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Is Platelet-Rich Plasma (PRP) a more effective treatment in reducing pain than corticosteroid (CS) injections in musculoskeletal injuries?

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A SELECTIVE EVIDENCE BASED MEDICINE REVIEW

In Partial Fulfillment of the Requirements For

The Degree of Master of Science

In

Health Sciences – Physician Assistant

Department of Physician Assistant Studies
Philadelphia College of Osteopathic Medicine
Philadelphia, PA

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ABSTRACT

OBJECTIVE: The objective of this selective EBM review is to determine whether or not, “Is Platelet-Rich Plasma (PRP) a more effective treatment in reducing pain than corticosteroid (CS) injections in musculoskeletal injuries?”

STUDY DESIGN: Review of three, double blind, randomized controlled trials (RCTs), published between 2013 and 2016, all in the English language were included. The articles compared platelet-rich plasma (PRP) and corticosteroid (CS) injections to a visually matched placebo of saline in regard to reduction of pain from baseline in varying different musculoskeletal injuries.

DATA SOURCES: Three RCTs were found using PubMed and Google Scholar. All articles were published in peer reviewed journals and selected based on their correlation to the topic of choice, the date of publication, and their ability in evaluating POEMs.

OUTCOMES MEASURED: Patient reported pain level, as measured by visual analog scale (VAS) score as well as joint specific scoring, such as the Patient-Rated Tennis Elbow Evaluation (PRTEE).

RESULTS: Forogh et al. and Mahindra et al. determined that both PRP and CS injections significantly reduced pain in knee osteoarthritis and chronic plantar fasciitis, respectively. However, Forogh et al. concluded that PRP had significantly better outcomes at 2 and 6 months follow up. Mahindra et al. concluded that CS injections had better outcomes at 3 weeks and 3 months follow up, whereas, PRP injections showed better outcomes at 3 months follow up. Krogh et al. determined that there was no significant difference in pain reduction comparing CS and PRP injections to a placebo injection.

CONCLUSION: Based off the data collected from the three RCTs, it is inconclusive whether platelet-rich plasma is a more effective treatment than corticosteroid injections in musculoskeletal injuries.

KEYWORDS: Platelet-Rich Plasma, Corticosteroids, Musculoskeletal Injuries

INTRODUCTION

Musculoskeletal injuries are very prevalent causes of morbidity in the United States today. Many of these injuries can be attributed to the elder population and may include osteoarthritis and falls.¹ The most common cause of injury in the youth population can be attributed to trauma such as motor vehicle accidents and sports injuries.¹ There are many different mechanisms, pharmacological therapies, and procedures that may be used to treat varying different musculoskeletal injuries. Treatment may be based on the part of the body injured or the structure of the body that has been injured.

Musculoskeletal injuries can be defined as any condition or injury that affect the bones, joints, or muscles.⁶ These can be painful, even debilitating, and can affect the everyday quality of life, activity, and productivity in these individuals. Over 6.8 million United States residents sought out medical care due to musculoskeletal related injuries in 2012.¹ Of these reported statistics, injuries most commonly occurred in the 18-64-year-old age range with sprains and strains accounting for a majority of these injuries.¹ Arthritis is the most common cause of disability, with approximately half of the United States population over the age of 65 being affected by this condition.⁶ In the year of 2011, the cost burden of these such musculoskeletal injuries in the United States costed approximately \$213 billion.⁶ Per person, the total cost for medical treatment of a musculoskeletal condition averaged about \$47, 800 in 2011.⁶ Furthermore, approximately 18% of all healthcare visits were related to musculoskeletal conditions in 2010.⁶ Musculoskeletal injuries are clearly a significant contributor to healthcare costs and prevalence today.

Due to the commonality of musculoskeletal injuries, there are numerous modalities used in the treatment of such conditions. Several studies have been completed in the comparison of PRP and CS injections with varying outcomes depending on the injury and length of time of

treatment.^{3,4,5} For example, one study on plantar fasciitis found that PRP was more effective long term compared to CS, however, another study found that there was no significant difference in the outcomes comparing PRP to CS.^{7,8,9} Other treatment modalities have also been used commonly in the treatment of musculoskeletal injuries. These treatments can include other types of injections, including hyaluronic acid, also physical therapy or occupational therapy, acupuncture or acupressure, osteopathic manipulation, chiropractic care, and therapeutic massage, or a combination of these. The decision regarding the treatment modality may be provider preference, age, and involved body part of injury.

