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Original research article

Functional improvement of lumbar discogenic pain with epidural injection of platelet rich plasma

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Abstract

Background: Platelet rich plasma (PRP) is an autologous platelet concentration in a small amount of plasma.

It has been employed in numerous medical sectors for over two decades. Fluoroscopic guided epidural injection of PRP has been found to be an effective treatment for lumbar discogenic pain in multiple researches. The goal of this study was to see how effective this new therapy technique was at relieving pain and improving functional outcome in patients with single-level lumbar discogenic pain.

Materials and Methods: In this prospective analysis, 33 patients having low back pain and unilateral radiculopathy whomever not responded to conservative treatment were enrolled. Under fluoroscopic guidance, all patients received an epidural injection of platelet-rich plasma (PRP). A systematic process was used to make PRP from the patient's own blood. The primary outcome measure was change in pain intensity from baseline to 24 weeks follow-up, as measured by VAS, SLRT, and secondary outcome measures included changes in functional status and quality of life, as measured by the Oswestry Disability Index (ODI) and RMDQ, respectively.

Results: The study included 33 patients, with a mean age of 44 years (range, 22-60 years). At 24th week follow-up, there was a significant improvement in pain intensity, as measured by VAS (mean difference-0.8; F value-261.366; $p<0.001$), SLRT (mean difference-74.4; F value-194.61; $p<0.001$) and functional outcome RMDQ (mean difference-3.4; F value-303.621; $p<0.001$), ODI (meandifference-11.2; F value-363.648; $p<0.001$).

Conclusion: The results of this study suggest that fluoroscopic guided epidural injections of platelet rich plasma may be an effective treatment for single level lumbar discogenic pain. This is a promising finding, as previous treatments for this condition have had limited success. More research is needed to confirm these results, but if they are borne out by further studies, this could be a major breakthrough in the management of discogenic pain.

Keywords: PRP, epidural, low back pain discogenic pain

Introduction

The global toll of low back pain and sciatica is significant. Low back pain has a significant impact on families, individuals, communities, and the health-care systems. In low-income countries, the consequences are disastrous. In 1998, the projected cost of back pain in the United States was $90.7 billion and 11 billion pounds in the United Kingdom in 2000, low back pain was discovered to be one of the most expensive disorders, with direct or indirect expenditures of $9.17 billion dollars had been estimated [1].

Low back pain affects huge proportion of population, a common cause to visit orthopedics OPD. Discogenic low back pain is most common cause of low back pain, contributing up to 39% cases. Disc herniation accounts for 30% cases and other causes have lower prevalence i.e. Facet joint arthropathy, sacroiliitis [2]. The prevalence of the Lumbar radiculopathy is 3-5% [3]. Most common age group is 30-50yr.

Pathogenesis of disc prolapse is degenerative and inflammatory changes around the disc which lead to increase in the levels of interleukin 1, interleukin 6 and interleukin 8. Which further lead to stimulation of nociceptive receptors [5].

Most patients with low back ache due to herniation of disc are managed conservatively by NSAIDS, muscle relaxant, intravenous or oral steroid, opioid and physiotherapy. Mostly conservative management

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have good prognosis However when in patient in whom conservative management do not provide satisfactory result then lumbar or caudal epidural steroid comes into role. Surgical management is reserved for the patient refractory to conservative management or have progressive neurological deficits [6].

There are some complications and limitations of steroid infiltration such as infection, haemorrhagic complication and rare but serious systemic complications such as fluctuation of glycemic levels in diabetics, suppression of hypothalamus-pituitary-adrenal axis, cushingoid syndrome [7].

For the management of discogenic LBP, new biological treatments are being researched. The use of platelet-rich plasma is one such treatment (PRP). Plasma incorporating concentrated platelets obtained from autologous blood is known as PRP. PRP proponents describe it as a "bridge" between conservative therapy and surgery. Platelets are high in growth factors and cytokines, which are intended to help the body to recover itself faster.

Platelet rich plasma is used in various clinical conditions for its healing properties due to growth factors8, hence our study Aims at verify the effectiveness with injection of platelet rich plasma via epidural route in treating single level lumbar discogenic pain.

Materials and Methods

Study design: Prospective Interventional study.

Study duration: Two years.

Study place: Department of Orthopaedics, JSS Hospital, Mysuru.

Sample size

The sample size for the study was calculated using the formula:

n= z2pq/d2.

Where: n = desired sample size when population > 10,000, z = level of significance at 95% CI (=1.96), p = proportion of the study population from similar study = 0.04, q = 1– 0.04 = 0.96 and d = degree of accuracy desired, usually set at 0.05.

Sample size (n) = z2pq/d2 = (1.96)2 x (0.04) x (0.96)/ (0.05)2 = 3.84 x 0.04 x 0.96/0.0025 =0.1474/0.0025= 58.98. The minimum sample size required for this study was 60.

The sample size could not be completed due to covid-19 restriction between the study period.

Sampling technique: Purposive sampling.

Study population and source of data

33 patients who presented to orthopaedics department at JSS hospital from September 2020 to March2022 with Low back pain with unilateral radiculopathy were included under the study population.

Subject eligibility

Inclusion criteria

1. Age between 18years to 60 years
2. Established case of single level lumbar disc lesion with unilateral lower limb radiculopathy
3. Failed appropriate conservative management.

Exclusion criteria

1. Spinal and Neural Congenital Anomalies.
2. Traumatic Spinal Injuries.
3. .Degenerative Lumbar Disc Diseases.
4. Inflammatory Spondyloarthropathy.
5. Infective Spondylodiscitis.
6. Demyelinating diseases.
7. Neoplastic lesion.
8. Progressive neurological deficits.
9. Failed back surgery syndrome.

Study assessments of end point

Patients administered with epidural autologous PRP will be followed up at the end of 2nd, 4th, 12th, 24th weeks to see functional outcome and possible complication.

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Pre-operative evaluation

All patients coming with low back pain with unilateral leg radiculopathy to the Orthopaedic OPD at JSS hospital will be subjected to-

1. Detailed history taking.
2. Thorough clinical examination and radiological investigation.
3. MRI scan of lumbosacral spine.
4. Routine blood investigations.
5. ECG and Chest X ray.

Fig 2: Picture showing clinical demonstration of SLRT

Roland-Morris Low Back Pain and Disability Questionnaire (RMQ)

Instructions

Patient name:_____ File #:_____ Date:_____

Please read instructions: When your back hurts, you may find it difficult to do some of the things you normally do. Mark only the sentences that describe you today.

- ☐ I stay at home most of the time because of my back.
- ☐ I change position frequently to try to get my back comfortable.
- ☐ I walk more slowly than usual because of my back.
- ☐ Because of my back, I am not doing any jobs that I usually do around the house.
- ☐ Because of my back, I use a handrail to get upstairs.
- ☐ Because of my back, I lie down to rest more often.
- ☐ Because of my back, I have to hold on to something to get out of an easy chair.
- ☐ Because of my back, I try to get other people to do things for me.
- ☐ I get dressed more slowly than usual because of my back.
- ☐ I only stand up for short periods of time because of my back.
- ☐ Because of my back, I try not to bend or kneel down.
- ☐ I find it difficult to get out of a chair because of my back.
- ☐ My back is painful almost all of the time.
- ☐ I find it difficult to turn over in bed because of my back.
- ☐ My appetite is not very good because of my back.
- ☐ I have trouble putting on my socks (or stockings) because of the pain in my back.
- ☐ I can only walk short distances because of my back pain.
- ☐ I sleep less well because of my back.
- ☐ Because of my back pain, I get dressed with the help of someone else.
- ☐ I sit down for most of the day because of my back.
- ☐ I avoid heavy jobs around the house because of my back.
- ☐ Because of back pain, I am more irritable and bad tempered with people than usual.
- ☐ Because of my back, I go upstairs more slowly than usual.
- ☐ I stay in bed most of the time because of my back.

