Intraarticular Platelet Rich Plasma vs Corticosteroid injections for Sacroiliac Joint Pain – A Double Blinded, Randomized Clinical Trial

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Running Title:

PRP vs Steroid Intraarticular Injections for Sacroiliac Pain

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Abstract

Objective: Using stringent inclusion criteria, a double-blinded study protocol, and fluoroscopic guided injections, we compare intraarticular sacroiliac joint platelet rich plasma injections to intraarticular steroids

Design: Double-blind, randomized controlled trial.

Setting: Two large university-based interdisciplinary spine centers.

Subjects: 26 patients after positive diagnostic block (>80% relief)

Methods: Subjects who a positive diagnostic block were randomized to either undergo a fluoroscopically-guided intra-articular injection of steroid or platelet rich plasma injection. Follow-up was at 1-month, 3 months, and 6-months. Outcomes included level of pain as indicated on a 0- to 100-mm Numeric Pain Rating Scale and functional disability score using the Oswestry Disability Index (ODI).

Results: At one, three, and six months, both groups improved, however subjects who received steroid injections reported lower pain scores than subjects who received platelet rich plasma. Using categorical data, we observed significantly more responders (defined as pain scores which improved by 50% or more from baseline) at one and three months in the group that received steroids compared to the group that received platelet rich plasma.

Conclusion: While both groups showed improvements in pain and function, the steroid group had significantly greater response and significantly more responders than the PRP group.

Introduction

Sacroiliac joint (SIJ) pain has been broadly defined as pain located in the area of the SIJ that can be elicited by various pain provocation tests and relieved after infiltration of the joint with local anesthetic [1]. Given the heterogeneity and size of the SIJ, the clinical presentation of SIJ pain can be quite variable. The prevalence of SIJ pain has been reported to range from 10-62% based on the clinical setting with a point prevalence around 25% [2]. This wide variation in prevalence rates is likely attributed to the use of different injection methods, differing diagnostic criteria, and variation in inclusion criteria.

Platelet-rich plasma (PRP) has emerged as a safe and promising treatment modality for reducing symptoms in musculoskeletal injuries[3,4]. Platelets are a source of growth factors (GFs) and other proteins which are essential for maintaining an optimal environment for the repair and regeneration of injured tissues. Growth factors contribute to repair activities including stimulating type I collagen synthesis, chemotaxis, stimulating the differentiation of mesenchymal cells to those involved in repair, including fibroblasts and chondrocytes, and promotion of angiogenesis [5].

Given the role of platelets and their secreted GFs in the physiologic response to injury, current research has postulated that PRP can similarly mimic elements of the body's healing process and be beneficial in augmenting joint repair. Previous studies have

reported positive outcomes in using PRP to treat a variety of conditions, including chronic tendinopathy, soft tissue injuries, and ligamentous injuries [6].

Currently, there is limited high-quality research evaluating the efficacy of PRP for SIJ pain. Utilizing stringent inclusion criteria, a double-blinded study protocol, and fluoroscopic-guidance for injections, our hypothesis is that PRP would provide similar or better pain and functional improvement when compared with intraarticular steroid injections.

Methods

This is a double-blind, randomized controlled trial conducted at two university-based interdisciplinary spine centers. Institutional Review Board approval was obtained at both Columbia University Medical Center and Weill Cornell Medical Center.

The following inclusion screening criteria were used identify patients: 1) chronic unilateral low back pain with NPRS of at least 5, without radiculopathy; 2) positive response to at least 3 pain provocation maneuvers, such as distraction test, thigh thrust, Gaenslen's test, compression test, sacral thrust [7]; 3) lack of improvement in symptoms despite at least 4 weeks of physical therapy. Patients were excluded from the study if they were less than 18 or over 80 years of age, had midline pain above the level of L5, or exhibited signs of nerve root impingement. Those with coagulopathy, systemic infection,

and pregnancy were also excluded. No patients included had prior sacroiliac joint injections or interventional procedures.