A common treatment for varying musculoskeletal injuries is the use of corticosteroid (CS) injections as well as an emerging treatment modality for these injuries is the use of platelet-rich plasma (PRP) injections. Platelet-rich plasma aids in the healing of injured tissues due to its introduction of increased concentrations of growth factors as well as bioactive molecules which, therefore, creates an optimized healing environment.^{2,3} The growth factors included have effects on cell proliferation, chemotaxis, cell differentiation, and angiogenesis.⁴ These injections have recently been used to aid in wound and bone healing, alloplastic surgeries, as well as healing muscle and tendon damage.⁴ Intra-articular corticosteroid injections are historically and frequently used in the treatment of acute as well as chronic inflammatory conditions.³ Corticosteroid anti-inflammatory properties are a result of the inhibition of anti-inflammatory cytokines that block their pathway that leads to the inflammatory actions.³ The effectiveness of both of these treatment modalities have been compared in various studies including plantar fasciitis, lateral epicondylitis, and knee osteoarthritis, as well as many other musculoskeletal injuries.^{3,4,5}

OBJECTIVE

The objective of this selective EBM review is to determine whether or not, “Is Platelet-Rich Plasma (PRP) a more effective treatment in reducing pain than corticosteroid (CS) injections in musculoskeletal injuries?”

METHODS

Articles were found using PubMed and Google Scholar. Three randomized controlled trials were used in this review. Patients older than 18 years of age with a diagnosed musculoskeletal injury based on the specific injuries’ criteria were utilized in this study. The experimental intervention was platelet-rich plasma injections and corticosteroid injections. The control utilized were injections of normal saline.^{4,5} The reduction of pain from baseline in patients receiving PRP injections compared to CS injections were compared at different intervals in time as well as compared to various different musculoskeletal injuries. The outcome evaluated in all three studies was the efficacy in reduction of pain when PRP injections were used compared to the reduction of pain with CS injections, as demonstrated by the visual analog scale (VAS) score in addition to injury specific pain scores.

All randomized controlled trials were published in peer reviewed articles, written in the English language, and found on PubMed or Google Scholar databases. The keywords used in the searches were “platelet-rich plasma,” “corticosteroid,” and “musculoskeletal injuries.” The articles were selected based on relevance and that the outcomes of the studied mattered to the patients (POEMs). The inclusion criteria were studies that were RCTs published after the year 2007. Exclusion criteria included patients under the age of 18 years old, those that did not have a diagnosed musculoskeletal injury, patients that did not respond to conservative therapy, and patients whom have received previous treatment for these injuries with PRP or CS injections.

Table 1: Demographics and Characteristics of Included Studies

Study	Type	# Pts	Age (yrs)	Inclusion Criteria	Exclusion Criteria	W/D	Interventions
Forogh ¹	RCT	41	61.1± 7.0	-Pain intensity a ≥60 in the VAS at the time of admission -Pain >3 mo -Undergoing at least 2 OA treatments with no benefit	-History of collagen vascular, CV diseases, DM, cancer, immunosuppression, Hep B or C, knee injections, infection, arthroscopy or surgery, active lumbosacral radiculopathy, or drug abuse	2	-PRP: 20 mL whole blood, 2 mL ACD-A, centrifuged or 12 mins at 1600 and 2000 -CS: 40 mg of methylpredni solone acetate
Mahindra ²	RCT	75	30.7 ± 7.42 33.9 ± 8.61 35.4 ± 9.54	-Heel pain and tenderness of calcaneal tuberosity -No response to 3 mo of conservative therapy	-Use of NSAID within 1 week of injection	0	-CS: 40 mg methylpredni solone -PRP: 27 mL whole blood with 3 mL of citrate dextrose centrifuged for 12 mins at 3200rpm -Normal saline
Krogh ³	Double Blind RCT	60	>18	-LE symptoms for >3 mo -US with signs of tendinopathy of at least grade 2 assessed at baseline	-<18 yo -CS injection within the past 3 mo -Previous tennis elbow surgery, inflammatory diseases, neck pain, shoulder pain, and other chronic widespread pain syndromes	0	-CS: 1 mL triamcinolone 40 mg/mL -Saline: 3 mL saline 0.9% -PRP: 27 mL of whole containing 3 mL sodium citrate, centrifuged for 15 mins at 3200rpm

OUTCOMES MEASURED

The primary outcome measured in all three studies was change in pain on visual analog scale score or injury specific questionnaire from individual baseline. On this scale, patients are able to rate their pain on a scale of 0 (no pain) to 10 (worst pain ever experienced). Forogh et al utilized the 20-meter-walk test, active and passive knee range of motion, and flexion contracture before the injections and again after injection for knee osteoarthritis.³ Mahindra et al. incorporated the American Orthopaedic Foot and Ankle Society (AOFAS) and Hindfoot score to evaluate chronic plantar fasciitis.⁴ Krogh et al. utilized the Patient-Rated Tennis Elbow Evaluation (PRTEE) questionnaire to allow patients to evaluate their pain.⁵