Fig 3: RMDQ (Roland morris disability questionnaire)

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SECTION 1 - PAIN INTENSITY
- ☐ I have no pain at the moment.
- ☐ The pain is very mild at the moment.
- ☐ The pain is moderate at the moment.
- ☐ The pain is fairly severe at the moment.
- ☐ The pain is very severe at the moment.
- ☐ The pain is the worst imaginable at the moment.

SECTION 2 - PERSONAL CARE (washing, dressing etc.)
- ☐ I can look after myself normally, without causing extra pain.
- ☐ I can look after myself normally, but it is very painful.
- ☐ It is painful to look after myself and I am slow and careful.
- ☐ I need some help, but manage most of my personal care.
- ☐ I need help every day in most aspects of self-care.
- ☐ I do not get dressed, wash with difficulty and stay in bed.

SECTION 3 - LIFTING
- ☐ I can lift heavy weights without extra pain.
- ☐ I can lift heavy weights, but it gives extra pain.
- ☐ Pain prevents me from lifting heavy weights off the floor, but I can manage if they are conveniently positioned (e.g., on a table).
- ☐ Pain prevents me from lifting heavy weights but I can manage light to medium weights if they are conveniently positioned.
- ☐ I can lift only very light weights.
- ☐ I cannot lift or carry anything at all.

SECTION 4 - WALKING
- ☐ Pain does not prevent me walking any distance.
- ☐ Pain prevents me walking more than 1 mile.
- ☐ Pain prevents me walking more than ½ of mile.
- ☐ Pain prevents me walking more than 100 yards.
- ☐ I can only walk using a stick or crutches.
- ☐ I am in bed most of the time and have to crawl to the toilet.

SECTION 5 - SITTING
- ☐ I can sit in any chair as long as I like.
- ☐ I can sit in my favourite chair as long as I like.
- ☐ Pain prevents me from sitting for more than 1 hour.
- ☐ Pain prevents me from sitting more than ½ an hour.
- ☐ Pain prevents me from sitting more than 10 minutes.
- ☐ Pain prevents me from sitting at all.

SECTION 6 - STANDING
- ☐ I can stand as long as I want without extra pain.
- ☐ I can stand as long as I want but it gives me extra pain.
- ☐ Pain prevents me from standing for more than 1 hour.
- ☐ Pain prevents me from standing for more than ½ an hour.
- ☐ Pain prevents me from standing for more than 10 minutes.
- ☐ Pain prevents me from standing at all.

SECTION 7 - SLEEPING
- ☐ My sleep is never disturbed by pain.
- ☐ My sleep is occasionally disturbed by pain.
- ☐ Because of pain, I have less than 6 hours of sleep.
- ☐ Because of pain, I have less than 4 hours of sleep.
- ☐ Because of pain, I have less than 2 hours of sleep.
- ☐ Pain prevents me from sleeping at all.

SECTION 8 - SEX LIFE (if applicable)
- ☐ My sex life is normal and causes no extra pain.
- ☐ My sex life is normal but causes some extra pain.
- ☐ My sex life is nearly normal but is very painful.
- ☐ My sex life is severely restricted by pain.
- ☐ My sex life is nearly absent because of pain.
- ☐ Pain prevents any sex life at all.

SECTION 9 - SOCIAL LIFE
- ☐ My social life is normal and causes me no extra pain.
- ☐ My social life is normal, but increases the degree of pain.
- ☐ Pain has no significant effect on my social life apart from limiting my more energetic interests, e.g., sports, etc.
- ☐ Pain has restricted my social life and I do not go out as often.
- ☐ Pain has restricted my social life to my home.
- ☐ I have no social life because of pain.

SECTION 10-TRAVELLING
- ☐ I can travel anywhere without pain.
- ☐ I can travel anywhere but it gives extra pain.
- ☐ Pain is bad but I manage journeys over 2 hours.
- ☐ Pain restricts me to journeys of less than 1 hour.
- ☐ Pain restricts me to short necessary journeys under 30 minutes.
- ☐ Pain prevents me from travelling except to receive treatment.

Fig 4: Oswestry Disability Questionnaire

Fig 5: Visual Analogue Scale

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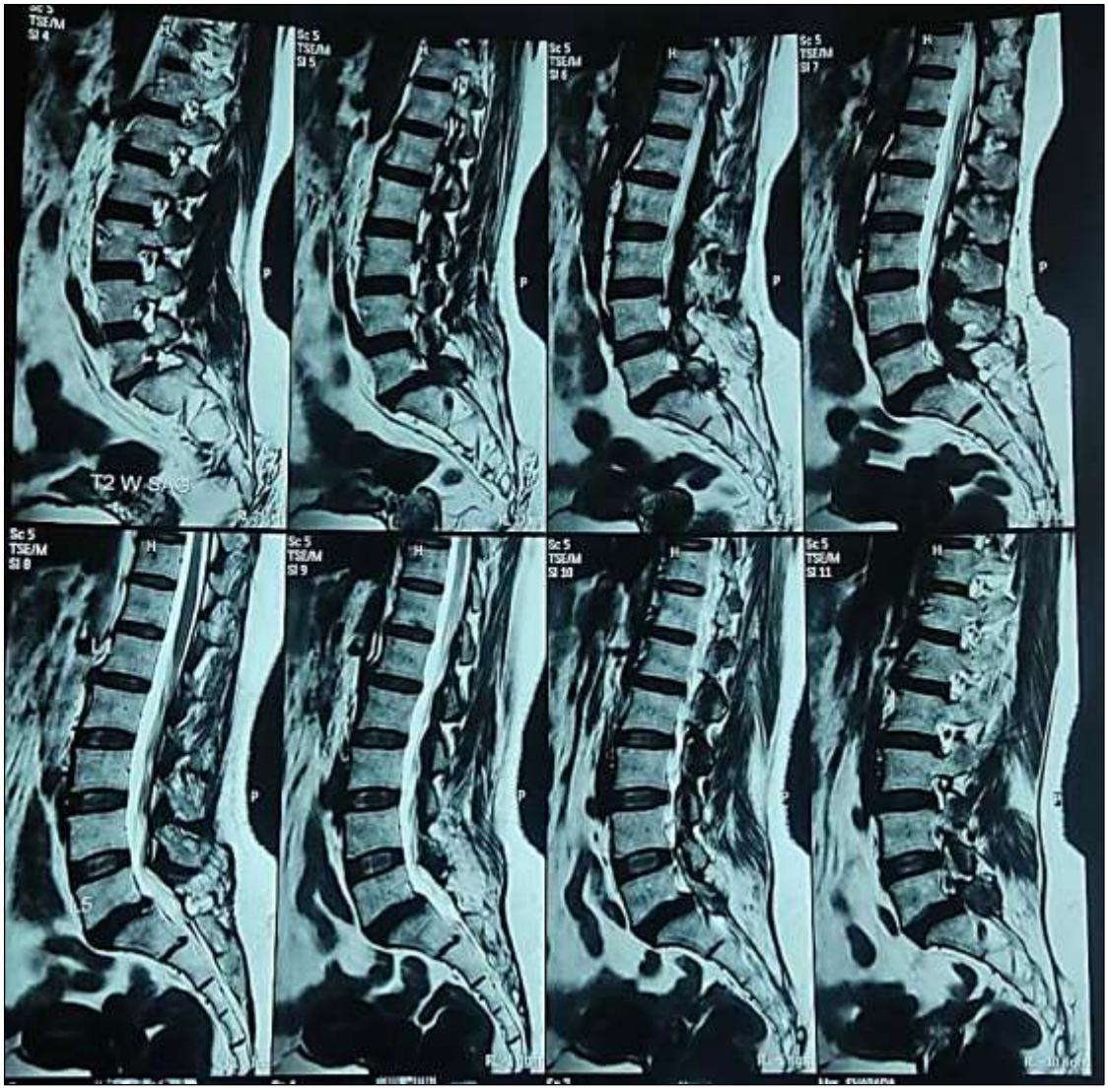