A total of 64 patients met screening inclusion criteria and proceeded with a diagnostic intra-articular block using 2% lidocaine, using Spine Intervention Society (SIS) guidelines [8]. Patients were positioned prone and the injection site was prepped and draped using sterile technique. The injection site was marked and the overlying skin was anesthetized using 1% lidocaine. Using intermittent and live fluoroscopy, a 22-gauge 3.5-inch spinal needle was introduced into the inferior margin of the SIJ and 0.5-1 mL of contrast medium (Omnipaque) was injected to confirm intra-articular placement of the needle. Once confirmed, the joint was infiltrated with 2 mL of 2% lidocaine. Thirty minutes after the first screening block, patients were asked to quantify pain based on the NPRS. Only those who responded with >80% pain relief directly after confirmed intraarticular block were included in the study [9].

Of the initial 64 patients, 30 patients had a positive diagnostic intraarticular block. 27 patients did not achieve the threshold of pain relief (80%). In 7 patients, despite multiple attempts, we were not able to achieve satisfactory intraarticular flow. After a positive diagnostic block, 4 patients decided to disenroll in randomization and move forward with PRP injection directly (Figure 1).

A total of 26 patients were randomized to either undergo an intra-articular corticosteroid injection or PRP injection into the SIJ. Each of the 26 procedures were double-blinded.

Only the research coordinator and one nurse (who did not perform any follow-up evaluations) were aware of which patient received which injection. All 26 patients had blood drawn peripherally to ensure blinding; for those randomized to the steroid group this blood was discarded rather than being placed in PRP centrifuge. Approximately 60 mL of blood was drawn and centrifuged for 15 minutes. EmCyte PurePRP® II kits were used. The EmCyte PurePRP® II kits are reported to produce a reduced Red Blood Cells PRP product with platelet concentration of $> 1 \times 10^6$ platelets per μL [10]. The true makeup and platelet concentration of the PRP injectate is beyond the scope of this study. Blood was obtained and handled in sterile conditions during all steps of PRP preparation.

The nurse then placed either PRP or steroid into a sterile 6cc syringe and covered the syringe with opaque tape to blind the proceduralist. Intraarticular SIJ injections were again performed using SIS guidelines with 22-gauge 3.5-inch spinal needle introduced into the inferior margin of the SIJ and 0.5-1 mL of contrast medium (Omnipaque) used to confirm intra-articular placement of the needle. Once the needle was in place and adequate flow pattern obtained under fluoroscopy, the covered sterile syringe was then handed to the proceduralist for injection. The steroid group received a single injection consisting of a combination of 1 mL of betamethasone sodium phosphate and acetate suspension (6mg/mL) and 1 mL of 2% lidocaine. The PRP group received a single injection of 2mL PRP.

Two primary outcomes were evaluated at 1-month, 3 month, and 6-month intervals: level of pain as indicated on a 0- to 100-mm NPRS and functional disability score using the

Oswestry Low Back Pain Disability Questionnaire. The 1-month follow-up assessment was obtained through an office visit encounter. For the subsequent 2nd and 3rd month assessment, a phone call follow-up was performed. Any complications pre and post-procedure were also recorded throughout the duration of the study.

Statistical analyses were conducted using IBM SPSS version 27. Differences in categorical demographic and outcome data of subjects who received PRP and subjects who received steroid injections were evaluated using Fisher exact tests. The Shapiro-Wilk test was utilized to evaluate the normality of continuous data and all data were found to be normally distributed. Continuous demographic and outcome data differences between groups were compared using independent sample t-tests. Repeated sample one-way ANOVA analyses were conducted to assess longitudinal changes in NPRS and ODI scores within and between PRP and steroid groups. To preserve statistical power, the 6-month visit outcomes were excluded from the ANOVA analyses due to extensive missing data (4/11 (36.4%) in the steroid group and 3/15 (20.0%) in the PRP group).

Results

There were no significant differences in the age, gender, ethnicity, or race between subjects who received PRP and subjects who received corticosteroid (Table 1). There was no significant difference between NPRS or Oswestry Disability Index (ODI) scores in subjects who received PRP versus steroid injections at baseline.

