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ORTHOPEDICS | RESEARCH ARTICLE

Treatment of unresolved lower back pain with platelet-rich plasma injections

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Abstract: Background: Platelet-Rich Plasma (PRP) is a non-invasive modality that has been used to treat musculoskeletal conditions for the past two decades. Based on our research, there were no publications that studied the effect of PRP on unresloved lower back pain. The aim of this study was to report the clinical outcomes of patients who received PRP injections to treat unresolved lower back pain.

Methods: 67 patients underwent a series one, two, or three PRP injections into the ligaments, muscle, and fascia surrounding the lumbar spine. Patients who received two treatments received injections a mean 24 days apart and patients who received three treatments received injections a mean 20.50 days apart. Baseline and post-treatment outcomes of resting pain, active pain, lower extremity functionality scale, and overall improvement percentage were compared to baseline and between groups.

Results: Patients who received one PRP injection reported 36.33% overall improvement and experienced significant improvements in active pain relief. These same patients experienced improvements in resting pain and functionality score, yet these results were not statistically significant. Patients who received a series of two and three treatments experienced significant decreases in resting pain and active pain and reported 46.17% and 54.91% total overall improvement respectively. In addition, they were able to perform daily activities with less difficulty than prior to treatment.

ABOUT THE AUTHORS

The authors of this study are apart of a private clinical practice called the Darrow Stem Cell Institute, which treats degenerative musculoskeletal conditions and sports injuries with regenerative medicine therapies. Our research department is dedicated to educate both the medical community and our patients about the efficacy of regenerative medicine with our clinical practice outcomes. This will be our 4th publication in the treatment of different musculoskeletal conditions with Bone Marrow Concentrate and Platelet-Rich Plasma Therapies.

PUBLIC INTEREST STATEMENT

Low back pain is one of the most common musculoskeletal issues, plaguing over 25 million Americans, and costing in excess of 102 billion dollars each year. Patients ailing from this condition are forced to choose from the conservative treatments, which are unreliable and invasive surgeries. The objective of this study was to provide insight on a minimally invasive surgical alternative that uses components of a patient's own blood to regrow tissue and relieve pain, called Platelet-Rich Plasma (PRP) Therapy. PRP therapy has been used for the past two decades for different musculoskeletal conditions. To our knowledge, this is the first study that examined PRP's clinical effect on lower back pain when injected into the ligaments, muscles, and fascia surrounding the lumbar spine. Our hope is by providing continual research about the efficacy of regenerative medicine it can reach and educate more people.

Conclusions: These results demonstrate that PRP injections may be a viable conservative approach to treat lower back pain. Additional research is needed to confirm these findings.

Subjects: Biology; Orthopedics; Joint Replacement; Sports Medicine; Complementary & Alternative Medicine

Keywords: lower back pain; platelet-rich plasma; non-invasive modality; regenerative medicine; surgical alternative

1. Introduction

Low back pain (LBP) is one of the most common musculoskeletal issues, affecting over 25 million Americans, and costing in excess of 102 billion dollars each year (Balague, Mannion, Pellise, & Cedraschi, 2012; Bevers et al., 2017; Martin et al., 2009; Nahin, 2012). Lifetime prevalence of LBP has been estimated to be as high as 84% (Balague et al., 2012). However, chronic LBP that is defined as pain that lasts greater than 3 months is reported to have a 23% prevalence (Herndon, Zoberi, & Gardner, 2015). LBP may originate from multiple underlying etiologies creating a challenge for physicians. This uncertainty accounts for the continued rise in treatment costs without a similar increase in the number of office visits associated with LBP (Bevers et al., 2017). General recommendations for the treatment of LBP begins by ruling out serious pathoanatomical causes, such as spinal disease or radiculopathies, thereby leading to a diagnosis of non-specific back pain (Herndon et al., 2015).

Magnetic resonance imaging (MRI) is used to rule out serious etiologies; however, it is not recommended for non-specific LBP due to a lack of evidence of improved symptoms and high false positives rates (Ash et al., 2008; Chou & Huffman, 2007; Jarvik, Hollingworth, & Martin et al., 2003; Modic et al., 2005). Studies have shown that abnormal MRI findings are present in up to 90% of asymptomatic patients due to normal aging and lead to unnecessary treatments that carry increased risks of adverse complications or side effects (Ash et al., 2008; Chou & Huffman, 2007; Jarvik et al., 2003; Modic et al., 2005). Despite recommendations, MRI orders for LBP continue to increase with a parallel increase in the rates of narcotic prescriptions, epidural steroid injections and surgical interventions, without an improvement in self-reported health status (Carrino et al., 2002; Friedly, Chan, & Deyo, 2007; Gray et al., 2006; Jarvik et al., 2003; Luo, Pietrobon, & Hey, 2004; Martin et al., 2008, 2009; Weiner, Kim, Bonino, & Wang, 2006).

