# Efficacy of Intra-articular Injection of Platelet Rich Plasma in Improving Pain and Function in Knee Osteoarthritis

Nimrah Patail, DO and Tyler Williams, DO
Faculty Advisor: Dr. Ehdaie
Houston Methodist Family Medicine Residency Program

## RESEARCH OBJECTIVE

To assess the efficacy of intra-articular injection with Platelet Rich Plasma in comparison with Normal Saline placebo in reducing pain and stiffness and improving physical function in knee osteoarthritis as measured by overall WOMAC (Western Ontario and McMaster Universities Osteoarthritis Index) scores.

## INTRODUCTION

- Osteoarthritis is commonly encountered in primary care Settings as it affects an estimated 32.5 million adults in the United States.
- Pain from Osteoarthritis significantly limits patients' function and quality of life.
- Intra-articular PRP injection is a newer treatment modality that needs more investigation to explore its potential utility.

## DESIGN

-Evidence-based review of Double Blind RCTs
-PubMed search using key words: "knee osteoarthritis", "platelet rich plasma", "WOMAC", "randomized controlled trial", "injection"

## METHODS

**Major inclusion criteria**

Adults (age 20-80) with radiographically confirmed OA, without prior PRP injection or surgical procedures in participating knee

**Major exclusion criteria**

prior knee injection or surgery, on anticoagulant, concomitant symptomatic knee injury, hematologic diseases.

**Setting:**

-outpatient centers in the USA, India and Taiwan

**Intervention:**

-Randomized patients received either a single or series of PRP injections, or a single or series of Normal Saline placebo injection and followed for up to 12 months.

**Outcome Measured:**

-Patients completed the WOMAC Index at baseline 0 months, and again, at various intervals for up to 12 months
-improvement in total WOMAC scores was used as a primary endpoint in each of the studies.

**Study Funding / Sponsors / Potential Conflicts of Interest**

Study 1 : Funded by Kaohsiung Veterans General Hospital Research Grant

Study 2: Financial support from Prof D.S. Grewal Memorial Orthopedics Society, Chandigarh and Indian Arthroplasty Assoc.

Study 3: Author is a consultant for Arthrex Inc., who provided funding for this study

## RESULTS TABLES

**Table 3.** WOMAC and IKDC Clinical Scores for PRP, HA, and NS Groups

| | Baseline (T1) | 1 mo (T2) | 2 mo (T3) | 6 mo (T4) | 12 mo (T5) | Post Hoc Test[†] ($P < .05$) |
|---|---|---|---|---|---|---|
| WOMAC score | | | | | | |
| PRP | 52.81 ± 18.14 | 60.91 ± 17.35 | 63.84 ± 17.86[‡§] | 62.28 ± 18.47[‡§] | 63.71 ± 20.67[‡§] | T2 > T1; T3 > T1; T3 > T2; T4 > T1; T5 > T1 |
| Change from baseline, % | — | 15[¶] | 21[¶] | 18[¶] | 21[¶] | |
| HA | 52.67 ± 18.06 | 60.29 ± 20.95 | 57.32 ± 21.85 | 52.9 ± 19.76 | 49.33 ± 21.51 | T2 > T1; T2 > T4; T2 > T5 |
| Change from baseline, % | — | 14[¶] | 9 | 0 | −6 | |
| NS | 48.59 ± 16.92 | 54.26 ± 17.16 | 49.79 ± 17.47 | 49.7 ± 15.61 | 46.94 ± 16.74 | T2 > T1; T2 > T4; T2 > T5 |
| Change from baseline, % | — | 12[¶] | 2 | 2 | −3 | |
| IKDC score | | | | | | |
| PRP | 35.71 ± 13.77 | 43.61 ± 14.86 | 47.83 ± 15.85[‡] | 47.13 ± 16.24[‡§] | 49.93 ± 17.74[‡§] | T2 > T1; T3 > T2; T4 > T2; T5 > T2 |
| Change from baseline, % | — | 22 | 34 | 33[¶] | 40[¶] | |
| HA | 35.93 ± 12.71 | 43.57 ± 15.67 | 42.29 ± 17.18 | 40.29 ± 15.76 | 38.64 ± 16.09 | T2 > T1; T2 > T4; T2 > T5 |
| Change from baseline, % | — | 21 | 18 | 12 | 8 | |
| NS | 33.3 ± 10.52 | 38.65 ± 11.07 | 35.56 ± 11.35 | 34.2 ± 11.11 | 32.96 ± 11.15 | T2 > T1; T2 > T4; T2 > T5 |
| Change from baseline, % | — | 16 | 7 | 3 | −1 | |

### STUDY 1

a total of 87 osteoarthritic Knees (53 patients) were randomly assigned to 1 of 3 groups, receiving 3-weekly injections of either leukocyte-poor PRP (31) knees, Hyaluronic Acid (29 knees), or normal saline placebo (27 Knees).