At 1M, 3M, and 6M, subjects who received steroid injections reported lower NPRS scores, indicating less pain, than subjects who received PRP (Figure 2). Using categorical data, we observed significantly more responders (defined as NPRS scores that improved by 50% or more from baseline) at 1M and 3M in the group that received steroid injections compared to the group that received PRP. There was no significant difference in the number of responders at 6M (Table 1).

The repeated measures ANOVA analysis indicated a significant main effect of NPRS, suggesting that subjects in both treatment groups reported improvement in pain across study visits ($F(2, 42) = 22.210$, $p < .0005$). There was also a significant main effect of treatment group, indicating that subjects who received steroid injections reported less pain than subjects who received PRP injections across study visits ($F(1, 21) = 8.682$, $p = .008$). There was a statistically significant interaction effect between the treatment group and NPRS ($F(2, 42) = 15.557$, $p = .005$), indicating that subjects who received steroid injections had a steeper drop in pain scores from baseline to 1 month than subjects who received PRP.

From a functional perspective, at 1M and 3M, subjects who received steroid injections had lower ODI scores than subjects who received PRP, but these differences were absent at 6M (Figure 3). Mauchly's Test of Sphericity found that the assumption of sphericity had been violated, $\chi2(2) = 15.714$, $p < .0005$, thus a Greenhouse-Geisser correction was used for the present repeated measures ANOVA analysis. This analysis indicated a significant main effect of ODI, suggesting that subjects in both treatment groups reported

improvement in function across study visits ($F(1.310, 28.818) = 23.229$, $p < .0005$). There was also a significant main effect of treatment group, indicating that subjects who received steroid injections reported less pain that subjects who received PRP across study visits ($F(1, 22) = 7.767$, $p = .011$). There was no significant interaction between ODI and treatment group ($F(1.310, 28.818) = .479$, $p = .545$).

Discussion

This randomized, controlled, double-blinded study evaluated pain and functional improvements in patients who received intraarticular platelet-rich plasma injections versus steroid injections.

Overall, pain scores decreased over time for both the steroid and PRP groups. In all time points, at 1, 3, and 6 months, the steroid group showed statistically significant greater improvements in pain than the PRP group. There were noted differences in pain scores over time – the steroid group showed a faster decline in NPRS for the steroid group than the PRP group, particularly between baseline and one month. The mean NPRS scores in the PRP group improved from 5.63 at baseline to 4.68 at 1 month, 4.07 at 2 months, and 4.38 at 6 months. None of these improvements at any time period showed a mean score difference of >2.0 or >30% from baseline, and as such may not be considered clinically meaningful [11]. Using categorical data (NPRS decrease of greater than 50%), there were significantly more responders in the steroid group at 1 and 3 months, however no difference at 6 months. In the PRP group, out of 14 participants who followed up at one month, only 21.4% (n=3) reported an NPRS decrease of >50% at 1 and 3 months. The

same 3 responders maintained benefit at 3 and 6 months. In comparison, 80% of participants in the steroid group reported an NPRS decrease of >50% at 1 month, and 70% at 3 months.

Analysis of functional outcomes with ODI yielded similar results. Over time, ODI scores decreased over time for both groups. However, at time points of 1 and 3 months, the steroid group had a greater decrease in ODI when compared to the PRP group.
The mean ODI scores in the PRP group improved from 17.07 at baseline to 12.36 at 1 month (28% improvement), 13.07 at 2 months (23% improvement), and 12.58 at 3 months (26.3% improvement). While the minimal clinically important difference in ODI is debated [12], none of these changes showed mean ODI improvement of greater than 5 points.

There is limited prior research evaluating the efficacy of PRP for SIJ pain. A single randomized controlled trial in 2017 by Singla *et. al.* [13] compared leukocyte-free PRP injections with 40mg/mL of methylprednisolone using ultrasound guided SIJ injections and reported statistically significant improvement in pain with PRP versus the steroid group at 6 weeks and 3 months follow up. This study, while well-designed overall, was non-blinded, utilized ultrasound guidance, and included patients without a diagnostic block to confirm true SIJ pain. Though the efficacy of ultrasound and fluoroscopy guided SIJ injections for pain is reported as equivalent [14, 15], there is significantly variability in true inter-articular injection rates using ultrasound. The percentage of true intra-

articular injection rates have been reported as 50% by Soneji et al., [12], 76.7% by Pekkafahli et al., [16], and 87.3% by Lee et al.[17].

