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Are Plasma Rich Platelets More Effective In Decreasing Chronic Lower Back Pain As Compared To Epidural Injections In Young Adults?

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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, Pennsylvania

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ABSTRACT

Objective: The objective of this selective EBM review is to determine whether or not PRP injections are more effective in decreasing chronic lower back pain as compared to epidural injections in young adults.

Study Design: Systematic review of three English language randomized controlled trials (RCTs), all published after 2012.

Data Sources: Two double-blind RCTs and one randomized open blinded end point (PROBE), which analyzed the effectiveness of PRP and epidural injections in young adults with chronic lower back pain. All studies were found using PubMed.

Outcome(s) Measured: Each of the articles analyzed the pain relief and function ability stated by the patient post PRP injections and epidural injections. These outcomes were measured using the visual analog scale score (VAS), the average of Numeric Rating Scale (NRS), the Oswestry Disability Index (ODI), the Modified Oswestry Disability questionnaire (MODQ), and the Functional Rating Index (FRI). Significance was determined using p-values for all three studies.

Results: Manchikanti et al. (2014) found that there was no significant difference between the use of local anesthetic alone compared to local anesthetic and steroid when treating chronic lower back pain in regards to pain and function measured by NRS and ODI scores. Singla et al. (2017) found that the pain significantly decreased at 6 weeks in patients treated with PRP injections compared to the group treated with steroid injections. This study also showed that the efficacy of PRP injections at 3 months was 90% compared to only 25% in the group with steroid injections. Tuakli-Wosornu et al. (2016) found that patients treated with PRP injections showed statistically significant improvements in pain and function 8 weeks post-procedure in regards to NRS best pain and FRI score.

Conclusions: the results from the three randomized controlled studies demonstrated that PRP injections are more effective in decreasing chronic lower back pain compared to epidural steroid injections by having less procedures, less adverse effects and providing lasting pain relief.

Key words: chronic lower back pain, platelet rich plasma, steroid injections.

INTRODUCTION

Low back pain is a very common condition in adults. Approximately, 80% of adults experience at least one episode of low back pain during their lifetime and approximately 20% of these patients have another episode within six months.¹ According to the National Institute of Neurological Disorders and Stroke “back pain is caused by general degeneration of the spine associated with normal wear and tear that occurs in the joints, discs, and bones of the spine as people get older” The cause of low back pain is very complex, although the most common cause is degenerative changes in the lumbar spine.²

This condition is the most common cause of disability among Americans between 45 and 65 years of age;¹ and it is the second most common cause of primary care visits.³ The cost of lumbar epidural steroid transforaminal treatment based on setting arrangement is between \$2,600 to \$3,000 per year.¹ Therefore making it difficult for patients who do not have health insurance coverage to afford these treatments. Today, low back pain is estimated to be the third largest condition of health care spending at \$87.6 billion.⁴

Aside from plasma rich platelet injections there are several non-invasive methods to treat low back pain such as acupuncture, physical therapy, physiotherapy, NSAIDs and opioids. In addition, there are other treatments that are more invasive such as radiofrequency neurotomy, epidural steroid injections, and if all these fail, then surgery. The three studies that will be discussed are recent RCTs that evaluate the efficacy of plasma rich platelet injections compared to epidural steroid injections.

Plasma rich platelets (PRP) is a biological blood-derived product that can be injected to various tissues since it releases high concentrations of platelet-derived growth factors that

enhance the body's natural healing process.² However, there is very little research on the topic due to the lack of standardization of graft preparation.³

OBJECTIVE

The objective of this selective EBM review is to determine whether or not PRP injections are more effective in decreasing chronic lower back pain as compared to epidural injections in young adults.

METHODS

All three articles were obtained via a search of the PubMed database using the keywords chronic lower back pain, platelet rich plasma, and steroid injections. Only randomized control trials published after 2012 were selected, based on the relevance and the importance of outcome to the patient. The articles chosen were published in English in peer-reviewed journals. Inclusion criteria included randomized controlled trial prospective studies; and they included patients who were at least 18 years old with chronic lower back pain for more than three months treated with either PRP or steroids injections in the lumbar area below L3. Exclusion criteria included patients who used PRP in another joints or tissues.