WOMAC score was collected at baseline and at 1, 2, 6, and 12 months after

### STUDY 2

A total of 78 patients (156 knees) with bilateral OA were divided randomly into 3 groups.

Group A (52 knees) received a single injection of PRP,
group B (50 knees) received 2 injections of PRP 3 weeks apart, and
group C (46 knees) received a single injection of normal saline.

statistically significant improvement in all WOMAC parameters was noted in groups A and B within 3 weeks and lasting until the final follow up at 6 months, with Slight worsening at the 6-month follow up

**TABLE 3**
Mean Scores and Percentage Change in Each Parameter of the WOMAC Score Compared With Baseline at Each Follow-up for All 3 Groups

| | Follow-up* | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Group A | | | | Group B | | | | Group C | | | |
| WOMAC Parameter | 0 | 1st | 2nd | 3rd | 0 | 1st | 2nd | 3rd | 0 | 1st | 2nd | 3rd |
| Pain | | | | | | | | | | | | |
| Mean | 10.18 | 4.26 | 3.74 | 5.00 | 10.62 | 4.38 | 4.88 | 6.18 | 9.04 | 8.48 | 10.35 | 10.87 |
| *P* value | Mean scores decreased significantly[†] | | | | Mean scores decreased significantly[†] | | | | Slight increase (significant)[‡] | | | |
| % change[‡] | | −61 | −70 | −58 | | −61 | −57 | −42 | | 4 | 18 | 25 |
| *P* value | At each follow-up, the percentage benefit from baseline was greater in groups A and B than in group C ($P < .001$); no difference between groups A and B | | | | | | | | | | | |
| Stiffness | | | | | | | | | | | | |
| Mean | 3.12 | 2.12 | 1.76 | 2.10 | 3.50 | 2.28 | 2.00 | 1.88 | 2.70 | 2.76 | 2.91 | 2.76 |
| *P* value | Mean scores decreased significantly[†] | | | | Mean scores decreased significantly[†] | | | | Slight increase (not significant) | | | |
| % change[‡] | | −29 | −48 | −31 | | −36 | −47 | −52 | | −2 | 10 | 2 |
| *P* value | At each follow-up, the percentage benefit from baseline was greater in groups A and B than in group C ($P < .001$); no difference between groups A and B | | | | | | | | | | | |
| Physical function | | | | | | | | | | | | |
| Mean | 36.56 | 18.98 | 16.98 | 20.08 | 39.10 | 18.30 | 18.82 | 22.40 | 33.80 | 34.54 | 37.43 | 39.46 |
| *P* value | Mean scores decreased significantly[†] | | | | Mean scores decreased significantly[†] | | | | Slight increase (significant)[‡] | | | |
| % change[‡] | | −48 | −58 | −50 | | −54 | −54 | −42 | | 1 | 11 | 20 |
| *P* value | At each follow-up, the percentage benefit from baseline was greater in groups A and B than in group C ($P < .001$) | | | | | | | | | | | |
| Total | | | | | | | | | | | | |
| Mean | 49.86 | 25.36 | 22.48 | 27.18 | 53.20 | 24.96 | 25.70 | 30.48 | 45.54 | 46.78 | 50.70 | 53.09 |
| *P* value | Mean scores decreased significantly[†] | | | | Mean scores decreased significantly[†] | | | | Slight increase (significant)[‡] | | | |
| % change[‡] | | −50 | −60 | −51 | | −55 | −54 | −43 | | 2 | 12 | 20 |
| *P* value | At each follow-up, the percentage benefit from baseline was greater in groups A and B than in group C ($P < .001$) | | | | | | | | | | | |