One consideration for the differences in outcomes may be due to posterior element pain. Our study specifically evaluated intra-articular SIJ pain using strict inclusion criteria after fluoroscopically guided diagnostic blocks. However, the entire SIJ complex can cause pain, including the posterior extra-articular elements and dorsal ligaments. The Singla study, which relied on ultrasound guidance, may have been injecting PRP not only into the joint space itself, but along the posterior complex as well. By placing PRP not only intraarticular, but also along the posterior ligamentous complex, perhaps a more robust response was achieved.

Of note, of the initial 64 patients screened in clinic, less that 50% (30) patients had a positive diagnostic block. 34 patients had either no response to diagnostic block or did not achieve the threshold of pain relief (80%). This is consistent with the findings by Schnieder et. al, which did not show association between diagnostic blocks and exam maneuvers [18]. In 11% of patients (n=7), even in experienced hands (all physicians with at least 5 years of experience as an attending), we were not able to achieve adequate intraarticular flow.

Our results for PRP injections into the SIJ do not show the same results as the 2017 Singla study, which found increased benefit and longer lasting duration in the PRP group as compared to the steroid group. In this study, using stringent inclusion criteria, the PRP

group showed limited improvement overall in pain and function, with the steroid group showing greater benefit in both NPRS and ODI at 1 and 3 months, using both mean and categorical data analysis. We did not observe any major or minor complications in either the PRP or steroid group.

This study has several limitations. Given stringent inclusion criteria and non-industry funding, we were limited to a small sample size due to the cost of the PRP kits. Several patients were lost-to-follow-up, particularly at 6 months (3/15 in the PRP group, 4/11 in the steroid group). Multiple attempts were made to contact these patients without success. In order to preserve statistical power given the lost-to-follow-up patients, the 6-month visit outcomes were excluded from the ANOVA analyses. Furthermore, because we did not follow patients beyond 6 months, were not able to determine the durability of pain relief for either group beyond this time. Our study group had a predominance (81%) of female patients and 77% of trial patients identified as white; these demographics may limit the ability to generalize our results.

Lastly, there is significant variability regarding the type and constitution of PRP used today. This is the subject of numerous other articles and discussions. These differences are outside the scope of this study; our goal was to evaluate the benefit of PRP vs. the standard of care, i.e. steroid injections. We utilized the EmCyte PurePRP kit for this study based on what was available to us at our institutions. A separate study evaluating outcomes between different types of PRP injections should be considered.

Conclusion

Using stringent criteria to identify those patients with true SIJ pain, we noted improvements in pain and function for both PRP and steroid injection groups, however observed a significantly greater response in pain at all time points (1,3 and 6) months in the steroid group when compared to the PRP group. We also saw a significantly greater functional response at 1 and 3 months in the steroid group. These differences between the steroid and PRP group were not observed at 6 months, with both groups maintaining some functional benefit. This study does not replicate findings described in prior studies, and indeed emphasizes the importance of continued research into the potential benefits of regenerative medicine therapies.

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Table 1. Subject Demographics and Outcome Data

	PRP (N=15)	Steroid (N=11)	p-value
Mean Age (SD)	51.47 (18.97)	46.00 (13.57)	.424
Gender (%)			.654
Male	3 (20.0%)	2 (18.2%)	
Female	12 (80.0%)	9 (81.8%)	
Ethnicity (%)			.619
Hispanic	2 (13.3%)	1 (9.1%)	
Non-Hispanic	13 (86.7%)	10 (90.9%)	
Race (%)			.783
White	12 (80.0%)	8 (72.7%)	
Black/African-American	1 (6.7%)	0 (0.0%)	
Other	2 (13.3%)	3 (27.3%)	
Mean NPRS 0M (SD)	5.63 (1.82)	5.95 (1.30)	.130
Responder 1M			.011
Yes	3 (21.4%)	8 (80.0%)	
No	11 (78.6%)	2 (20.0%)	
Responder 3M			.035
Yes	3 (21.4%)	7 (70.0%)	
No	11 (78.6%)	3 (30.0%)	
Responder 6M			.141
Yes	3 (25.0%)	4 (66.7%)	
No	9 (75.05)	2 (33.3%)	
Mean ODI 0M (SD)	17.07 (6.78)	13.45 (4.06)	.640