Fig 6: MRI of L-S Spine with IVDP at L5-S1 (T2 weighted)

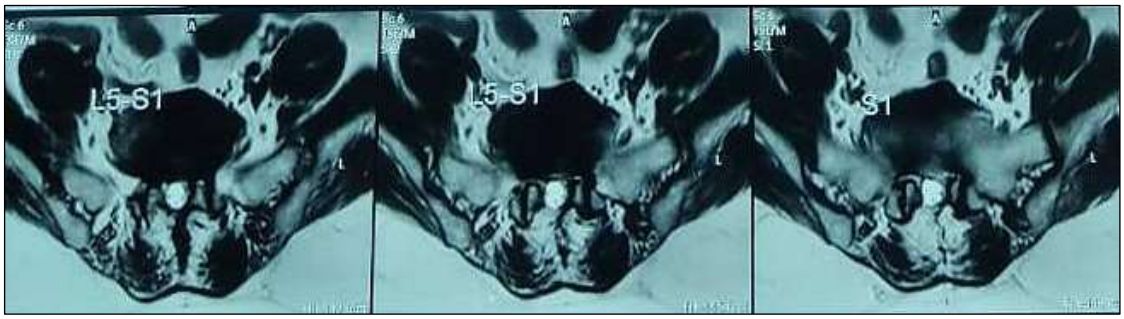

Fig 7: T2 weighted MRI film of L-S spine

Showing IVDP at l5-s1 level

Methodology

PRP Prepration

Double spin method was used for the preparation of PRP as done by Augustus D *et al.* [18]. A total of 20 mL blood was drawn from the patient. The blood was placed in six 2.7ml vaccutainers containing acid citrate dextrose. All of the containers have been filled to the vaccutainers mark. The vaccutainers are then placed in the centrifugation machine's slot in a way that they should counter balance. The initial centrifugation was performed at 1500 RPM for about three minutes. This leads the blood to be divided in the two layers. RBCs are concentrated at the bottom, whereas plasma and platelets are concentrated at the top then using a long 18 G needle and syringe, the top layer is then transferred to new vaccutainers, Which was PRP.

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Role of PRP

PRP comprises a naturally occurring concentration of cytokines and growth factors such as vascular epidermal growth factor, endothelial growth factor, transforming growth factor-1, insulin-like growth factor and platelet-derived growth factor.[19] Because of its ability to promote cell differentiation, proliferation, migration, and production of collagen and ECM proteins, growing researches have revealed the repair and regenerative ability of PRP in many deteriorated or damaged tissues including ligaments, tendons, and cartilage [20, 21, 22]. Moreover, PRP also have an anti-inflammatory property by.

Preventing the activation of inflammatory mediators a long with inhibiting metalloproteinases enzymes and CO-Xenzymes, making it a potential strategy for the treatment of discogenic LBP [23, 24].

A variety of techniques can be used to create autologous of platelet rich plasma. The duration and rate of centrifugation differ. A double centrifugation method adopted by Augustus D *et al*. was to separate blood into plasma and RBC. The generated plasma was isolated into platelet-poor plasma and platelet-rich plasma using a second step of centrifugation. Furthermore, using the trial and error process on a regular basis, we were able to standardize the formulation of platelet-rich plasma. The Platelet rich plasma is also known as autologous platelet gel, platelet rich concentrate, and platelet releasate. Platelet rich plasma is autologous blood with a platelet content above the standard range [18].

According to Hall MP *et al*. platelet rich plasma has growth factor concentrations that are 1-25 fold higher and platelet concentrations that are two to eight significantly greater [25].

In a publication entitled "What is PRP and What Is Not PRP?" by Marx R.E. *et al*. described that the elevation of healing will be connected with at least 10 lakh platelets per ml in five ml of plasma [26]. In a literature publication, Alsousou J. *et al*. defined PRP as having a concentration that is five times the normal count [27].

The method utilised to create the PRP also influences the concentration of growth factors. According to author Augustus *et al*., growth factors are similar as IGF-1, HGF, and PDGF are higher in single centrifugation method than in double centrifugation. We decided against performing growth factor assays because they were not commercially viable [18].

Depending on the concentration of WBC, PRP can be separated into high WBC PRP and low WBC PRP. The WBC count was shown to be low in platelet poor plasma and high in platelet rich plasma, according to Augustus D *et al*. They discovered that the kinds of WBC did not significantly differ between platelet rich plasma and platelet-poor plasma. There was discussion over the concentration of WBC in PRP.[18] Some researcher's proposed avoiding WBC exposure to tissues in order to minimize inflammatory response. WBCs have antimicrobial properties and produce more growth factors, according to Bielecki T.M. *et al*. [28].

Once liberated from circulation, platelets in PRP become active. For platelet activation, several researchers have employed various methods.

According to Kenneth S. Lee *et al*., rupturing the skin during an injection causes bleeding, which provides the clotting agent thrombin, which is required to activate platelets. Administering compounds to activate platelets, such as calcium chloride, type 1 collagen, and bovine thrombin. The needling approach developed by Kenneth S. Lee *et al*. was applied in this work to activate platelets [29].

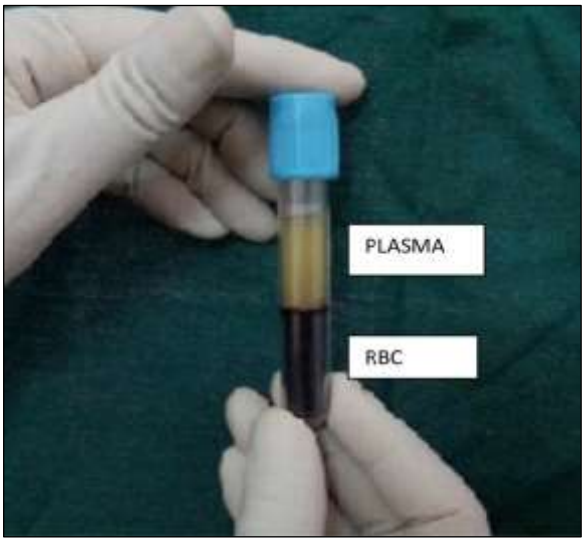

Fig 8: Showing plasma separated from RBC after 1st centrifugation

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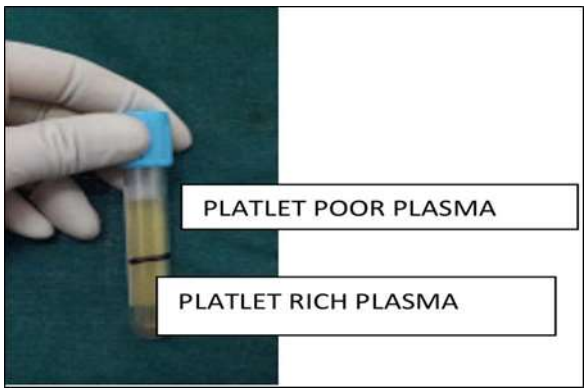

Fig 9: Showing PRP

In operation theatre
Patient positioned on operating table, all vital monitoring devices connected and patient started on Normal saline.

