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Evaluation of clinico-radiological outcomes in patients with lumbar degenerative disc diseases treated with intradiscal PRP versus steroids: A prospective double blinded randomized controlled trial

[1]Dr. Bhupinder Singh Brar, [2]Dr. Vivek Jha, [3]Dr. Guncha Kalia, [4]Dr. Bhandari Vaibhav, [5]Dr. Neelam Gupta, [6]Dr. Mandeep Kaur Nanda, [7]Dr. Monika Sharma

[1]Professor and HOD, Department of Orthopaedics, MMMCH, Solan, Himachal Pradesh, India
[2]Assistant Professor, Department of Orthopaedics, MMMCH, Solan, Himachal Pradesh, India
[3]Professor, Department of Orthopaedics, MMMCH, Solan, Himachal Pradesh, India
[4]PG Resident, Department of Orthopaedics, MMMCH, Solan, Himachal Pradesh, India
[5]Professor and HOD, Department of Pathology, MMMCH, Solan, Himachal Pradesh, India
[6]Professor, Department of Anaesthesiology, MMMCH, Solan, Himachal Pradesh, India
[7]Associate Professor, Department of Radiodiagnosis, MMMCH, Solan, Himachal Pradesh, India

Corresponding Author:
Dr. Bhandari Vaibhav (drvaibhav2408@gmail.com)

Abstract

Context: To evaluate clinico-radiological outcomes in patients with lumbar degenerative disc diseases treated with intradiscal PRP versus steroids.
Design: Prospective double blinded randomized controlled trial.
Aims: The aim of the study was to compare and assess radiological changes and clinical outcome in patients with degenerative disc diseases when treated with intradiscal platelet rich plasma and intradiscal steroid.
Objectives: To compare clinical outcome in PRP and steroid treated patients, to compare radiological changes in PRP and steroid treated patients, to assess clinical outcome in PRP and steroid treated patients at subsequent follow ups, to assess radiological changes in PRP and steroid treated patients at subsequent follow up.
Settings and Design: Prospective double blinded randomized controlled trial.
Methods and Material: Adults (18-50 years) with chronic low back ache (> 6 months) non-radiating who were unresponsive to conservative treatment. A total 40 patients were randomized to receive intradiscal PRP (Group A) or steroid (Group B) after provocative discography in the department of Orthopaedics in Maharishi Markandeshwar Medical College and Hospital, Solan between the time period of November 2019 to September 2021 based on inclusion and exclusion criteria were enrolled for platelet rich plasma and steroid infiltration in a randomized manner. Pain relief as assessed by change in VAS score, functional assessment using change in Modified oswestry disability index (MODI). Pfirrman and MSU grades as assessed by MRI.
Statistical analysis used: The sociodemographic data was presented in form of number and percentage. The collected data was recorded on a predefined proforma and was compiled in Microsoft excel worksheet and analyzed using statistical software's SPSS (Standard protocol for social sciences) version 20 and Medcalc 19.5 were used for analysis. Adequate and

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appropriate statistical tests were applied and were used for the assessment of level of significance. All the test were applied by taking significance level p <0.05 as significant.
Results: Average age of the study population was 36.55±8.04 years in group A and 38.15±7.94 years in group B. Mean duration of complain was 10.90±3.48 in group A and 11.50±2.91 in group B with female preponderance in both groups. Majority of patients were with PIVD L4-L5 in both the groups' p value (0.6457). The outcome was assessed by visual analogue scale score with statistically significant p value 0.0460* post 6 months from 0.8817 which was at presentation and modified oswestry disability index score at presentation with p value (0.1025) which reduced with significant p value (<0.0001*). Radiologically outcome was assessed by Pfirrman and Michigan state university grading at 6 months post intervention and was found to be statistically insignificant with p value of 0.1675 and 0.1578 respectively.
Conclusions: Both platelet rich plasma and steroid are effective, safe and easy method in treating low back ache. However, we conclude that platelet rich plasma is a superior treatment option for long term duration and outcome success.