This review is comprised of a set of three randomized controlled trials that were selected based on relevance and patient oriented evidence that matter (POEMs). Manchikanti et al.¹ used a RCT double blind study to compare two groups. Group I received lidocaine and a sodium chloride solution while group II received lidocaine plus betamethasone. The outcomes measured were pain relief and functional status using Numeric Rating Scale (NRS) and the Oswestry Disability Index (ODI). Singla et al.² used a prospective randomized open blinded end-point study (PROBE) to compare two groups. Group S received methylprednisolone and lidocaine while group P received leukocyte-free PRP and calcium chloride. The outcomes measured were

intensity of pain and functional disability with visual analog scale (VAS) and Modified Oswestry Disability Questionnaire (MODQ). Tuakli-Wosornu et al.³ used a double-blind RCT to compare intradiscal PRP injections vs. a contrast agent. The outcomes measured were improvement in pain and function with Functional Rating Index (FRI) and Numeric Rating Scale (NRS). All three of the studies determined significance using p-values.^{1,2,3} A summary of the demographics of each study can be found in Table 1 below.

Table 1: Demographics and Characteristics of Included Studies.

STUDY	TYPE	# PTS	AGE (yrs)	Inclusion criteria	Exclusion criteria	W /D	Interventions
Manchikanti, 2014 ¹	Double blind RCT	120	43 ± 12 years	- Pts who were at least 18 y/o with chronic lower back pain and lower extremity pain of at least 6 months, only disc herniations at L4-L5 and L5-S1, all pts must have PT along with exercise program and nonsteroidal anti-inflammatory therapy.	- Hx of previous lumbar surgery, radiculitis w/o disc herniations, pts with B/L radiculopathy, radiculitis secondary to spinal stenosis, and pts with other uncontrolled medical illnesses.	0	Group 1 received local anesthetic with saline whereas pts in group 2 received local anesthetic and steroid.
Singla, 2017 ²	Open blind RCT	40	18-65	- Pts of either sex with chronic low back pain (predominantly below the L5 vertebra) of moderate intensity for > 3 months, Pts having unilateral SIJ pathology on X-ray, magnetic Patients having unilateral SIJ pathology on X-ray, MRI, or nuclear scan with 3 or more positive provocative tests.	- Systemic infection or localized infection at the anticipated introducer entry site, spinal pathology that may impede recovery, pregnancy, Active radicular pain, Immunosuppressive conditions, allergy to medications used in the procedure; narcotic use, contraindications pertaining to the use of platelet concentrate.	0	A mixture of 2% lidocaine with methylprednisol one or PRP with calcium chloride.
Tuakli-Wosornu, 2016 ³	Double blind RCT	51	44 ± 9 years	- Refractory low back pain persisting for > 6 months, failure of conservative treatment measures, maintained intervertebral disk height of at least 50%, disk	- Presence of a known bleeding disorder, current anticoagulation therapy ,pregnancy , systemic or skin infection over the puncture site, allergy to	4	A single Intradiscal PRP injection vs. visualized matched placebo

				protrusion less than 2 mm on MRI or CT, concordant pain on discography, presence of a grade 3 or 4 annular fissure as determined by discography, Absent contraindications (eg, spinal stenosis)	contrast agent, presence of a psychiatric condition, solid bone fusion preventing access to the disk, severe spinal canal compromise at the levels to be investigated, extrusions or sequestered disk fragments, previous spinal surgery, spondylolysis, spondylolisthesis.		
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OUTCOMES MEASURED

The outcomes measured in each of the three studies were functional ability and back pain relief. Both are considered patient-oriented outcomes because they significantly impacted a patient’s quality of life. Manchikanti et al. measured pain with the Numeric Rating Scale (NRS) and also measured functional ability with the Oswestry Disability Index (ODI).¹ These were measured at 3,6,12,18, and 24 months. This study also measured secondary outcomes such as opioid intake, employment, and work status among both groups, but were not examined in this review.

Singla et al. measured the pain intensity with the visual analog scale (VAS) from pre-injection to follow-ups in both groups at 2,4,6 weeks and 3 months.² The disability of the patient was measured by Modified Oswestry Disability Questionnaire (MODQ) score. These were also measured at 2,4,6 weeks and 3 months. This study also compared post-injection complications among both groups, but these were not examined in this review.

Tuakli-Wosornu et al. measured function and pain related with Functional Rating Index (FRI) and Numeric Rating Scale (NRS).³ This study also measured secondary outcomes among both groups, but these were not examined in this review.