RESULTS

Two studies compared the efficacy of PRP injections and CS injections to a placebo.^{4,5} One study compared the efficacy of PRP directly to CS injections.³ Each study assessed the pain for each specific injury at baseline before treatment was given.^{3,4,5} Forogh et al. evaluated the intervention at 2 months, and 6 months, Krogh et al. evaluated the intervention at 3 months, 6 months, and 12 months, and Mahindra et al. evaluated the intervention at 3 weeks and again at 3 months.^{3,4,5} All three studies were double-blinded studies comparing the effectiveness of PRP and CS injections in musculoskeletal injuries.^{3,4,5}

The study conducted by Forogh et al. comparing platelet-rich plasma versus corticosteroid injections in knee osteoarthritis was conducted in Tehran, Iran at the Physical Medicine and Rehabilitation Clinic in Firouzgar Hospital.³ Inclusion and exclusion criteria for this study can be found in Table 1. Forogh et al. evaluated 48 knees in 41 patients with 24 knees divided evenly into the PRP injection group and CS injection group evenly.³ Of the initial 41 patients and 48 knees, 2 patients were lost to follow-up and four patients were excluded due to seeking other treatment modalities, leaving a total of 39 knees being included in the statistical

analysis.³ The PRP was prepared by drawing 20 mL of autologous blood with the addition of anticoagulant citrate dextrose solution, Solution A. This then went through two centrifuge procedures at 1600 relative centrifugal force (RCF) for 6 minutes and then 2000 RCF for 6 minutes, which produced 5 mL of PRP.³ This solution was activated by combining 0.5 mL of calcium gluconate.³ One mL of Depo-Medrol containing 40mg of methylprednisolone was utilized for the CS group.³ Efficacy was evaluated based on the patient reported VAS-based pain intensity, 20-meter-walk test, as well as active and passive range of motion.³ Results were calculated based on the change from baseline pain, pain at 2 months, and pain at 6 months following the injection.³ This data indicated that platelet-rich plasma treatment significantly relieved pain at both 2 months and 6 months follow-up, whereas, the corticosteroid treatment was only effective in relieving pain at the 2 month follow-up. Statistical significance was set at $p < 0.05$ in this study.³ One patient reported dissatisfaction following the PRP injection due to increased knee and lumbar pain.³ No other adverse events were reported by participants in this study.³

Table 2: Efficacy in Pain Reduction Evaluated by Mean Change in VAS in Forogh et al.

	Baseline	2-month	6-month	p-value
Platelet-Rich Plasma (N=23)	81.3 ±13.4	45.1±23.4	44.6±15.6	<0.05
Corticosteroid (N=16)	77.8±13.8	65.3±19.3	72.5±16.2	<0.05

Krogh et al. conducted their study comparing the pain efficacy of PRP and CS injections to a placebo in patients with lateral epicondylitis (LE) in Denmark in the Rheumatology Unit at the Region Hospital Silkeborg after patients were referred by general practitioners, rheumatologists, or orthopaedic specialists.⁴ Patients included and excluded in this study can be found in Table 1. The primary efficacy outcome was changes in intensity of pain 3 months after the injection using the Patient-Rated Tennis Elbow Evaluation (PRTEE) questionnaire that

evaluates pain as a score ranging from 0 to 50 points.⁴ Three months was the chosen length of time evaluated due to the fact that the study gave patients the option to withdraw from the trial if they did not achieve a satisfactory treatment response at 3 months.⁴ Sixty patients with LE were included in the study and randomly divided with 20 patients in each arm of the study.⁴ Each injection was ultrasound guided with the elbow bent at 90 degrees.⁴ The PRP was prepared using 27 mL of autologous blood mixed with 3 mL of sodium citrate, then centrifuged at 3,200 RCF for 15 minutes.⁴ The CS group was injected with 1mL containing 40mg of triamcinolone and the placebo injection consisted of 3 mL of saline.⁴ After 3 months Krogh et al. determined there was no significant difference in pain reduction between any of the groups.⁴ However, at the one month evaluation, CS showed significant improvement in pain compared to the PRP and saline placebo groups.⁴ Due to the large number of drop out participants at 6 and 12 months, these results were not included in the study.⁴ There were no serious adverse events in any of the groups with no reports of infections after any injection therapies received.⁴

Table 3: Efficacy in Pain Reduction Evaluated by Mean Change in PRTEE in Krogh et al.