Position
Prone position was used.

Fig 10: Showing position of the patient in theatre

Painting and Draping
Chlorhexidine solution was used to paint the back of the patient and draped with a disposabledrape.

Identification of the spinal level and PRP injection
Under anteroposterior fluoroscopy guidance, target interlaminar space was identified using 27 G needle after giving 2ml of 1% lidocaine. After confirmation of the level, 18G Touhey needle insertedvertically and walk off lamina onto the ligamentum flavum, stylet from the Touhey needle was removed and loss of resistance (LOR) syringe was connected and epidural space was identified with loss of resistance technique. 2ml of the dye is injected in epidural space and confirmed under C-ARM.
After confirmation 5 ml of Platelet rich plasma was administrated into the epidural space.
Following which patient was shifted to the post-operative ward for observation for 2 hours. After 2 hours patient is reassessed for VAS and SLRT and patient was shifted to IP ward. After 24 hours patient was discharged with the following advice:

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1. Avoid lifting heavy weights.
2. Bending forward.
3. Avoid long distance travel.
4. Rest for one week.

Follow up:

1. **At 2nd week:** Patient was reassessed with VAS score, SLRT, ODI and RMDQ.
2. **At 4th week:** Patient was reassessed with VAS score, SLRT, ODI and RMDQ.
3. **At 12th week:** Patient was reassessed with VAS score, SLRT, ODI and RMDQ.
4. **At 24th week:** Patient was reassessed with VAS score, SLRT, ODI and RMDQ.

Fig 11: Showing identification of target level by using C-arm

Fig 12: Showing confirming the epidural space with the help of radio opaque dye

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Fig 13: Infiltration of the PRP in the epidural space

Results

The statistical analysis of the data was performed by using SPSS 23.0. Descriptive statistics were calculated and summarized. Which includes frequency, percentage, mean and standard deviation. Inferential statisticshad been carried out in the study. Six time points comparison was done using repeated measures ANOVA and pair wise comparison done by Bonferroni post hoc test. Level of significance was set at 5%.

Table 1: Showing age distribution of patients

Age	Frequency	Percent
≤30	6	18.2
31-40	8	24.2
41-50	8	24.2
>50	11	33.3

The above table shows 11(33.3%) are of age group >50 years, 8 (24.2%) are in the age group of31-40, 41-50 and 51-60 and 6 (18.2%) are in the less than 30 age group.

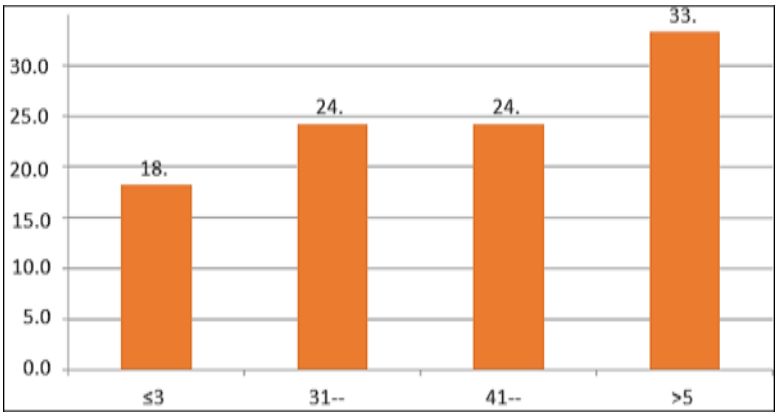

Fig 1: Graph showing age distribution of the patients

Table 2: Showing occupation of the patients

Frequency		Percent
Business	5	15.2
Farmer	11	33.3
House wife	10	30.3
Job	4	12.1
Student	2	6.1
Vendor	1	3.0
Total	33	100.0

The above table shows 10(30.3%) are house wife, 11 (33.3%) are farmers, 5 (15.2%) are doing business, 2 (6.1%) are students and 1(3%) are vendors.

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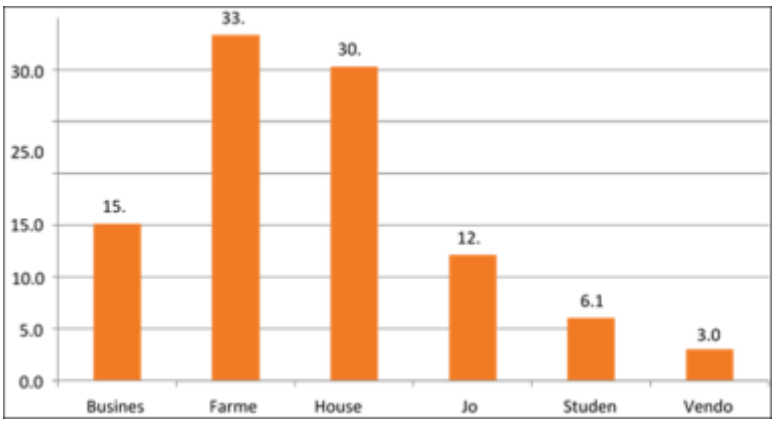

Fig 2: Showing percentage distribution of subjects on the basis of occupation

Table 3: Showing gender distribution of subjects

Gender	Frequency	Percentage
Male	21	63.6
Female	12	36.4

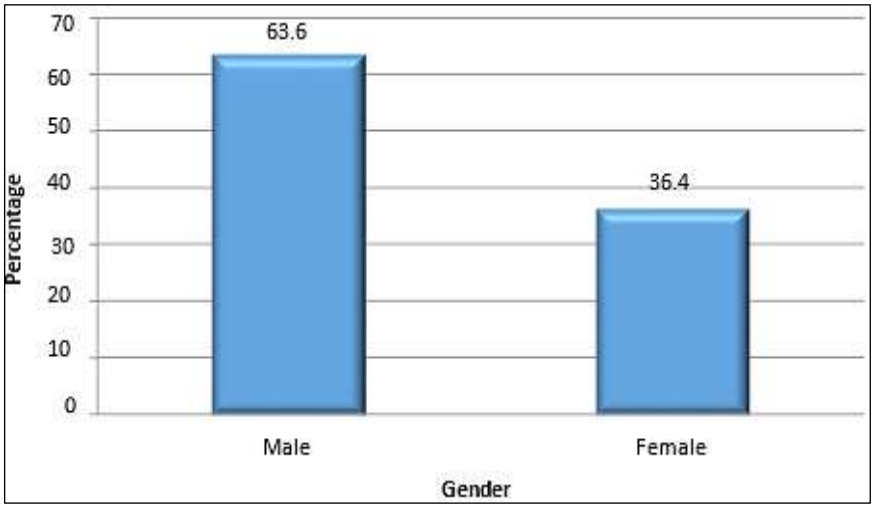

Fig 3: Showing gender distribution of subjects

Table 4: Showing mean, SD and Repeated measures p value of VAS score of subjects across six time points

VAS	Mean	SD	F value	P value
Prior to injection	8.3	0.7	261.366	<0.001*
After 2 hours	6.2	1.1		
2nd week	4.7	1.5		
4th week	3.5	1.6		
12th Week	2.1	1.5		
24th Week	0.8	1.2		

*Significant.