Platelet-rich plasma (PRP) therapy is a non-invasive, nonsurgical biologic intervention that has gained attention in the treatment of degenerative and musculoskeletal conditions (Andia & Abate, 2013; Andia et al., 2014). PRP is isolated from autologous blood and contains an assortment of signaling cytokines that modulate inflammation and angiogenesis as well cell migration and proliferation, all of which are important in the healing process (Andia, Sanchez, & Maffulli, 2010; Bosch, Moleman, Barneveld, Weeren, & Schie, 2011; Lyras et al., 2010, 2009). Studies have also found that PRP effects gene expression and downstream processes that produce pain. Thereby, PRP may play role in reducing or modulating the amount of pain produced by the body (Andia, Rubio-Azpeitia, & Maffulli, 2015). Due to these properties, patients with chronic non-specific LBP may experience therapeutic effects from PRP therapy.

It is well documented in research that PRP has demonstrated increased tendon and ligament healing through injections (Yuan, Zhang, & Wang, 2013). At our clinic we inject PRP into the muscles, fascia, and ligaments surrounding the lumbar spine to improve patients' spinal stability. Many of our patients may be diagnosed with herniated discs, facet arthropathy, degenerative disc disease, spinal stenosis, scoliosis, spondylosis, spondylolisthesis, or other pathology. We have found that the actual pain generator may not even be noted in the diagnosis. Strengthening the support of the spine may not only relieve patients' current pain regardless of the diagnosis but may lower their risk for future discogenic problems.

To our knowledge, PRP research for LBP has primarily focused on discogenic etiology. The goal of our study was to determine the therapeutic effect of PRP therapy for chronic non-specific LBP regardless of the diagnosis. Determining the clinical efficacy of PRP for the reduction of low back pain is essential to improve patient outcomes and prevent unnecessary and risky treatments.

2. Methods

1. Patients

This study reports clinical practice outcomes in which variables were administered prospectively and data were analyzed retrospectively. Patients who were included in this study underwent a series of one, two, or three PRP treatments for lower back pain. The procedures were performed at a solo practitioner private practice from July 2016 to April 2018. Patients who did not have at least one-month follow-up after the first injection were excluded. All treatments were prescribed on an individual basis, as recommended by a physician. Written informed consent was obtained prior to each treatment.

As stated in our previous knee osteoarthritis publication, (Shaw, Darrow, & Derian, 2018) if a patient at our clinic requires multiple injections, we direct them to receive injections approximately 14 days apart, however, scheduling conflicts often cause injection intervals more than 14 days. At the 14 day time period, there is growth factor secretion from various cell types that participate in the late phases of wound healing, which can enhance tissue regeneration (Barrientos, Stojadinovic, Golinko, Brem, & Tomic-Canic, 2008; Enoch & Price, 2004). Patients were instructed not to use non-steroidal anti-inflammatory drugs during treatment since they significantly impair platelet function (Schippinger, Prüller, & Divjak et al., 2015). In addition, they were instructed not to participate in any strenuous physical activity for the duration of treatment. Patient characteristics can be found in Table 1. This study was constructed to follow all ethical guidelines directed by the Declaration of Helsinki.

2. Procedure

48-cc of blood was drawn into six 8.5 mL ACD solution A tubes. The blood was then spun in a centrifuge, and the top layer without visible red blood cells was isolated to yield 12-cc PRP. The PRP was then split into 4-cc portions and was added to three 6-cc syringes. 2-cc of Lidocaine was added to each syringe to ensure less post-injection stiffness. The injection sites were sterilized with 4% Hibiclens. The PRP was injected by the physician into the tender or painful areas along the enthesis of the insertion of the quadratus lumborum, thoracodorsal fascia, iliac crest, interspinous and supraspinous ligaments, gluteus attachments to the pelvis, sacroiliac ligaments, etc, as determined per patient's complaints and tenderness.

