

Unveiling the Clinical Response to Platelet-Rich Plasma in Knee Osteoarthritis

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INTRODUCTION: Leukocyte-poor platelet-rich-plasma (LP-PRP) is an autologous biologic that has been shown to decrease inflammation and pain in knee osteoarthritis (KOA) patients similar to conventional pharmacologic therapies.¹ However, current literature regarding PRP lacks appropriate power to drive clinical decisions, due to the lack of preparation standardization and uncertainty around the mechanism of action that promotes a positive response to treatment.² The purpose of this study is to identify key demographic factors, cellular and molecular components of LP-PRP that influence better PROMIS Pain and Function outcomes in patients treated for symptomatic KOA.

METHODS: In this retrospective cohort study, de-identified data from 34 patients ages 30-85 diagnosed with KOA (KL grades I-IV) and symptomatic knee pain treated with a single, intra-articular PRP injection. A total of 34 LP-PRP samples were collected, 8 of which were bilateral (n=16 knees) and 18 unilateral knees. Completed cases with PROMIS Pain and Function scores were gathered at baseline and 3-months following LP-PRP injection. The change between baseline and 3-month PROMIS Pain and Function scores were calculated. Patients defined as a “responder” had a difference of 10% from baseline PROMIS, while non-responders did not reach that threshold. Multiplex immunoassays were conducted using a Human XL Cytokine 46-plex Luminex assay to measure protein concentrations and correlations were calculated and displayed as a heat map (**Figure 2C**) where red denotes positive and blue denoted negative relationships between markers.

RESULTS: A total of 13 and 21 samples evaluated had OA grades I-II, III-IV. BMI ranged from 16 – 32 (mean = 25.6). Of patients who reported, 9 samples had an acute injury while 20 samples had a chronic injury. A total of 18 cases were unilateral while 16 cases were bilateral. There was a significant difference in PROMIS Pain between baseline and 3-months post-injection (baseline: 55.0 ± 6.3 , 3-month: 61.6 ± 7.2 , $p < 0.05$). Of the completed cases, 8 subjects had a positive response at 3-months post-injection compared to baseline, while 2 subjects responded negatively to LP-PRP (**Figure 1**). Detectable inflammatory, anti-inflammatory, and degenerative factors were detectable in 8 positive responders and 2 negative responders to LP-PRP treatment (**Figure 2A**). Of the responders, there was a significant increase in GCSF (mean = 37.8 ± 9.48 , $p = 0.03$), IL-12 (mean = 24.5 ± 11.3 , $p = 0.03$), and IL-1b (mean = 4.5 ± 1.55 , $p = 0.004$) concentrations compared to patients who did not respond (**Figure 2B**). GCSF positively correlated with RANTES ($p = 0.71$) and PDGF AB/BB ($p = 0.74$). IL-1b was positively correlated with IL-13 ($p = 0.77$) (**Figure 2C**). Furthermore, of those who reported a secondary procedure (e.g., injection, surgery) up to 6 months after LP-PRP injection, 6 had repeat PRP, 1 had a repeat of either HA or steroid, and 1 had an undisclosed type of non-surgical intervention. For surgical interventions, 2 had cartilage repair, 4 had total knee arthroplasty, and 2 had an undisclosed surgical intervention.

DISCUSSION: The main finding of the study was a significant reduction in PROMIS Pain observed in 8 joints from 7 subjects’ treatment with a single intra-articular LP-PRP injection. Of the responders, there was a significant increase in GCSF, I-1b, and IL12. Further investigation is necessary to determine the association between these inflammatory factors in knee OA. Limitations include heterogeneity of donor, including grade of OA and other biological factors (e.g., amount of sleep, physical activity, eating habits) which could transiently affect the collected LP-PRP sample. Another limitation included unanticipated decreased patient follow-up over time.

SIGNIFICANCE/CLINICAL RELEVANCE: The molecular analysis of the clinical responder’s LP-PRP will help provide data necessary to personalize PRP formulations in the future to improve treatment efficacy of KOA.

REFERENCES:

¹ Di Martino A, et al. Leukocyte-Rich versus Leukocyte-Poor Platelet-Rich Plasma for the Treatment of Knee Osteoarthritis: A Double-Blind Randomized Trial. *Am J Sports Med.* 2022;50(3):609-617.

² Hurley ET, et al. Experts Achieve Consensus on a Majority of Statements Regarding Platelet Rich Plasma Treatments for Treatment of Musculoskeletal Pathology. *Arthroscopy.* 2023 Aug 23; S0749-8063(23)00673-4.

IMAGES AND TABLES:

