anitua et al.<sup>1</sup> about 14 years back in 2004 published this article "Autologous platelets as a source of proteins for healing and tissue regeneration". PRP has been used in many different types of regeneration therapy.

Many randomized controlled trials have proved its simplicity and superiority over other interventional procedures in recent publications too. Shen et al.<sup>2</sup> in their meta-analysis proved its superiority in 2017 in this article "The temporal effect of platelet-rich plasma on pain and physical function in the treatment of knee osteoarthritis: systematic review and meta-analysis of randomized controlled trials."

Different animal experiments like the published article by Yin et al.<sup>3</sup> proved it in animals too. Several other studies proved its efficacy in osteoarthritis of knee.<sup>4-6</sup>

Nusstein et al.<sup>7</sup> in a study has shown that even lignocaine injection in ligament can produce an increase of pain in 20% patients and injection of artiacaine increased pain in 31% patients on next day.

Despite hundreds of publications on PRP injection in osteoarthritis of the knee, there is a scarcity of literature about the post-procedure pain and discomfort after PRP injections. One published literature has shown the increase of pain after local anesthetic injection in ligaments in 20–31% patients.

## METHODS

### Study Design—Retrospective Study

*Study settings:* This study was completed after compiling data available at RG Kar Medical College pain clinic in patients where PRP was injected for OA knee.

After preparation of autologous PRP, it is injected at either superolateral or inferolateral aspect of the knee joint. Average pain for next 7 days was recorded by verbal rating scale. After collecting data, the two groups were compared for the average post-procedure pain and total incidence of post-procedure pain.

Most of the previous studies for PRP in OA knee do not mention about post-procedure pain. We expect that in some population of patients, there will be an increase in pain at the injection site. Thus, we shall compare the difference of pain in two different groups.

All available data from 1st July 2017–30th June 2018 was collected and analyzed for statistical significance. Patients were divided into two groups based on site of injection.

- *Group A:* Patients received PRP injection at the inferolateral side of the knee.
- *Group B:* Patients received PRP injection at the superolateral side of the knee

Average pain score at rest of 7 days post-injection period is measured by verbal rating scale and compared with pre-injection rest pain.

- *Place of study:* Pain Clinic, Department of Anesthesiology, RG Kar Medical College and Hospital, Kolkata.
- *Period of study:* One year from 1st July 2017 to 30th June 2018.
- *Study population:* Men and women aged 40–80 years who received platelet-rich plasma injection of osteoarthritis of the knee at RG Kar Medical College and Hospital, Kolkata.

The sample size was calculated based on a similar study where an increase in pain was noticed in about 20% of patients after injection of lignocaine and 31% with artiacaine. We assumed that PRP will increase the pain further because of possible regeneration process in next 7 days. We assumed that pain will increase in at least 10 to 20% situation after injection of PRP in standard inferolateral injection site based on earlier publication. We also assumed that SL injection site will produce less pain and there is no chance of touching injured cartilage at SL approach and taken at VRS anticipated as  $5 \pm 1$ . We have taken the alpha error as 0.05, beta error as 0.2 and power of study 0.8.

### Study Parameters

- Mean pain in group A— $6 \pm 1$
  - Anticipated mean pain in group B—5
  - Alpha 0.05
  - Beta 0.2
  - Power 0.8
- Thus, the sample size calculated was 32

### Inclusion Criteria

- ASA grade 1 and 2
- Patients aged 40–80 years.
- Patients gave consent for the study.
- VRS score  $\geq 3$

### Exclusion Criteria

- Patients refusal or non-cooperative patients,
- Patients aged  $<40$  and  $>80$  years of age,
- Patients not intelligent enough to give VRS score

## Study Variables

- Age
- Sex
- Site of injection

## Data Collections and Interpretation

- Data were collected from the records of a pain clinic.
- Any other side/adverse effects if recorded were excluded from the study.

## Procedures

All data of patients who fulfill the inclusion and exclusion criteria was recorded in a master/grand chart for further analysis.

## Outcome Definitions and Parameters

The primary outcome is a comparison of two groups. The secondary outcome is the calculation of incidence of post-injection pain after PRP injection in OA knee.

**Table 1:** Comparison of age

	Group A (IL inj)	Group B (SL inj)
Sample size (n)	35	34
Range	43–74 years	44–78 years
Arithmetic mean	58.97+ 8.08 years	59.53+8.3 years
95% CI for the mean	56.1944 to 61.7456	56.7401 to 62.3199
Standard deviation	8.08	8.3
Statistical difference between two groups*	$p = 0.7780$	

\*Two groups are comparable as  $p$  value is not significant, which was calculated using independent samples student's  $t$ -test

**Table 2:** Male/female sex ratio between two groups

	Group A (IL)	Group B (SL)
Sample size (n)	35	34
Male	13 (37.14%)	15 (44.11%)
Female	22 (62.85%)	19 (55.88%)
Statistical difference between two groups*	$p = 0.5552$	

\*Using Chi-square test for the comparison of two proportions (from independent samples)

**Table 4:** Post-procedure VRS compared between two groups

	Group A (IL)	Group B (SL)
Sample size (n)	35	34
VRS range	1–8	1–7
Mean VRS	4.62 + 1.7	4.74 + 1.4
95% CI for the mean	4.036 to 5.204	4.2515 to 5.2285
Statistical difference between two groups*	$p = 0.1415$	

\*Using Chi-square test for the comparison of two proportions (from independent samples)

Data obtained was entered in the master data sheet. Parametric test, e.g.,  $t$ -test was applied to see the statistical significance of the difference in age and non-parametric test, e.g. Chi-square test was applied for the male/female ratio in two groups. Mann–Whitney U test was done for non-parametric data of pain score between two groups. Statistical analysis was done by using appropriate statistical software/formula.

## RESULTS

Two groups were compared using  $t$ -test and were found similar (Table 1).

Male/female sex ratio between two groups was compared and found comparable with of statistically significant difference (Table 2).

Pre-procedure VRS were compared with non-parametric Mann–Whitney U test and were also found comparable with no statistically significant difference (Table 3).

Post-procedure VRS were compared between two groups using non-parametric Mann–Whitney U test and were also found comparable with no statistically significant difference (Table 4).

Post-procedure inj pain after 7 days were compared with Mann–Whitney U test with pre-procedure pain and there were a statistically significant reduction of pain score at 7th day and no increase of pain (Table 5).

## DISCUSSION

This retrospective study reveals that post-procedure injection pain does not depend on the injection site in PRP

**Table 3:** Pre-procedure VRS compared between two groups

	Group A (IL)	Group B (SL)
Sample size (n)	35	34
VRS range	5–8	3–8
Mean VRS	6.31+ 1.1	5.76 + 1.46
95% CI for the mean	5.9321 to 6.6879	5.2506 to 6.2694
Statistical difference between two groups*	$p = 0.1416$	

\*Using Chi-square test for the comparison of two proportions (from independent samples)

**Table 5:** Comparison between pre- and post-procedure injection pain

	Pre-procedure pain	Post-procedure pain
Sample size (n)	69	69
VRS range	3–8	1–8
Mean VRS	6.04 + 1.31	4.68 + 1.55
95% CI for the mean	5.7253 to 6.3547	4.3076 to 5.0524
Statistical difference between two groups*	$p < 0.00001$	

\*Using Chi-square test for the comparison of two proportions (from independent samples)

injection in osteoarthritis of the knee. It was also found that at 7th-day the pain was reduced that pre-procedure pain. The increase of post-injection pain was found in some patients which were not statistically significant.

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