3. Outcomes

The outcomes of interest in this study were changes to resting pain and active pain (numerical pain scale [NPS]), overall improvement (percentage scale), and function (scored questionnaire) as seen in Figure 1. Data was collected at follow-ups after each treatment and were performed at

Table 1. Patient characteristics

	N	Mean (SD)
Age	67	53.51 (16.52)
BMI	67	26.90 (5.66)
Years of Pain	67	10.17 (11.32)
Gender %		
Female	27	40.30%
Male	40	59.70%

Figure 1. Patient Questionnaire.

Lower Extremity Functionality Questions

Please describe the deg ree of difficulty you have performing these activities with your injured lower body part

	Activities	Extreme Difficulty	Quite a Bit of Difficulty	Moderate Difficulty	A Little Bit of Difficulty	No Difficulty	N/A
1	Job, housework, or school activities	0	1	2	3	4	N/A
2	Hobbies, recreational, or sport activities	0	1	2	3	4	N/A
3	Squatting	0	1	2	3	4	N/A
4	Walking two blocks	0	1	2	3	4	N/A
5	Going up stairs	0	1	2	3	4	N/A
6	Rolling over in bed	0	1	2	3	4	N/A
7	Standing for an extended period of time	0	1	2	3	4	N/A
8	Lifting a heavy objecting	0	1	2	3	4	N/A
9	Getting in and out of your car	0	1	2	3	4	N/A
10	Bending to the floor	0	1	2	3	4	N/A

Total:_____

Resting Pain Level: 0 (No pain) 1 2 3 4 5 6 7 8 9 10 (Extreme pain)

Active Pain Level: 0 (No pain) 1 2 3 4 5 6 7 8 9 10 (Extreme pain)

Improvement Since Date of First Treatment (%) 0 10 20 30 40 50 60 70 80 90 100

approximately one month, three months, six months, and annually after the first injection. The functionality portion of the questionnaire, which assessed the degree of difficulty in performing daily activities, was based on 10 of 20 activities assessed in the Lower Extremity Functional Scale, (Binkley, Stratford, Lott, & Riddle, 1999) but also included a "not applicable (N/A)" response option. This scale has been shown to be a reliable functionality questionnaire for LBP (Liang, Hou, & Chang, 2013). The NPS to assess resting and active pain used a scale of 0 (no pain) to 10 (extreme pain) (Childs, Piva, & Fritz, 2005). Lastly, the form included a subjective measure of how much overall improvement the patient experienced following treatment on a scale of 0% to 100%.

4. Statistical analysis

Baseline and postintervention data were compared using means and standard deviations. Each follow-up response was compared with its corresponding baseline response using the Wilcoxon signed rank test. Intergroup comparisons were performed using the Wilcoxon sum rank test. Covariates were not accessed in this report. Statistical significance was set at P less than 0.05 and statistical analysis was performed using R 3.5.1 (R Foundation for Statistical Computing, Vienna, Austria).

3. Results

In total, there were 141 PRP treatments performed on 67 patients' lower backs. On average, patients had experienced 10.17 years of lower back pain prior to treatment. The two-treatment

patients received injections a mean 24 days apart and the three treatment patients received injections a mean 20.50 days apart. Patient results can be found in Table 2–4 and Figure 2.

Patients experienced successive decreases in resting and active pain with the increased number of PRP treatments. Patients who received one PRP injection reported a 1.13 (P = 0.016) decrease in active pain, which is a 16.98% decrease compared to baseline. Patients who received a series of two PRP injections experienced a 1.20 (P = 0.005) and 1.83 (P = 0.002) decrease in resting pain and active pain respectively. That is a 31.15% decrease in resting pain and 26.34% decrease in active pain compared to baseline. Patients who received a series of three PRP treatments experienced a 1.91 (P = 0.001) and 3.09 (P < 0.001) decrease in resting and active pain respectively. That is a 51.85% decrease in resting pain and a 43.31% decrease in active pain compared to baseline. The three treatment group showed statistically significant results in terms of resting pain to the one treatment group and significant active pain relief compared to the one and two treatment group.

When patients were asked a percentage of overall improvement they also reported successive increases. Patients who received one treatment reported 36.33% total overall improvement, two treatment patients reported 46.17% total overall improvement, and three treatment patients reported 54.91% total overall improvement. 35 out of 67 patients experienced at least 50% overall improvement compared to baseline.