RESULTS

In the study by Manchikanti et al.¹, 120 patients with chronic low back pain and with disc herniations at levels L4-L5 and L5-S1 were enrolled. Patients were assigned randomly via computer to two groups with 60 patients in each group: Group I was treated with 1.5 ml of preservative-free lidocaine 1% followed by a 0.5 ml sodium chloride solution, while group II was treated with preservative-free lidocaine 1% followed by 3 ml of betamethasone. All patients continued drug therapy with opioids or nonsteroidal anti-inflammatory drugs at a lower dose. All the injections were performed by one physician in an interventional pain management center based on Consolidated Standards Reporting Trials (CONSORT) guidance. An intention to treat analysis was used when data was missing or unavailable. At baseline, both groups had similar clinical characteristics with no statistical differences regarding the NRS and ODI as described in table 2. This study showed that there is no superiority from using steroids injections over lidocaine injections for low back pain. Both showed significant and similar improvement of at least 50% in pain and function in responsive patients. In addition, at 2 years, 65% of patients who received lidocaine alone showed improvement in comparison to 57% who received steroids.

Table 2: Comparison of NRS and ODI at baseline and at 2 years.

Time Points	Numeric Pain Rating Scale		Oswestry Disability Index	
	Group I Mean ± SD	Group II Mean ± SD	Group I Mean ± SD	Group II Mean ± SD
Baseline	8.3 ± 0.9	8.2 ± 0.9	29.9 ± 4.8	28.0 ± 5.3
24 months	4.0* ± 1.6	4.2* ± 1.6	14.9* ± 6.9	14.1* ± 6.5

* significant difference with baseline values within the group (P <0.001)

Manchikanti et al. Transforaminal epidural injections in chronic lumbar disc herniation - a randomized, double blind, active control trial.

Table 3: Efficacy of lidocaine injections compared lidocaine with steroid injections at 2 years.

CER	EER	RBI	ABI	NNT
0.7	0.6	-0.14	-0.01	-10

Local adverse events including 28 (4.6%) intravascular infiltrations and 9 (1.5%) nerve root irritations were obtained during the entire the study.

In the study by Singla et al.,² forty patients were selected who met the criteria between the ages of 18 and 65 years old with chronic low back pain predominantly below L5. Patients were assigned randomly via computer to two groups with 20 patients in each group. Group S was treated with 1.5 ml of methylprednisolone and 1.5 ml of 2% lidocaine with 0.5 ml of saline, while Group P received 3 ml of leukocyte-free PRP with 0.5 ml of calcium chloride. All pain medications were discontinued, including NSAIDs, before the start of this study. The injections were administered only once and patients followed up at 2,4,6 weeks and 3 months. Data analysis was performed using Statistical Package for the Social Sciences version 20. All tests were evaluated for 95% confidence limits. A P-value of less than 0.05 was considered as statistically significant. At the baseline parameters, both groups had similar clinical characteristics with no statistical differences regarding the VAS score, this held true at both 2 weeks and 4 weeks according to the study. At three months, the percentage of pain free in group P was 90% compared to 25% in group S. The MODQ scores were very similar in both groups at pre-injection, 2 weeks and 4 weeks; however, at 6 weeks and 3 months it was much lower in Group P compared to Group S as expressed in this article. No major post-injections complications were reported in any of the groups other than temporary pain and stiffness in Group P that subsided within 2 days of onset. The odds of achieving reduction in VAS >50% from baseline in group P were 10.91 times higher than in group S at 6 weeks, and 37.28 times higher at 3 months as described in table 5.²

Table 4: Efficacy of PRP injections compared to steroid injections at 3 months.