The above table depicts, mean VAS score before injection is 8.3±0.7, and it improved to 0.8±1.2 by the end of 24 weeks. The reduction in VAS score across six time points from before injection to 24th week is statistically significant with $p<0.05$.

Table 5: Showing mean difference and Bonferroni test p value for multiple comparison of VAS score

(I) factor1	(J) Factor	Mean Difference (I-J)	Std. Error	P Value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Before injection	2 hours	2.091*	0.118	<0.001	1.716	2.465
	Week 2	3.530*	0.226	<0.001	2.813	4.247
	Week 4	4.758*	0.282	<0.001	3.863	5.652
	Week 12	6.182*	0.28	<0.001	5.293	7.071
	Week 24	7.485*	0.25	<0.001	6.69	8.279
2 hours	Week 2	1.439*	0.211	<0.001	0.771	2.108

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	Week 4	2.667*	0.267	<0.001	1.819	3.514
	Week 12	4.091*	0.3	<0.001	3.141	5.041
	Week 24	5.394*	0.275	<0.001	4.522	6.266
Week 2	Week 4	1.227*	0.223	<0.001	0.52	1.935
	Week 12	2.652*	0.249	<0.001	1.863	3.44
	Week 24	3.955*	0.263	<0.001	3.12	4.79
Week 4	Week 12	1.424*	0.163	<0.001	0.907	1.941
	Week 24	2.727*	0.243	<0.001	1.955	3.499
Week 12	Week 24	1.303*	0.154	<0.001	0.815	1.791

Indicates the mean difference is significant at the .05 level.

The above table depicts the mean reduction in VAS score

- Before injection to after 2 hours is 2.091.
- 2 hours to week 2 is 1.439.
- Week 2 to week 4 is 1.227.
- Week 4 to week 12 is 1.424.
- Week 12 to week 24 is 1.303.

The reduction in VAS score between each pair of time points is statistically significant with $p<0.05$.

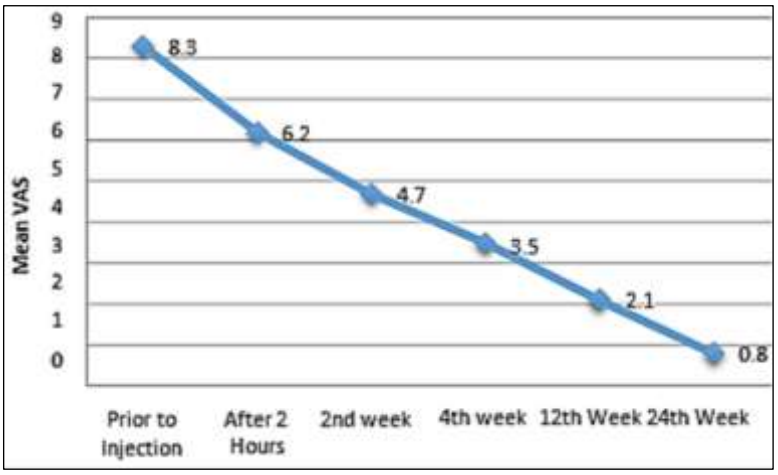

Fig 4: Showing mean VAS score of subjects across six time points

Table 6: Showing mean, SD and Repeated measures p value of SLRT score of subjects across six time points

SLRT	Mean	SD	F value	P value
Prior to injection	22.7	6	194.61	<0.001*
After 2 hours	41.6	7.6		
2nd week	51.4	10.3		
4th week	57.7	11.6		
12th Week	65.9	10.9		
24th Week	74.4	9.6		

*Significant.

The above table depicts, mean SLRT score before injection is 22.7±6, post 2 hours of injection it improved to 41.6±7.6 and sustained until last follow-up. The improvement in SLRT score across six time points from before injection to 24th week is statistically significant with p value < 0.05.

Table 7: Showing mean difference and Bonferroni test p value for multiple comparison of SLRT score

(I) Factor	(J) Factor	Mean Difference (I-J)	Std. Error	P value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Before injection	2 hours	-18.848*	1.182	<0.001	-22.596	-15.101
	Week 2	-28.636*	2.071	<0.001	-35.204	-22.069
	Week 4	-35.000*	2.406	<0.001	-42.632	-27.368
	Week 12	-43.182*	2.387	<0.001	-50.752	-35.612
	Week 24	-51.667*	2.199	<0.001	-58.642	-44.691
2 hours	Week 2	-9.788*	1.572	<0.001	-14.774	-4.802
	Week 4	-16.152*	2.15	<0.001	-22.972	-9.331
	Week 12	-24.333*	2.148	<0.001	-31.146	-17.521
	Week 24	-32.818*	2.075	<0.001	-39.401	-26.235

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Week 2	Week 4	-6.364*	1.448	0.002	-10.956	-1.771
	Week 12	-14.545*	1.662	<0.001	-19.818	-9.273
	Week 24	-23.030*	2.075	<0.001	-29.612	-16.449
Week 4	Week 12	-8.182*	1.039	<0.001	-11.479	-4.885
	Week 24	-16.667*	1.638	<0.001	-21.862	-11.471
Week 12	Week 24	-8.485*	1.12	<0.001	-12.037	-4.933

*Indicates the mean difference is significant at the .05 level.

The above table depicts the mean improvement in SLRT score.

- Before injection and after 2 hours is 18.848,
- 2 hours to week 2 is 9.788
- Week 2 to week 4 is 6.364,
- Week 4 to week 12 is 8.182
- Week 12 to week 24 is 8.485.

The improvement in SLRT score between each pair of time points is statistically significant with p<0.05.

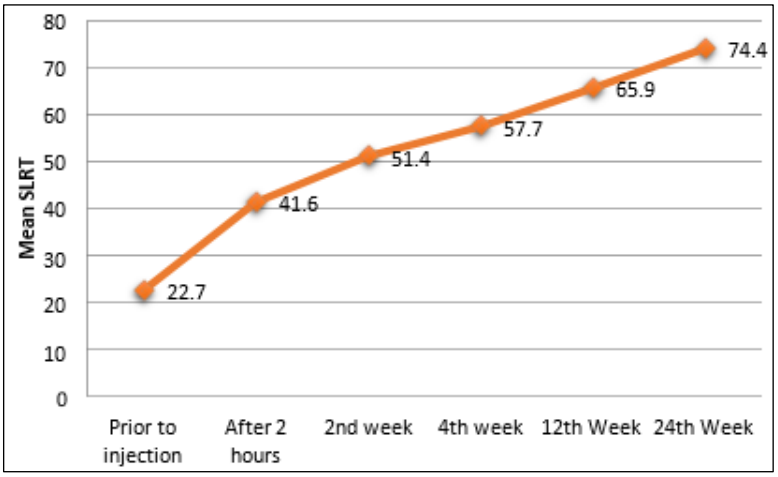

Fig 5: Showing mean SLRT score of subjects across six time point

Table 8: Showing mean, SD and Repeated measures p value of RMDQ score of subjects across six time points

RMQ	Mean	SD	F value	P value
Prior to injection	18.6	1.2	303.621	<0.001*
After 2 hours	17.3	1.8		
2nd week	14.6	2.7		
4th week	12.2	3.4		
12th Week	9.3	3.3		
24th Week	5.5	3.4		

*Significant.