Keywords: Degenerative disc disease, intradiscal injection, platelet rich plasma, PRP, steroid, low back pain

Introduction

Low back pain (LBP) is a very frequent ailment in the twenty-first century, with 80 percent of the global population suffering from it at some point [1]. It is the second most prevalent reason for a doctor's visit in developed countries and it is also one of the most expensive disease of the healthcare system [2-4].
As a result, LBP sufferers are estimated to 600 million worldwide and is currently a serious socioeconomic issue [5]. It is now widely accepted that degeneration of the intervertebral disc (IVD), a fibrocartilaginous junction located between two vertebrae, is responsible for 40% of chronic LBP patients [6, 7].
On the intervertebral disc, the consequences of degenerative illness and ageing are strikingly comparable. As a result, biochemical degradation and a decrease in the mechanical qualities of the intervertebral discs are prevalent difficulties among the elderly, owing to their proclivity for traumatic injury during regular physical activities. Excessive stress of the disc, according to *in vitro* research, is more likely to fail the vertebral endplate than the disc itself [8]. As a result, herniation and fissures in a healthy disc can only occur when significant bending and compressive pressures are coupled [9].
The nucleus pulposus tissue is thought to be the source of degeneration [10]. The nucleus begins to acquire a more fibrotic structure as a result of these metabolic changes and the growing likeness of a solid tissue (rather than a fluid-filled structure due to the decreasing water content). The annulus and nucleus become histologically identical in the latter stages of degeneration. These alterations in the nucleus are accompanied by an immediate loss of functioning and gradual calcification of the cartilaginous endplates. Because there is minimal or no osmotic transfer through the endplates, blood vessels and nerve terminals are observed to grow from the vertebral bodies to inside the disc [11].
Disc degeneration at the rim of the endplate is frequently accompanied by the growth of osteophytes. It's been suggested that this is a remodelling phenomenon, in which the alterations expand the endplate's cross-sectional area and spread the loads across a larger region. These mineralized tissues, on the other
Hand, do not have a constant pattern and frequently have random shape. According to the literature, these mineralized deposits contribute to the functional spinal unit's overall resistance, particularly under bending stresses [12].
Furthermore, zygapophyseal joint osteoarthritis frequently occurs after disc degeneration as a result of substantial changes in the load-sharing relationship between the anterior and

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posterior spinal columns. Changes in the morphology of the intervertebral disc constituents caused by degeneration are reflected in their biomechanical behaviour as well [13].
In the early stages of the disease, treatment options such as physical therapy, analgesics and anti-inflammatories are aimed at addressing the symptoms. In more advanced cases, epidural steroid injections can be utilized to address radicular symptoms and ultimately surgical treatment, including fusions, may be undertaken to help alleviate symptoms. Platelet-rich plasma (PRP) also has been an alternative strategy in IVD regeneration with documented success due to its multiple growth factors [14].
So, the purpose of this prospective double blinded randomized controlled trial study is to evaluate the clinico-radiological outcome after treated with intradiscal PRP and steroids in patients with lumbar degenerative disc diseases. The efficacy, reparative and regenerative effect of intradiscal PRP and steroids and the association between the severity of inflammatory endplate changes are being investigated. The null hypothesis is there is that no association between outcome and following above treatments in MRI.

Subjects and Methods

This was a prospective, double blinded, randomized controlled trial of 40 participants with chronic low back ache for more than 6 months non-radiating pain treated with intradiscal PRP and steroid injection for 20 patients each in a tertiary care center. This proposed study was undertaken with approval of Institutional Ethical Committee. Single injections of autologous PRP by buffy coat method or steroid into symptomatic degenerative disc diseases and evaluating long term efficacy of either modalities as assessed by VAS score, MODI score. Group A patients were injected with 1.5 ml PRP intradiscally via 18G Chiba needle and group B patients with 1.5ml intradiscal dexamethasone (8mg) and 0.5ml bupivacaine (0.5%) via 18G Chiba needle. After procedure, hemodynamic parameters were monitored and recorded every 5 minutes for 30 minutes for any complications.

Participant recruitment

Ninety-one participants were assessed for eligibility at a single academic outpatient department between time period of November 2019 to September 2021 based on inclusion and exclusion criteria (Table no 1). Fifty-one participants were not enrolled in the study (26 did not meet inclusion criteria and 25 declined to participate). A total of 40 participants who met the inclusion criteria were randomized for inclusion into the study.