CER	EER	RBI	ABI	NNT	P-value
0.3	0.9	2.6	-0.67	2	0.01

Table 5: Patients with reduction of VAS at different times (pain reduction) and MODQ (disability)

Time Points	VAS		MODQ			P-value	95 % CI
	Group P	Group S		Group P	Group S		
2 weeks	12 (60 %)	15 (75%)	Baseline	48 %	45 %	0.001	27.0 – 159.66
3 months	18 (90 %)	5 (25 %)	3 months	28 %	14 %		

In the study by Tuakli-Wosornu et al.,³ forty-seven patients were studied who had refractory low back pain for longer than 6 months with the presence of grade 3 or 4 annular fissure (< 2ml) seen in discography. The treatment group included 29 participants while the control group included 18 participants. The treatment group received 3-4 ml of PRP while the control group received 1-2 ml of contrast agent. A P-value of less than 0.05 was considered as statistically significant. These injections were administered only once and patients were analyzed at baseline, 1 week, 4 weeks, and 8 weeks. In addition, twenty eight patients came back at 6 months for follow up and 21 patients came back a year later for a last follow up. At baseline there was no significant difference between both groups. At the 8 week follow up, the comparisons between both groups demonstrated significant improvement in the PRP group compared to the control group regarding the FRI score (P= 0.03) and the NRS (P=0.02). Fifty six percent of the patients treated with PRP were satisfied with the treatment compared to 18% of the patients in the control group. No complications were reported in either group.

Table 6: Efficacy of PRP injections compared to placebo group at 8 weeks.

CER	EER	RBI	ABI	NNT	P-value
0.18	0.56	2.1	0.38	3	0.01

Table 7: Comparison of NRS (best pain) and FRI score at baseline and at 8 weeks.

Time Points	Numeric Pain Rating Scale		Functional Rating Index		P-value	
	Control Mean \pm SD	PRP Mean \pm SD	Control Mean \pm SD	PRP Mean \pm SD	NRS	FRI
Baseline	2.08 \pm 1.7	2.81 \pm 1.8	45.37 \pm 15.6	51.47 \pm 15.6		
8 weeks	2.72 \pm 2.1	2.00 \pm 2.1	44.45 \pm 19.6	37.99 \pm 19.6	0.03	0.02

At 6 months NRS P=0.01, FRI P= 0.01. At 1 year NRS P=0.01, FRI P= 0.01

DISCUSSION

Steroid injections have been commonly used to treat chronic lower back pain, but usually the patient needs to have several injections done in order to experience pain reduction of at least 50%.¹ PRP is a relatively new procedure that holds promise given the need for fewer procedures and longer lasting pain relief, however, this procedure is not yet covered by health insurance companies.⁵ According to Dr. Verma, an orthopedic surgeon, the average price of a single PRP injection is \$750. Patients with lower back pain often may need more than one injection in one procedure.⁵ This causes a major limitation for patients since they have to pay out of pocket for this procedure. In 2013, Hsu et al. reported that PRP is more expensive than steroid injections when used in short-term treatment, but less expensive when used for long-term treatment.⁶

According to the FDA guidelines, PRP injections have not been approved by the FDA since it does not follow the regulatory pathway that includes animal and clinical trials. However, it has clearance from the Center for Biologics Evaluation and Research (CBER), a provider of the FDA, to be used to mix with bone graft materials to enhance bone graft handling in orthopedic practices. Therefore, if PRP is used outside that setting, it would be considered “off

label” which means that the clinician can use them as long as they are well informed about the product and its scientific rationale, as well as to maintain records of its use and side effects.⁷

This systematic review of three randomized controlled trials analyzed the efficacy of PRP injections compared to steroid injections regarding long lasting back pain relief. In the study by Singla et al.,² the follow-up duration was very short with respect to evaluating if chronic lower back pain could have long-lasting pain relief. A longer follow-up of at least 2 years is suggested. In addition, this study was open-blinded, which could result in bias. In the study by Manchikanti et al.,¹ all patients continued taking drug therapy with opioids or NSAIDS, so the results might not be due to the steroids. However, the major limitation of this study it was that the steroids were compared to a placebo instead of PRP. In the study by Tuakli-Wosornu et al.,³ the major limitation was the short follow-up time of the placebo group lasting 8 weeks.

Finally, regarding possible complications of PRP injections showed no complications, only temporary pain and stiffness with 2 days post-procedure.²

CONCLUSION

Based on the information obtained from these three randomized controlled studies, both injections demonstrated efficacy in low back pain relief. However, platelet rich plasma injections demonstrated to be more effective over steroid injections in decreasing chronic back pain and improving functional ability with lasting results and less adverse effects in adults in two studies. Future studies may benefit from a longer follow up time such as 2 years. They may also benefit from a comparison of baseline lumbar MRI versus last follow up MRI to compare if there is any difference in regards to disc heights pre and post treatment.

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