	Baseline	Pain at 1 month	Pain at 3 months	Confidence Interval (CI)
Platelet-Rich Plasma	27.5	-0.5	-6.0	95%
Corticosteroid	28.0	-9.8	-7.1	95%
Saline (placebo)	25.0	-1.7	-3.3	95%

Mahindra et al. conducted their study comparing the efficacy in pain reduction of chronic plantar fasciitis using PRP, CS, and a placebo injection in India at the Department of Orthopaedics, Dayanand Medical College and Hospital.⁵ The inclusion and exclusion criteria for this study is noted in Table 1. The primary efficacy outcome was reduction in pain from baseline at 3 weeks and at 3 months following a PRP, CS, or placebo injection utilizing the VAS and the American Orthopaedic Foot and Ankle Society (AOFAS) Ankle and Hindfoot score.⁵ This study included 75 patients with chronic plantar fasciitis and randomly divided these patients into three

groups evenly.⁵ Each injection was given at the patient's point of maximal tenderness in the heel.⁵ The PRP injection was prepared with 27 mL of autologous blood combined with 3 mL of citrate dextrose solution and then centrifuged at 3200 RCF for 12 minutes, creating 2.5 to 3 mL of PRP.⁵ 2 mL of 40 mg of methylprednisolone was used for the CS injections and the placebo group received normal saline.⁵ In both the PRP and CS groups, mean VAS score decreased significantly from pre-injection baseline scores with no significant difference in pain in the placebo group at 3 weeks follow-up and 3 months follow-up.⁵ However, at 3 weeks follow-up the CS group received better outcome scores compared to the PRP group and at 3 months the PRP groups received better outcome scores compared to the CS group, but this difference was determined to not be significant.⁵ There were no adverse events reported by patients included in this study.⁵

Table 4: Efficacy in Pain Reduction Evaluated by Mean Change in VAS in Mahindra et al.

	Pre-injection	3 weeks	3 months	p-value
Platelet-Rich Plasma (PRP)	7.44±1.04	3.76±1.53	2.52±1.71	<0.05
Corticosteroid (CS)	7.72±1.17	2.84±1.46	3.64±1.62	<0.05
Placebo (normal saline)	7.56±1.15	7.12±1.12	7.44±1.04	<0.05

DISCUSSION

Musculoskeletal injuries are common conditions in the United States and will continue to be in the future. Therefore, it is important to determine the method of treatment that is most beneficial to patients in the reduction of their pain due to these injuries. Both CS injections and PRP injections are widely used treatment modalities for these such injuries today.

Forogh et al. determined that pain relief from PRP injections was significantly greater than pain relief in those that were treated with corticosteroids.³ Krogh et al. concluded that there was no significant difference in reduction of pain at 3 months follow-up when comparing PRP

and CS to placebo.⁴ However, Krogh et al. was able to determine that CS was associated with significant short term relief of pain at one month follow up.⁴ Mahindra et al. determined that both PRP and CS injections were effective in reducing pain at three weeks and three months follow up, however, PRP had significant better outcomes at three months follow up compared to CS therapy.⁵

Whereas CS injections are more likely to be covered by insurance, such as Medicare, PRP injections are not due to the lack of evidence of this newer procedure.^{10,11} Therefore, PRP injections can range anywhere from \$500 to \$2000 without insurance coverage.¹⁰ CS injections can range from \$3 to \$200.¹¹ Costs of these injections can vary according to location and the practitioner performing the injection.¹¹

Uses for CS and PRP injections include inflammatory arthritides, tendinopathies, and nerve compression syndromes with lack of evidence for various conditions.¹² Contraindications of both CS and PRP injections include periarticular infections, fractures, instability, septic arthritis, certain locations on the body, and juxta articular osteoporosis.¹² Complications due to these injections are very uncommon and may just be due to administration error.¹² CS and PRP injections are both approved by the FDA.^{13,14} However, there use of CS epidural spinal injections is not approved as well as several different PRP preparation systems.^{13,14}

Evaluation of data was limited due to small sample sizes, the allowance of individuals to drop out if not satisfied, differing prior treatments to trials, activity level post injections, and exact preparations of the PRP injections.^{3,4,5} It is also essential to take note that these studies took place in countries other than the United States. Treatments including other ethnicities would be beneficial in determining if PRP is more effective in reducing pain for the general population of the United States. All three studies also did not evaluate the reduction of pain greater than one

year following the injections, allowing this to be another limitation due to the lack of long-term efficacy in pain reduction.^{3,4,5}

CONCLUSION

Based on the results of this review, the data is conflicting in whether or not PRP injections reduce pain greater than CS injections in musculoskeletal injuries.^{3,4,5} While all three studies reported pain reduction with both the PRP and CS injections, it is unclear which is more effective in general.^{3,4,5} Evaluation of a longer duration would be beneficial in determining the reduction of pain long-term following either PRP or CS injections. Future studies can utilize a more specific pain rating scale for an injury to that specific structure that is being evaluated rather than a generalized pain scale utilized for all injuries for more accurate results in pain reduction. It may also be beneficial to educate patients in the trial that it may take time for the injection to become effective to prevent withdrawal due to dissatisfaction. In conclusion, these three studies indicated that PRP is an effective treatment for musculoskeletal injuries, however, a larger sample size, longer duration, and more specific pain scale is needed to completely determine its effectiveness when compared to CS injections.

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