Table 2. The baseline and post-treatment scores of patients who received 1 PRP treatments for lower back pain. N = 15

Number of Treatments	0	1	Difference	P-Value	Percent Difference
Resting Pain (0–10) Mean (SD)	3.67 (2.99)	3.13 (2.97)	−0.53	0.200	14.55%
Active Pain (0–10) Mean (SD)	6.73 (2.69)	5.60 (3.22)	−1.13	0.016	16.83%
Total Improvement (0–100%) Mean (SD)	-	36.33% (39.64)			36.33%
Functionality Score (0–40) Mean (SD)	20.60 (12.94)	21.80 (13.24)	1.20	0.130	5.83%
Follow up Time (mo.)	7.28				

Table 3. The baseline and post-treatment scores of patients who received a series of 2 PRP treatments for lower back pain. N = 30

Number of Treatments	0	2	Difference	P-Value	Percent Difference
Resting Pain (0–10) Mean (SD)	3.70 (2.39)	2.50 (2.52)	−1.20	0.005	32.47%
Active Pain (0–10) Mean (SD)	6.33 (2.67)	4.50 (3.30)	−1.83	0.002	28.95%
Total Improvement (0–100%) Mean (SD)	-	46.17% (36.24)			46.17%
Functionality Score (0–40) Mean (SD)	21.63 (8.12)	28.10 (9.84)	6.47	<0.001	29.89%
Follow up Time (mo.)	5.41				
Days between Injections	24.00				

Table 4. The baseline and post-treatment scores of patients who received a series of 3 PRP treatments for lower back pain. N = 22

Number of Treatments	0	3	Difference	P-Value	Percent Difference
Resting Pain (0–10) Mean (SD)	3.68 (2.87)	1.77 (3.90)	−1.91	0.001	51.85%
Active Pain (0–10) Mean (SD)	7.14 (2.08)	4.05 (2.77)	−3.09	<0.001	43.31%
Total Improvement (0–100%) Mean (SD)	-	54.91% (35.17)			54.91%
Functionality Score (0–40) Mean (SD)	19.82 (7.81)	26.82 (7.63)	7.00	<0.001	35.32%
Follow up Time (mo.)	4.22				
Days Between Injections	20.50				

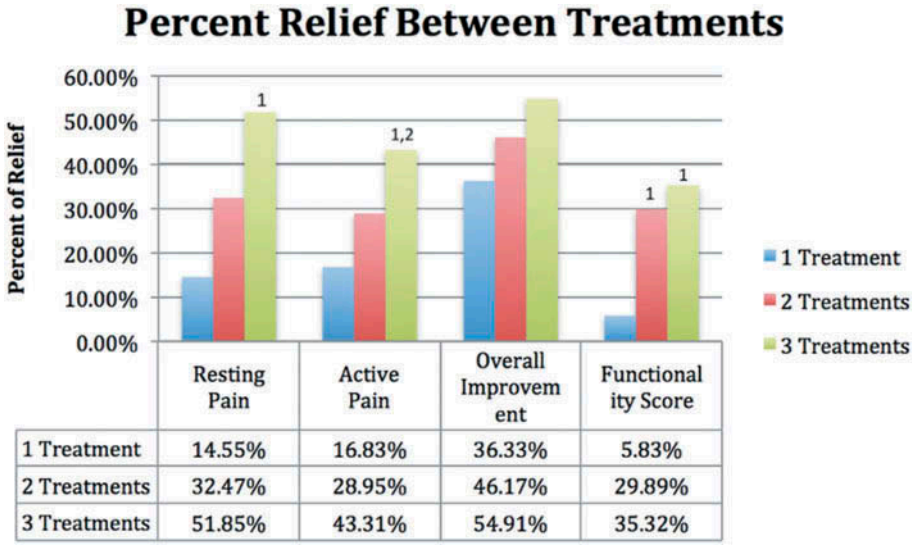

Figure 2. Comparing relief of active pain, resting pain, total overall improvement percentage, and functionality score by treatment number.

Legend: 1-Statistically significant (P < .05) compared with outcomes after first injection. 2-Statistically significant (P < .05) compared with outcome after second injection.

In terms of functionality score, two-treatment patients experienced less difficulty performing daily activities reporting a 6.16 (P = <0.001) increase, which is a 28.51% increase compared to baseline. Three treatment patients reported a 7.00 (P < 0.001) increase in functionality score, which is a 35.32% increase compared to baseline. The two and three-treatment groups experienced greater functionality score increases compared to the one-treatment group.