Table 1: Inclusion and exclusion criteria for study participation

Inclusion Criteria	Exclusion Criteria
Degenerative disc disease.	Non discogenic source of back pain
Age 18-50 Years.	Active moderate to severe lumbar radiculopathy
Chronic low back pain (VAS score more than 3).	Intradural disc herniation for more than 6 weeks
Failed management with physiotherapy and medications for 6 weeks duration.	Spinal fracture within past 6 months
No motor deficit in anti-gravity muscles.	
	Prior fusion at level.
	Lumbar spine surgery within 6 months.
	Steroid injection in spine in past 30 days.
	Any intradiscal injection other than contrast dye or anaesthetic within past 30 days.
	Inability to consent to procedure.
	Pregnant or breastfeeding.
	Severe psychological illness.

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	Severe uncontrolled medical condition.
	Active infection.
	Moderate to severe hepatic dysfunction.
	Inflammatory arthritis.
	Malignancy.
	Coagulopathy preventing spinal injection.
	Use of any investigational drug within past 30 days.
	Known allergy or sensitivity to citrate (used for processing PRP.

***Note:** Our standard physiotherapy prescription focuses on patient education regarding proper exercises, back care principles and back strengthening progressive exercise and stabilization instruction to increase core strength and flexibility in a spine safe manner. The program trial is usually twice weekly for a minimum of 6 weeks.

Results

This study was carried out in the Department of Orthopaedics in collaboration with Department of Blood Bank, Anesthesiology and Radiodiagnosis at a tertiary care centre. Comparison between Groups A vs Group B was done using different variables and p value was obtained.

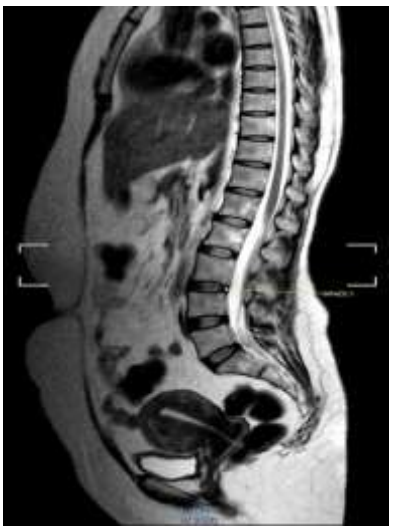

Fig 1: MRI at the time of presentation

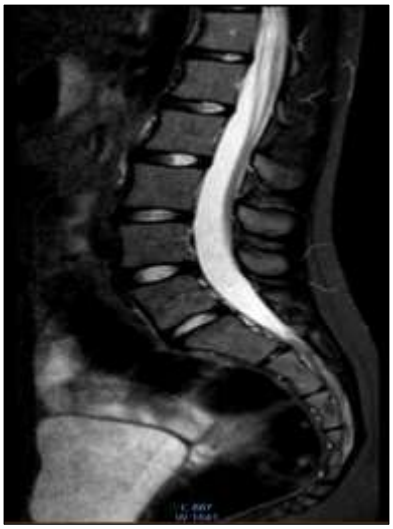

Fig 2: MRI post 6 months of PRP infiltration

Table 2: Comparison between the two groups according to mean age, duration of complaint, sex, age group, PIVD diagnosis distribution

Parameter		Group A	Group B	p value
Age (yr.) (Mean ± SD)		36.55±8.04	38.15± 7.94	0.2925
Duration of Complain (weeks) (Mean ± SD)		10.90± 3.48	11.50± 2.91	0.4103
Sex	Male	7 (35%)	9 (45%)	0.5653
	Female	13 (65%)	11 (55%)	
Age group	20-30 years	5 (25%)	3 (15%)	0.7954
	31-40 years	8 (40%)	10 (50%)	
	41-50 years	7 (35%)	7 (35%)	
PIVD diagnosis distribution	L3-L4	2 (10%)	3 (15%)	0.6457
	L4-L5	13 (65%)	9 (45%)	
	L4-L5,L5-S1	1 (5%)	2 (10%)	
	L5-S1	4 (20%)	6 (30%)	

*Significant (p-value < 0.05)

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Table 3: Comparison between the two groups according to Visual Analogue Scale (VAS)

VAS	Group A	Group B	Difference	95% CI	p-value
	Mean ± SD	Mean ± SD			
At presentation	5.75±0.72	6.50±1.192	0.75	0.2638 to 1.203	0.881
Post 6 Hour	4.68±0.84	3.73±0.70	-0.95	-0.4838 to 0.142	0.714
Post 3 Month	3.30±0.80	4.90±0.97	1.6	0.9941 to 1.304	0.01*
Post 6 Month	3.15±0.74	6.00±0.93	2.8	1.1435 to1.821	0.04*