The above table depicts, mean RMDQ score before injection is 18.6±1.2, and at the end of the follow up i.e. 24 weeks it improve to 5.5±3.4. The reduction in RMDQ Score across six time points from before injection to 24th week is statistically significant with *p*<0.05.

Table 9: Showing mean difference and Bonferroni test p value for multiple comparison of RMDQ score

(I) Factor	(J) Factor	Mean Difference (I-J)	Std. Error	p value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Before injection	2 hours	1.273*	0.181	<0.001	0.699	1.846
	Week 2	4.000*	0.384	<0.001	2.781	5.219
	Week 4	6.424*	0.479	<0.001	4.906	7.943
	Week 12	9.303*	0.443	<0.001	7.899	10.707
	Week 24	13.091*	0.469	<0.001	11.602	14.58
2 hours	Week 2	2.727*	0.329	<0.001	1.683	3.772
	Week 4	5.152*	0.435	<0.001	3.77	6.533
	Week 12	8.030*	0.421	<0.001	6.696	9.365
	Week 24	11.818*	0.438	<0.001	10.428	13.209
Week 2	Week 4	2.424*	0.289	<0.001	1.508	3.34
	Week 12	5.303*	0.398	<0.001	4.042	6.564
	Week 24	9.091*	0.467	<0.001	7.608	10.574

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Week 4	Week 12	2.879*	0.396	<0.001	1.623	4.135
	Week 24	6.667*	0.494	<0.001	5.101	8.232
Week 12	Week 24	3.788*	0.281	<0.001	2.896	4.68

Indicates the mean difference is significant at the .05 level.

The above table depicts the mean reduction in RMDQ score before injection to after 2 hours is 1.273, 2 hours to week2 is 2.727, Week2 to week4 is 2.424, week 4 to week 12 is 2.879 Week 12 to week 24 is 3.788.

The reduction in RMDQ score between each pair of time points is statistically significant with $p<0.05$.

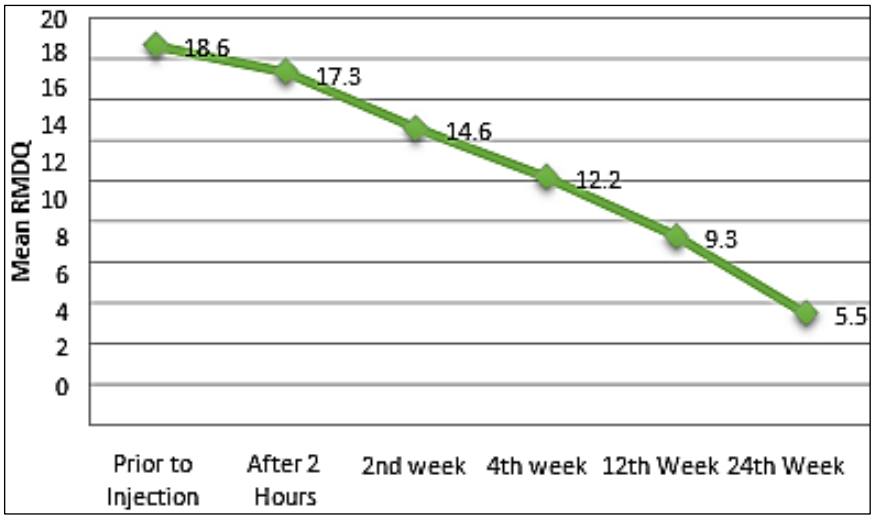

Fig 6: Showing mean RMDQ score of subjects across six time points

Table 10: Showing mean, SD and Repeated measures p value of ODI score of subjects across six time points

ODI	Mean	SD	F value	P value
Prior to injection	73.6	8.5	363.648	<0.001*
After 2 hours	69.1	8.5		
2nd week	56.9	7.9		
4th week	48.6	8.1		
12th Week	38.9	12.5		
24th Week	11.2	9		

*Significant.

The above table depicts, mean ODI score before injection is 73.6±8.5 and by the end of 24 weeks it improve to 11.2±9. The reduction in ODI score across six time points from before injection to 24th week is statistically significant with $p<0.05$.

Table 11: Showing mean difference and Bonferroni test p value for multiple comparison of ODI score

(I) Factor	(J) Factor	Mean Difference (I-J)	Std. Error	p value	95% Confidence Interval for Difference	
					Lower Bound	Upper Bound
Before injection	2 hours	4.485*	0.39	<0.001	3.249	5.72
	Week 2	16.667*	1.461	<0.001	12.033	21.3
	Week 4	25.030*	1.459	<0.001	20.402	29.659
	Week 12	34.606*	2.007	<0.001	28.242	40.971
	Week 24	62.364*	2.124	<0.001	55.627	69.1
2hours	Week 2	12.182*	1.473	<0.001	7.51	16.854
	Week 4	20.545*	1.536	<0.001	15.675	25.416
	Week 12	30.121*	2.109	<0.001	23.433	36.81
	Week 24	57.879*	2.123	<0.001	51.145	64.613
Week2	Week 4	8.364*	1.092	<0.001	4.899	11.828
	Week 12	17.939*	1.959	<0.001	11.726	24.152
	Week 24	45.697*	1.679	<0.001	40.371	51.023
Week 4	Week 12	9.576*	1.278	<0.001	5.521	13.631
	Week 24	37.333*	1.736	<0.001	31.828	42.839
Week12	Week 24	27.758*	1.975	<0.001	21.494	34.021

Indicates the mean difference is significant at the .05 level.

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The above table depicts the mean reduction in ODI Before injection to after 2 hours is 4.485 2 hours to week 2 is 12.182 Week 2 to week 4 is 8.364 Week 4 to week 12 is 9.576 week 12 to week 24 is 27.758. The reduction in ODI score between each pair of time pointsis statistically significant with $p<0.05$.