4. Discussion

Our study demonstrated that one, two or three PRP treatments were effective in significantly reducing active pain in the lower back. Additionally, functionality scores were significantly increased showing that patients were able to quickly return to everyday activities. Patients experienced an improvement in resting pain and functionality score after the one treatment, however, statistical significance was demonstrated only after the second and third treatments. Yet, self-reported mean total improvement was 36.33%, 46.17%, and 54.91% at the first, second and third treatments, respectively, suggesting an immediate clinical benefit.

Traditional treatments for chronic non-specific LBP include pharmacologic, steroid, or surgical interventions; however, the evidence for their efficacy is lacking and insufficient. For example,

long-term controlled studies found that pharmacologic treatment for chronic LBP may only provide three months of relief and the overall quality of evidence was low (Kuijpers et al., 2011). Steroid injections are another common treatment, yet the FDA issued a drug safety warning in 2014 stating the effectiveness of steroid use has not been established and that there is potential for serious adverse effects. Furthermore, studies have shown that steroid injections were not suggested for chronic LBP lasting greater than six months and, overall, did not improve pain or disability (Choi et al., 2013; Chou et al., 2015).

PRP is fast, non-invasive procedure that has been studied as an alternative treatment modality for low back pain and musculoskeletal injuries in the recent decade. The physiologic complexity of PRP bestows characteristics intriguing to investigators that involve immunomodulatory effects as well as angiogenic properties that facilitate healing. The exact mechanism of PRP is not known, but current research points to cytokines, growth factors and other proteins as the main medium through which PRP works (Dechellis & Cortazzo, 2011). Specifically, studies have shown that PRP contains vascular endothelial growth factor, epidermal growth factor, transforming growth factor β-1, platelet-derived growth factor, hepatocyte growth factor, insulin-like growth factor-I, basic fibroblast growth factor, and connective tissue growth factor responsible for significant tissue proliferation (Anitua et al., 2005; Dechellis & Cortazzo, 2011; Sys, Weyler, Zijden, Parizel, & Michielsen, 2011). PRP also contains certain chemokines and cytokines that are involved in the innate inflammatory and immunologic response that facilitate healing (Galliera, Corsi, & Banfi, 2011). Simultaneously, PRP modulates gene expression of specific chemokines that serve to regulate the immunoinflammatory reaction, preventing disproportionate responses and reducing pain (Andia et al., 2015).

Tissue healing is a complex mechanism acting through multiple physiologic pathways that may require time for molecular recruitment to reach satisfactory levels to observe clinically beneficial effects. Our results indicated significant improvement in all measurable outcomes after a series of two treatments and showed continued improvement after three treatments. Based on these results, it could be hypothesized that with each successive treatment further improvement may be demonstrated due to increased molecular involvement. Furthermore, combining other treatment modalities known to act through similar pathways may enhance the effects of PRP and increase the rate of healing. For example, investigators have demonstrated that hyperbaric oxygen combined with platelet concentrate increases the rate of bone healing. (Neves et al., 2013) Further research is needed to explore these avenues; however, the promise of PRP in the treatment of chronic LBP and other degenerative health issues offers hope to patients that have failed conservative treatment and are unable to find relief of their symptoms.

The limitations of our study include the limited sample size in the group of patients that received a total of one treatment. The improvement in resting pain and functionality scores were not statistically significant, but perhaps with a larger sample size, pain scores may be significant even after one treatment. Another limitation to our study was the population studied. According to epidemiologic studies, risk factors for chronic lower back pain include low educational status and lower socioeconomic levels (Hoy, Brooks, Blyth, & Buchbinder, 2010; Unde Ayvat, Aydin, & Ogurlu, 2012). Most insurance companies do not cover PRP and subsequently our patient population may not be representative of the general population suffering from chronic low back pain. In addition, the conclusions of this study were limited by not accounting for all variables that may have influenced patient outcomes, such as comparing age and BMI between groups. However, we plan on addressing different covariates in a separate study at a later date. The subjectivity of the measured variables may have introduced response bias and there was no control group to account for a placebo effect of the injections. Further randomized-controlled studies with larger sample sizes and longer follow-ups are warranted to further validate these results.

5. Conclusion

Our study demonstrated that PRP therapy reduced pain and increased functionality in patients with chronic non-specific LBP. The results of the study offer promise to patients that have failed conservative modalities and seek a quick, non-invasive treatment. Further research is warranted to determine the efficacy of widespread implementation of PRP as the standard of care for chronic non-specific LBP and other related chronic health issues.

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Conflict of Interest
Marc Darrow is the primary physician at the Darrow Stem Cell Institute, where all study procedures were performed.

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