*Significant (p-value < 0.05)

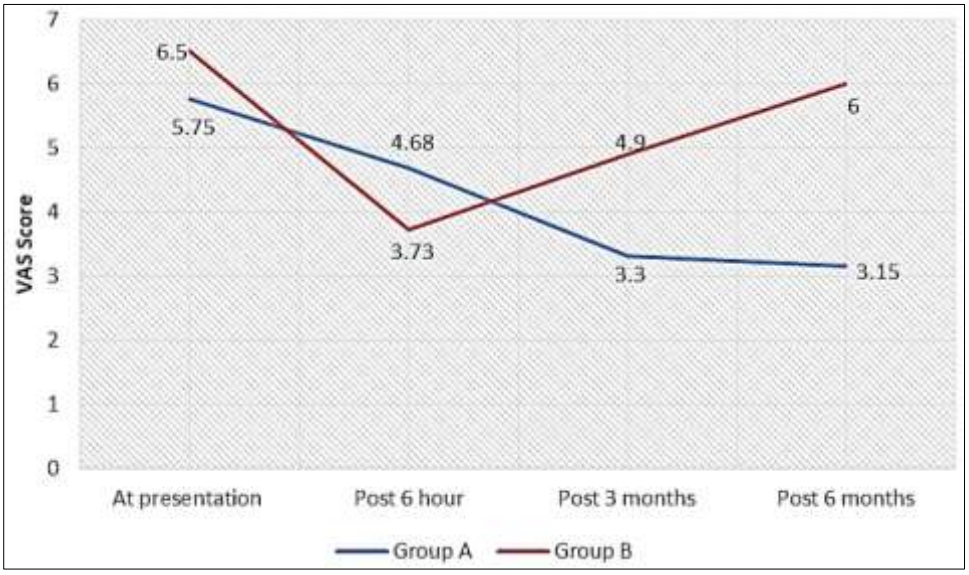

Table 4: Comparison between the two groups according to MODI Score

MODI Score	Group A	Group B	Difference	95% CI	p-value
	Mean ± SD	Mean ± SD			
At presentation	54.10±9.57	59.30±10.08	5.2	-1.0912 to11.4912	0.1025
Post 3 Month	42.60±8.76	52.40±9.21	9.80	4.0463 to 15.5537	0.0014*
Post 6 Month	28.00±4.10	37.80±5.39	9.80	6.7348 to 12.8652	<0.0001*

*Significant (p-value < 0.05)

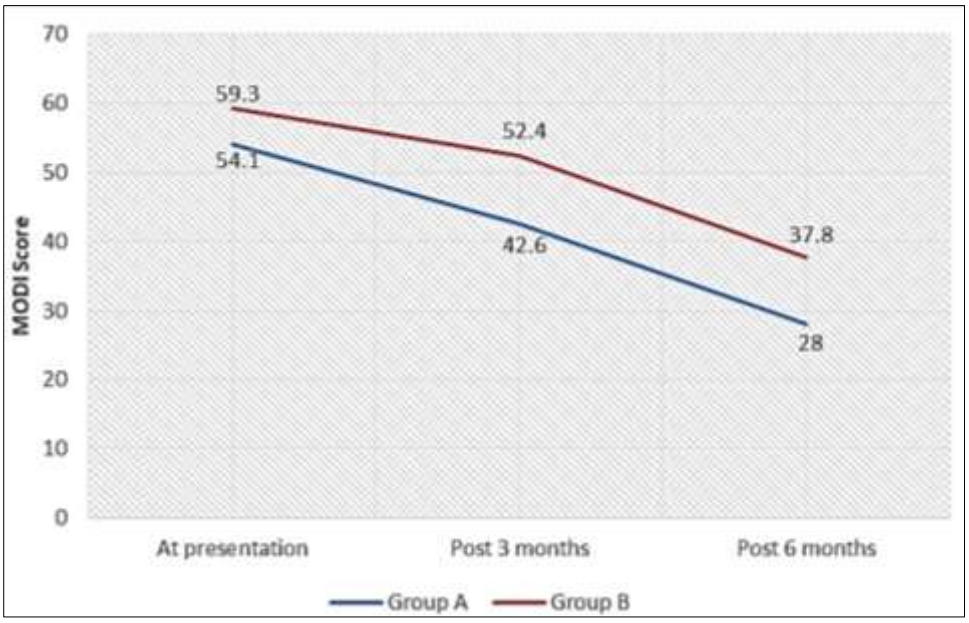

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Table 5: Comparison between the two groups according to Pfirrman and MSU grading