Figure 1: CONSORT Diagram

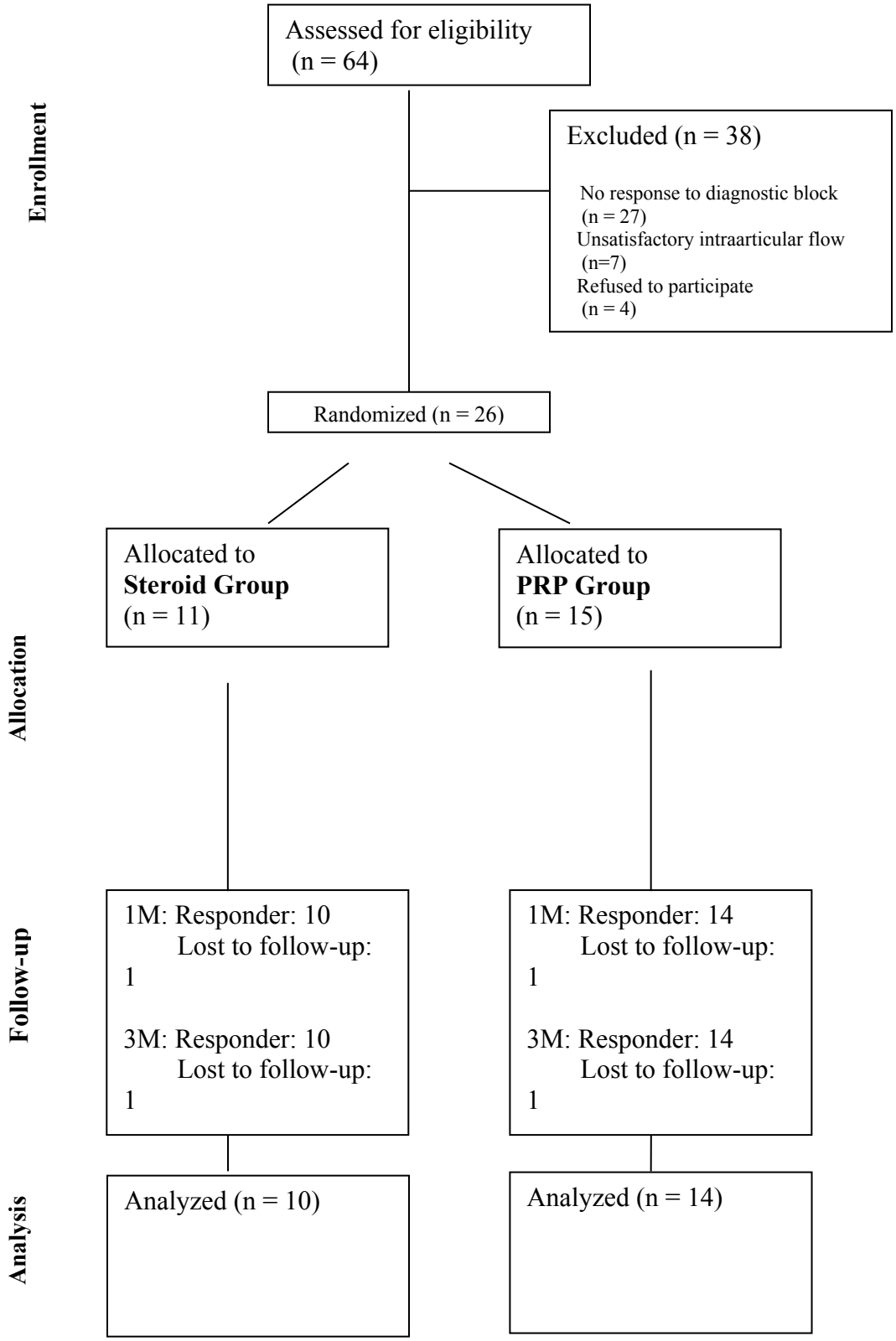
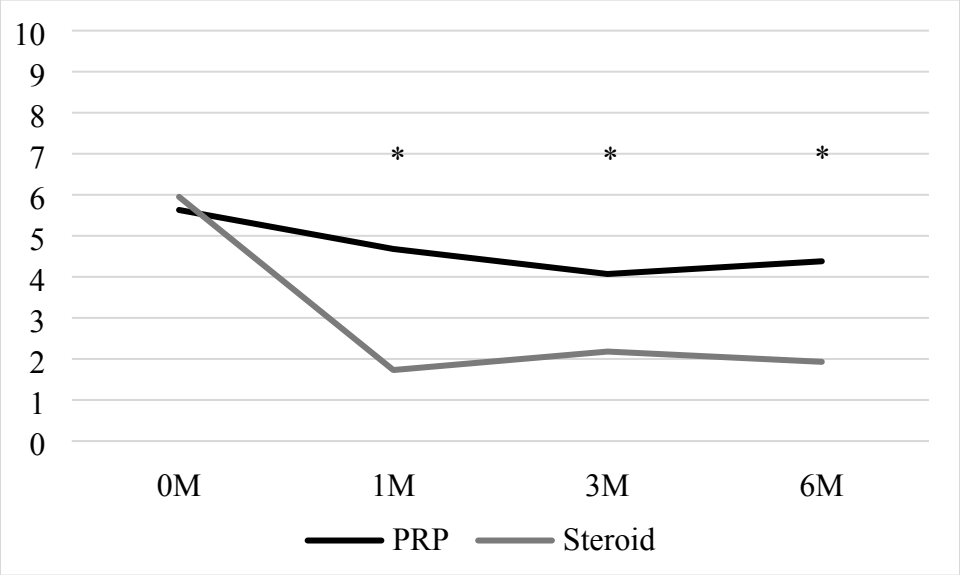
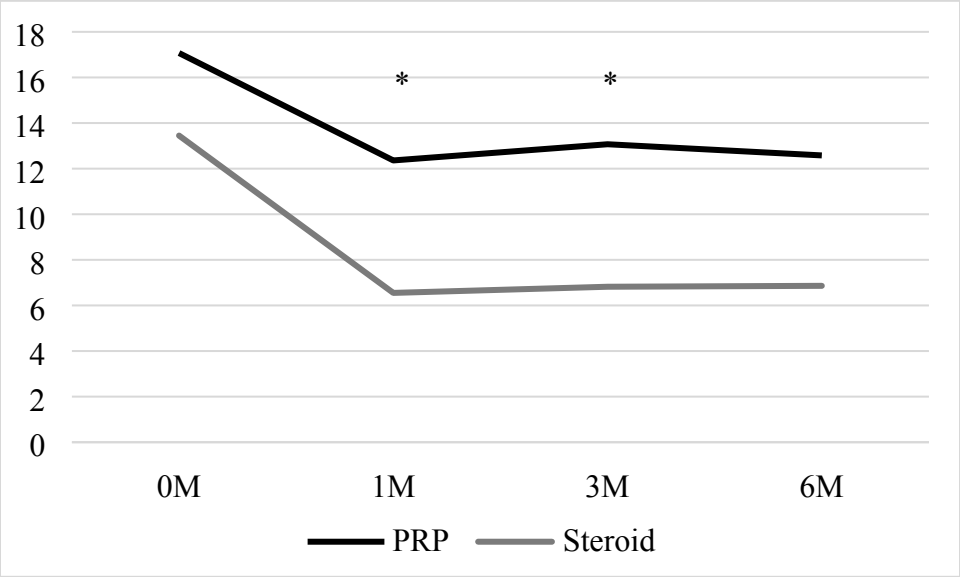


Figure 2. Mean NPRS scores by study visit



* $p < .05$

Figure 3. Mean ODI scores by study visit



* $p < .05$