TABLE 3
WOMAC Osteoarthritis Index Scores for ACP and Placebo Groups*

| WOMAC | Baseline | 1 Week | 2 Weeks | 2 Months | 3 Months | 6 Months | 12 Months |
|---|---|---|---|---|---|---|---|
| Overall | | | | | | | |
| ACP | 47 (41-53) | 35 (29-40) | 22 (15-29)[†] | 14 (5-23)[†] | 10 (3-18)[†] | 11 (3-20)[†] | 10 (4-17)[†] |
| Δ from baseline, % | | 26[‡] | 53[‡] | 70[‡] | 78[‡] | 72[‡] | 78[‡] |
| Placebo | 46 (40-53) | 38 (30-46) | 36 (28-44) | 31 (22-41) | 37 (30-45) | 44 (36-53) | 43 (33-54) |
| Δ from baseline, % | — | 18 | 22 | 32[‡] | 20 | 4 | 7 |
| Pain | | | | | | | |
| ACP | 10 (9-11) | 7 (6-8) | 4 (2-6)[†] | 3 (1-5)[†] | 2 (1-4)[†] | 3 (1-4)[†] | 2 (1-4)[†] |
| Δ from baseline, % | | 30[‡] | 59[‡] | 71[‡] | 79[‡] | 70[‡] | 76[‡] |
| Placebo | 11 (10-12) | 8 (6-10) | 8 (6-9) | 7 (5-9) | 8 (6-9) | 9 (7-11) | 9 (6-11) |
| Δ from baseline, % | | 24[‡] | 27[‡] | 34[‡] | 28[‡] | 13 | 19 |
| Stiffness | | | | | | | |
| ACP | 4 (4-5) | 3 (2-4) | 2 (1-3)[†] | 1 (1-2) | 1 (0-2)[†] | 1 (0-2)[†] | 1 (0-2)[†] |
| Δ from baseline, % | | 30[‡] | 53[‡] | 67[‡] | 76[‡] | 76[‡] | 77[‡] |
| Placebo | 4 (4-5) | 3 (2-4) | 3 (2-4) | 3 (2-3) | 3 (2-4) | 4 (3-5) | 4 (3-5) |
| Δ from baseline, % | | 27[‡] | 30[‡] | 43[‡] | 28[‡] | 9 | 6 |
| Physical function | | | | | | | |
| ACP | 32 (27-37) | 24 (21-28) | 16 (10-21)[†] | 9 (3-16)[†] | 7 (2-12)[†] | 8 (2-14)[†] | 7 (3-11)[†] |
| Δ from baseline, % | | 24[‡] | 51[‡] | 71[‡] | 78[‡] | 75[‡] | 78[‡] |
| Placebo | 31 (26-37) | 27 (21-32) | 25 (20-31) | 22 (15-29) | 27 (21-32) | 31 (25-37) | 30 (23-37) |
| Δ from baseline, % | — | 15 | 19 | 30[‡] | 15 | 0 | 3 |

### STUDY 3

114 patients were screened, and 30 were ultimately included in the study.

Randomized to receive either PRP (n=15) or saline placebo (n=15) for a series of 3 weekly injections.

WOMAC scores served as the primary efficacy outcome measure. Patients were followed for 1 year total.

## DISCUSSION

In knee osteoarthritis, PRP injection is clinically superior to Normal Saline placebo in achieving reduction in pain and stiffness, and improvement of physical function as measured by overall WOMAC scores at 6 months, up to 12months.

Further studies will be needed to discern the long-term effects of multiple injections and the ideal inter-injection timeframe, and to compare different PRP preparations against each other

Some study limitations:
- Strict inclusion and exclusion criteria make generalizability difficult
- Varying randomization across studies (ex. Randomization of patients vs. randomization of knees)
- lack of studies available regarding long-term safety, cumulative effects

In terms of practical application: cost is a current limiting factor for a large number of patients, as PRP injections are not routinely covered by insurance.

## CONCLUSIONS

| Author | WOMAC Changes (Initial-> 6 months) | | P-value |
|---|---|---|---|
| Lin, et al | IA Placebo= 45.54 -> 53.09<br>IA PRP= 49.85 -> 27.18 | Δ +7.55<br>Δ 22.67 | <.001 |
| Patel, et al | IA Placebo= 49.7 -> 48.59<br>IA PRP= 62.28 -> 52.81 | Δ 1.11<br>Δ 9.47 | <.05 |
| Smith, et al | IA Placebo= 46 -> 44<br>IA PRP= 47->11 | Δ 2<br>Δ 36 | <.05 |

| Clinical Recommendations | SOR | References |
|---|---|---|
| At 6 months, PRP injections resulted in a statistically significant improvement in Overall WOMAC scores in adults with knee osteoarthritis. | B | Lin, et al<br>Patel, et al<br>Smith, et al |

## FUTURE QUESTIONS FOR FURTHER STUDY

What is the ideal PRP preparation to receive maximal effect?

Is there any difference in effect between leukocyte-poor vs. leukocyte-rich PRP? (all studies included used leukocyte poor)

What are the cumulative, long-term effects of PRP injections?

## REFERENCES

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