		Group A				Group B			
		At presentation		Post 6 Month		At presentation		Post 6 Month	
		No	%	No.	%	No.	%	No.	%
Pfirrman grading	II	1	5	8	40	2	10	4	20
	III	19	95	12	60	18	90	16	80
P value		0.5483		0.1675		0.5483		0.1675	
MSU grading	1A	9	45	16	80	6	30	11	55
	1B	4	20	3	15	8	40	8	40
	2A	4	20	0	0	3	15	1	5
	2AB	2	10	0	0	2	10	0	0
	2B	1	5	1	5	1	5	0	0
p value		0.7217		0.1578		0.7217		0.1578	

*Significant (p-value < 0.05)

Discussion

LBP is one of the most common health problems and is frequently encountered by orthopaedicians. The multiple possible causes of this symptom make specific disease diagnosis difficult. This dilemma needs organized approach to differentiate between mechanical disorders and rare systemic disorders. The diagnosis of mechanical disorders is often straightforward and does not require radiological or laboratory evaluation. Most low back pain resolves without any intervention, but some reports suggest that episodes of back pain are persistent or recurrent in some patients [1]. Though the causes of chronic low back pain are numerous, lumbar disc degeneration is one of the most common causes. Surgical intervention may be necessary in cases of intractable LBP [2].

PRP is an autologous blood product with increased platelet concentration that has the ability to naturally enhance the healing process biologically. Due to the presence of numerous growth factors such as platelet-derived growth factor and transforming growth factor-beta.[3] These growth factors increase the collagen content, accelerate endothelial regeneration and promote angiogenesis in many different type of tissues. The concentration of growth factors parallels that of the increased concentration of the platelets and activate stem cells to promote the tissue repair and reduce apoptosis [22]. Platelet-rich plasma aids in tissue repair and healing in many different musculoskeletal disorders, such as osteoarthritis, lateral epicondylitis, rotator cuff disease, Achilles and patella tendinopathy, hamstring injuries and degenerative disc disease [24]. Many studies have shown that PRP injections can help with back pain caused by intervertebral disc degeneration [3].

The intervertebral disc is comprised of central nucleus pulpous and surrounding annulus fibrosus which allows mobility between opposing surfaces of the vertebral body.

When degenerative changes exist in the nucleus pulpous, some of the force between the vertebral end plates is exerted directly on the annulus fibrosus leading to tears and fissures in the disc. Although in the early phases these changes are microscopic in appearance, they cause an inflammatory reaction in the surrounding, sensitive, longitudinal ligaments of the spine. This creates a clinical picture of acute LBP [17].

Both steroids and non-steroidal anti-inflammatory drugs have partial effectiveness in treating pain associated with this inflammation. In treating pain due to inflammation steroids and anti-inflammatory agents can be used to relieve the symptom. Therefore, the rationale for using intradiscal steroids is to suppress the inflammation within the disc, thereby alleviating the patient's symptoms. Structurally, intradiscal steroids are thought to promote spinal segment stabilization by decreasing the radial bulges and increasing the disc height [17].

Intradiscal injections of PRP are gaining popularity as a new therapy option for CLBP, with promising results in terms of pain relief and improved functional abilities. As a result, we

conducted this prospective double-blind randomised controlled trial to assess the clinico-radiological outcome in patients with lumbar degenerative disc disease treated with intradiscal PRP and steroids.

In our study the mean age of the patients in group A was 36.55±8.04 years and the mean duration of complaint was 10.90±3.48 weeks and the mean age of the patients in group B was 38.15±7.94 years and the mean duration of complaint was 11.50±2.91 weeks. In the study conducted by Singla *et al*. [25] mean age of patients was 37±10.09 which was concordant with our study. Our study was also partially concordant with Morishita *et al*. [31] in which mean age was 34.14 years and majority of the patients had acute duration of symptoms < 12 weeks.