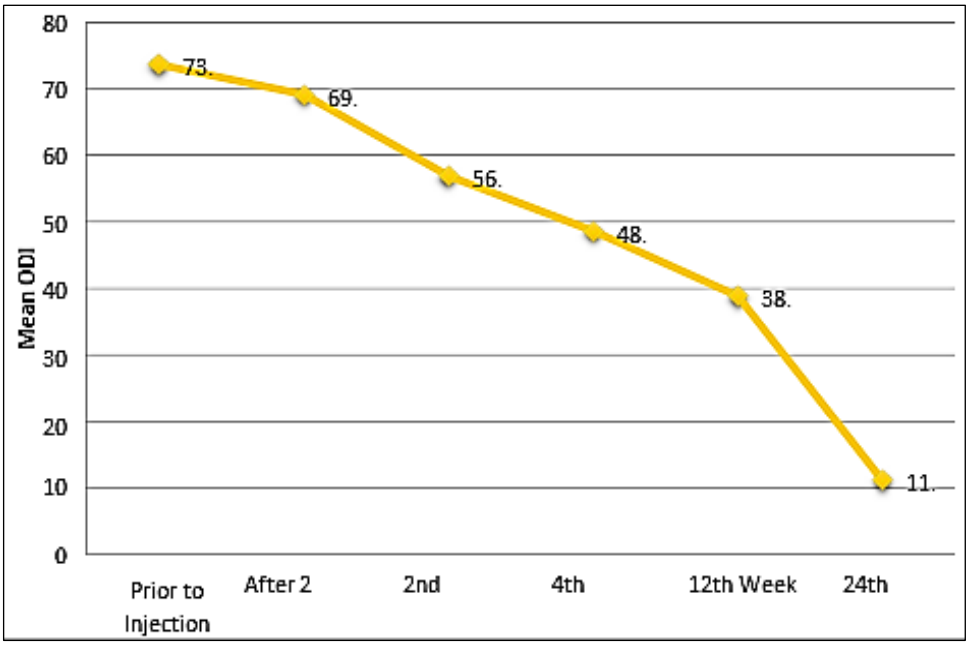

Fig 7: Showing mean ODI score of subjects across six time points

Discussion

Fluoroscopic guided epidural injection of platelet rich plasma (PRP) is a new, minimally invasive management option in single level lumbar discogenic pain.

According to the study, patients with single-level lumbar discogenic pain improved in functional outcome measures after receiving a platelet-rich plasma (PRP) epidural injection under fluoroscopic guidance.

Our study was a prospective, interventional study that included 33 patients who received PRP injections and were followed for 24 weeks.

Table 12: Comparing the age, SLRT, RMDQ, VAS, ODI of various studies with our study

	Age	SLR T	VAS	RMDQ	ODI
Tuakli *et al.* 2016 [12]	41.4	-	Baseline 79.8 ± 15.6	Baseline NR	Baseline NR
			Final F/U 58.2 ± 23.3	Final F/U NR	Final F/U NR
Comella *et al.* 2017 [30]	51.5	-	Baseline 56	Baseline NR	Baseline NR
			Final F/U 36	Final F/U NR	Final F/U NR
Akeda *et al.* 2017 [11]	33.8	-	Baseline 75 ± 13	Baseline 12.6 ± 4.1	Baseline NR
			Final F/U 29 ± 28	Final F/U 2.8 ± 3.9	Final F/U NR
Levi *et al.* 2016 [31]	47.5	-	Baseline 66.0± 12.2	Baseline NR	Baseline 31.0± 9.8
			Final F/U 41.4 ± 27.0	Final F/U NR	Final F/U 23.5 ± 16.2
Bhatia *et al.* 2016 [10]	NR	-	Baseline 61.0 ± 12.0	Baseline NR	Baseline NR
			Final F/U 37.0 ± 6.7	Final F/U NR	Final F/U NR
Our study	44	Base line 22.7 ± 6	Baseline 83.0 ± 0.7	Baseline 18.6±1.2	Baseline 73.6 ± 8.5
		Final F/U 74.4 ± 9.6	Final F/U 0.8±1.2	Final F/U 5.5±3.4	Final F/U 11.2 ± 9

Table 12 shows that the average age of the subjects was 43.6± 7.7 years. Patients in our study had an average age of 44 years, with 63.6% being male and 36.4% being female. Farmers (hard physical labour) and housewives were found to be the most afflicted by discogenic pain (32.21% and 35.7%, respectively), which could be attributed to their posture.

Tuakli-Wosornu *et al.* conducted a double-blind RCT research utilising PRP for discogenic LBP. Patients were given an intradiscal injection of PRP (treatment group) or a contrast agent (control group). When compared to the control group, the treatment group showed statistically significant improvements in numeric pain rating scale (NPRS) best pain, patient satisfaction (North American Spine Society Outcome Questionnaire) and functional rating index (FRI), at the 8-week follow-up. There were no reports of adverse effects such as disc infection, neurologic damage, or increasing herniation [12]. In our study we have observed that there was significant reduction in intensity of pain measured by using VAS scale which was statistically significant. There were no major adverse events reported expect the pain

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radiating to the other non-affected leg but got subsided at end of 24th week it was mainly due to strenuous activity or due to other underlying problem

Previous research on interlaminar CT guided epidural platelet rich plasma and steroid injection in lumbar radicular pain found no significant difference between the two groups in terms of ODI improvement (oswestry disability index) [9]. In the agreement of the this article, our study also showed improvement in disability and quality of life measure.

In a pilot study done by Bhatia *et al*. in which they infiltrated PRP in epidural space showed improvement in SLRT readings [10]. In the agreement of the this article, our study also showed improvement in SLRT range at the end of 24 weeks follow up. Also conclude that at the end of follow up there were no complications and patients were able to do all daily activities without any oral or parenteral route.

In a study conducted by Akeda *et al*. (2021), on safety and initial efficacy of intradiscal injection of autologous platelet-rich plasma (PRP) releasate in patients with discogenic low back pain. In this study the RMDQ score were significantly decreased at one month, and this was generally sustained throughout the observation period (12 months after treatment).13 In the agreement of the this article, our study also showed the reduction in RMDQ score across six time points from before injection to 24th week is statistically significant improvement.

In study done by Bodor *et al*., reported that there was positive impact of single intradiscal injection of PRP and this effect was sustained for almost 6-12 months. Half of them experienced "excellent" and half "good" in terms of pain resolution and returning to the daily activities of life. 32 Similar to the previous research, our study has found out to be effective in reduction of pain on 24 weeks of follow up.

Butternmann and Riew reported the cross over rate of epidural steroid injection to discectomy group in various trials [33, 34]. They both saw that cross over rate was roughly 50%. In Buttermann's randomised controlled trial, 27 of 50 (54%) patients who received epidural steroid injections required discectomy [33], Whereas in Riew's study, 29 of 55 (53%) patients crossed over [34]. In contrast to article, our study no participant had to undergo surgical intervention post administration of PRP injection.

Conclusion

PRP epidural injection may be a new minimally invasive modality of treatment for lumbar discogenic pain, since it demonstrated clinically significant improvement in radicular pain intensity in individuals with lumbar discogenic pain. Furthermore, there were statistically improvement in SLRT, disability, and quality of life which were maintained until the last 24-week follow-up.

We further conclude that PRP epidural injection is safe because it is not associated with any serious problems.

Limitation of the study

There are several potential limitations to this study. First, it is a small, single-center study. Second, the use of fluoroscopic guidance for the epidural injections may not be widely available. Third, the long-term efficacy of this intervention is unknown. Third the small sample size due to the covid pandemic.

References

1. D Hoy PB. Best Practice; Research Clinical Rheumatology. Best Pract. Amp Res Clin Rheumatol. 2010;24(6):769-81.
2. Zhang YG, Guo TM, Guo X, Wu SX. Clinical diagnosis for discogenic low back pain. International journal of biological sciences. 2009;5(7):647.
3. Berry JA, Elia C, Saini HS, Miulli DE. A review of lumbar radiculopathy, diagnosis and treatment. Cureus, 2019 Oct, 11(10).
4. Stafford MA, Peng P, Hill DA. Sciatica: a review of history, epidemiology, pathogenesis and therole of epidural steroid injection in management. Br J Anaesth. 2007 Oct;99(4):461-73.
5. Burke JG, Watson RW, McCormack DR, Dowling FE, Walsh MG, Fitzpatrick JM. Intervertebral discs which cause low back pain secrete high levels of proinflammatory mediators. The Journal of bone and joint surgery. British volume. 2002 Mar;84(2):196-201.
6. Baig MZ, Abdullah UE, Muhammad A, Aziz A, Syed MJ, Darbar A. Use of Platelet-Rich Plasma in Treating Low Back Pain: A Review of the Current Literature. Asian Spine Journal, 2020 Mar.
7. Goodman BS, Posecion LW, Mallempati S, Bayazitoglu M. Complications and pitfalls of lumbar interlaminar and transforaminal epidural injections. Current reviews in musculoskeletal medicine. 2008 Dec;1(3):212-22.
8. Cozma CN, Raducu L, Jecan CR. Platelet Rich Plasma-mechanism of action and clinical applications. Journal of Clinical and Investigative Surgery. 2016;1(2):41-6.
9. Bise S, Dallaudiere B, Pesquer L, Pedram M, Meyer P, Antoun MB, *et al*. Comparison of interlaminar CT-guided epidural platelet-rich plasma versus steroid injection in patients with lumbar radicular pain. European radiology. 2020 Jun;30(6):3152-60.
10. Bhatia R, Chop RAG. Efficacy of platelet rich plasma via lumbar epidural route in chronic prolapsed

ISSN:0975 -3583,0976-2833 VOL14, ISSUE 10, 2023

intervertebral disc patients-a pilot study. Journal of clinical and diagnostic research: JCDR. 2016 Sep;10(9):UC05.

11. Akeda K, Ohishi K, Masuda K, Bae WC, Takegami N, Yamada J, *et al*. Intradiscal injection of autologous platelet-rich plasma releasate to treat discogenic low back pain: a preliminary clinical trial. Asian spine journal. 2017 Jun;11(3):380.
12. Tuakli-Wosornu YA, Terry A, Boachie-Adjei K, Harrison JR, Gribbin CK, LaSalle EE, *et al*. Lumbar intradiskal platelet-rich plasma (PRP) injections: a prospective, double-blind, randomized controlled study. PM&R. 2016 Jan;8(1):1-0.
13. Akeda K, Ohishi K, Takegami N, Sudo T, Yamada J, Fujiwara T, *et al*. Platelet-Rich Plasma Releasate versus Corticosteroid for the Treatment of Discogenic Low Back Pain: A Double-Blind Randomized Controlled Trial. Journal of Clinical Medicine. 2022 Jan;11(2):304.
14. Navani A, Hames A. Platelet-rich plasma injections for lumbar discogenic pain: A preliminary assessment of structural and functional changes. Techniques in Regional Anesthesia and Pain Management. 2015 Jan;19(1-2):38-44.
15. Takeuchi M, Kamei N, Shinomiya R, Sunagawa T, Suzuki O, Kamoda H, *et al*. Human platelet-rich plasma promotes axon growth in brain-spinal cord coculture. Neuroreport. 2012 Aug;23(12):712-6.
16. Doss AX. Trigeminal Neuralgia Treatment: A Case Report on Short-Term Follow up After Ultrasound Guided Autologous Platelet Rich Plasma Injections. Webmed Central Neurology. 2012;3(5):WMC0-03381. Doi: 10.9754/journal.wmc.2012.003381
17. Kim HJ, Yeom JS, Koh YG, Yeo JE, Kang KT, Kang YM, *et al*. Anti-inflammatory effect of platelet-rich plasma on nucleus pulposus cells with response of TNF-α and IL-1. J Orthop Res. 2014 Apr;32(4):551-6. Doi: 10.1002/jor.22532. Epub 2013 Dec 11. PMID: 24338609.
18. Augustus D Moazzocca, *et al*. platelet rich plasma differs according to preparation method and human variability; JBJS A. 2012;94;308-16.
19. Alves R, Grimalt R. A review of platelet-rich plasma: history, biology, mechanism of action, and classification. Skin Appendage Disord. 2018;4(1):18-24.
20. Schneider A, Burr R, Garbis N, Salazar D. Platelet-rich plasma and the shoulder: clinical indications and outcomes. Curr. Rev Musculoskelet Med. 2018;11(4):593-597.
21. Dai WL, Zhou AG, Zhang H, Zhang J. Efficacy of platelet-rich plasma in the treatment of knee osteoarthritis: a meta-analysis of randomized controlled trials. Art Ther. 2017;33(3):659-670.
22. Wong CC, Ou KL, Lin YH, *et al*. Platelet-rich fibrin facilitates one stage cartilage repair by promoting chondrocytes viability, migration, and matrix synthesis. Int. J Mol. Sci. 2020;21(2):577.
23. Cao Y, Zhu X, Zhou R, He Y, Wu Z, Chen Y. A narrative review of the research progress and clinical application of platelet-rich plasma. Ann Palliat Med. 2021;10(4):4823-4829.
24. Urits I, Viswanath O, Galasso AC, *et al*. Platelet-rich plasma for the treatment of low back pain: a comprehensive review. Curr. Pain Headache Rep. 2019;23(7):52.
25. Hall MP, Band PA, Meislin RJ, Jazrawi LM, Cardone DA. Platelet-rich plasma: current concepts and application in sports medicine. JAAOS-Journal of the American Academy of Orthopaedic Surgeons. 2009 Oct;17(10):602-8.
26. Robert E Marx. Platelet rich plasma what is PRP and what is not PRP; Implant dentistry. 2001;10;225-230.
27. .Alsousou J, Thompson M, Hulley P, Noble A, Willett K. Review article, The biology of platelet rich plasma and its application in trauma and orthopedic surgery; JBJS B. 2009;91,987-994.
28. Bielecki TM, Gazdzik TS, Arendt J, Szczepanski T, Krol W, Wielkoszynski T. Antibacterial effect of autologous platelet gel enriched with growth factors and other active substances: an *in vitro* study. The Journal of bone and joint surgery. British volume. 2007 Mar;89(3):417-20.
29. Lee KS, Wilson JJ, Rabago DP, Baer GS, Jacobson JA, Borrero CG. Musculoskeletal applications of platelet-rich plasma: fad or future? American Journal of Roentgenology. 2011 Mar;196(3):628-36.
30. Comella K, Silbert R, Parlo M. Effects of the intradiscal implantation of stromal vascular fraction plus platelet rich plasma in patients with degenerative disc disease. Journal of translational medicine. 2017 Dec;15(1):1-8.
31. Levi D, Horn S, Tyszko S, Levin J, Hecht-Leavitt C, Walko E. Intradiscal platelet-rich plasma injection for chronic discogenic low back pain: preliminary results from a prospective trial. Pain medicine. 2016 Jun;17(6):1010-22.
32. Dregalla RC, Uribe Y, Bodor M. Human mesenchymal stem cells respond differentially to platelet preparations and synthesize hyaluronic acid in nucleus pulposus extracellular matrix. The Spine Journal. 2020 Nov;20(11):1850-60.
33. Buttermann GR. Treatment of lumbar disc herniation: epidural steroid injection compared with discectomy: a prospective, randomized study. JBJS. 2004 Apr;86(4):670-9.
34. Riew KD, Park JB, Cho YS, Gilula L, Patel A, Le6n1ke LG, *et al*. Nerve root blocks in the treatment of lumbar radicular pain: a minimum five-year follow-up. JBJS. 2006 Aug;88(8):1722-5.