Among age groups of the studied cases by Shanmugam and Shivakumar [27] showed that the most common affected age group was between the age of 51-60 years (53.33%) while in our study, in both the groups majority of the patients were between the age of 31-40 years. These partially differences may be attributed due to the different setting and locality.

In group A and group B categories, males were 35% and 45% while females were 65% and 55% respectively. Female preponderance was observed in our study which was concordant with study reported by Laxmaiah Manchikanti and colleagues [2] who reported overall increasing prevalence of CLBP, among women aged 21 to 34 and among men aged 45 to 54. Female patients exhibited more severe disc degeneration than male subjects, according to the researchers [15-16].

L4-L5 was the most prevalent PIVD diagnosis in group A and group B (65% and 45% respectively), whereas L5-S1 was the second most common (20% and 30% respectively). Our study was concordant with study conducted by Akeda *et al*. [21] in which PIVD at L4-L5 level was most common. Also, in the study reported by Gurmeet Singh Sarla [29] 80% of the disc prolapse in the lumbar spine occur at L4-L5 and L5-S1 levels which was also concordant with our study.

The outcome of low back pain was assessed by pain VAS score at presentation, post 6-hour, post 3 months and 6 months in both the groups. There was significant reduction in group B as compared to group A only in post 6-hour period. VAS score significantly reduced post 6 months in group A as compared to group B. It is possible that over time the effect of PRP on IVD could have been enhanced due to its repairative and regenerative effect. Comella *et al*. [26] reported reduction in pain and discomfort with intradiscal PRP according to both VAS and present pain index. VAS scores statistically improved from average of 5.6 at baseline to 3.6 at 6 months which was concordant with our study. Levi *et al*. [23] also reported successful outcome of intradiscal PRP at 6 months with a 50% decrease in VAS score with poor early results at 1 month which may reflect the mechanism of action of PRP and time required for treatment effect to occur.

Our study was also concordant with Tavares *et al*. [20] where they reported intradiscal injections of lidocaine and prednisolone acetate to reduce pain intensity for LBP with active discopathy at 1 month, but not at 3 or 6 months. Nyugen *et al*. [19] reported that for persistent low back pain caused by active discopathy, a single glucocorticoid intradiscal injection could reduce low back pain for a month but not for a year which had partially similar results with our study.

In our study MODI Score significantly decreased from baseline 54.10±9.57 to 42.60±8.76 and 28.00±4.10 in group A and from baseline 59.30±10.08 to 52.40±9.21 and 37.80±5.39 in group B from at the time of presentation to post 3 and 6 months respectively. Karamanakos *et al*. [28] reported chronic low back ache successfully treated with a single intradiscal injection of autologous PRP where ODI scores reduced from baseline 74 to 34 and 22 at two and one year follow up which was concordant with our study. Cao *et al*. [18] reported intradiscal steroid injection in LBP and found that no difference of improvement by MODQ score was seen among the patients at 3 and 6 months which related with our study.

Akeda *et al*. [21] found no significant progression of disc height narrowing and ossification

following the injection of PRP releasate into the targeted disc in their research of intradiscal injection of autologous PRP releasate to treat discogenic LBP. Quantitative MRI assessment was done between baseline and follow ups. No significant change was found at baseline and at follow up in both nucleus pulposus and annulus fibrosus on T2 weighted maps. These findings were found to be consistent with our research and no statistically significant difference was seen ($p > 0.05$).

In our study, we also found that in both the groups patients initially presented with varying MSU grades; grade 1A, 1B, 2A, 2AB and 2B but at 6 months majority of patients in both the groups had grade 1A. Hosseini and colleagues [30] evaluated the therapeutic efficacy of intradiscal injection in reducing pain and improving patient's performance in different types of MSU grades for disc disease. Further studies are needed to evaluate PRP and steroid efficacy on MSU grading.

Limitations

The small sample size with single centre study and short follow up was one of the limitations of our study. Further research is needed to evaluate the efficacy of this treatment.

Conclusion

Our study concluded that intradiscal injection of PRP for the management of CLBP is an effective, safe, cheap and better treatment modality in comparison to intradiscal steroid. It results in significant reduction in pain and improved functional status as seen by reduction in VAS scores, MODI score. Although these results are promising, further studies are needed to define the subset of participants most likely to respond to biological intradiscal treatment and the ideal cellular characteristics of the intradiscal PRP injectate.

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