ORIGINAL RESEARCH

A comparative study to assess the clinical outcomes in osteoarthritis of the knee between intra-articular platelet rich plasma (PRP) injections vs intra-articular corticosteroid injections

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Received date: 06 January, 2024 Acceptance date: 17 February, 2024

ABSTRACT
Osteoarthritis (OA) is by far the most common form of joint disease throughout the world. It is strongly associated with age, and extremely common in older people, Some studies estimate that over 80% of people over 55 years of age have osteoarthritis of at least one joint. It mainly affects the hips, knees, spine, hands and feet. Hip and knee OA are the most important because of the high prevalence of pain and disability that they cause in older adults. **Methodology:** Patients visiting the department of orthopaedics, narayan medical college and hospital that meet the inclusion criteria. Patient were be divided into 2 groups randomly (30 in each group).one group was administered intra- articular corticosteroid injection (1 ml of triamcinolone acetonide with 1ml of 2% lignocaine without epinephrine). And the other group was administered intra-articular prp injection into the affected knee (5 ml of prp). Following treatment they were assessed using mcmaster universities arthritis index (womac)[56], visual analogue scale (vas), scoring systems which will be recorded through questionnaires prior to the injection to record baseline scores and post injection then at 6weeks,3,6 and 12months follow-up. **Result:** Significant difference was seen in mean WOMAC scores in Group A and Group B at 1 week, 4weeks, 8 weeks, 12 weeks and 12 months but no significant differences were observed at 6 months. Significant differences were seen in the VAS score for Group A and Group B subjects at 1 week, 4 weeks, 8 weeks, 12 weeks, 6 months and 12 months when compared using independent t test as $p<0.05$. **Conclusion:** for a long duration relief of symptoms and the functional outcome, intraarticular PRP is better than Triamcinolone acetonide injections.
Keywords: Osteoarthritis, Platelet Rich Plasma, Intra-articular Injection, Triamcinolone acetonide, WOMAC Scale, VAS Scale

INTRODUCTION

As the average human lifespan increases, there is an increased chance of damage to the articular cartilages that causes pain. This in turn will contribute to a decrease in the quality of life that result in poor socioeconomic effects. Cartilage lesions can cause significant morbidity as articular cartilage tissues have limited healing potency.[1] Although hyaline cartilage is well known for its smooth surface and excellent ability to withstand huge amounts of pressure, the regenerative ability of cartilage tissue is poor with increasing age. [2]

Osteoarthritis (OA) is by far the most common form of joint disease throughout the world. It is strongly associated with age, and extremely common in older people, Some studies estimate that over 80% of people over 55 years of age have osteoarthritis of at least one joint.

It mainly affects the hips, knees, spine, hands and feet. Hip and knee OA are the most important because of the high prevalence of pain and disability that they cause in older adults.[3]

In the past several decades, the major treatment for severe degenerative osteoarthritis (OA) has been

to replace the articular surfaces. In cases of early OA, the major treatment option is a conservative therapy for pain reduction because there is nothing known to stop the progression of degeneration sequences. Although joint replacement treatment has developed significantly from technical point of view, it is still insignificant when viewed from a regenerative perspective. Recently, new reparative methods, including platelet -rich plasma (PRP) treatment, to treat early OA and cartilage lesions are getting clinical attention.

PRP consists of a volume of plasma with a platelet concentration 2-6 times above baseline values that are obtained from the patient's own blood.[4] As such, PRP is safe from immune reaction and blood diseases because it is obtained from autologous blood and the application of PRP in the outpatient clinic is possible. In addition, it is cheap and effective, and no additional procedures are required.[5]

Platelet-rich preparations containing a large pool of growth factors (GFs) and proteins stored in the alpha granules of platelets. These GFs and proteins have been implicated in tissue repairing mechanisms and have been found to take part in the regeneration of articular cartilage.[6]

They are directed at stimulating repair and replacing damaged cartilage, which is incapable of repair, given its avascular, aneural and hypocellular nature. Various growth factors (platelet-derived growth factor, transforming growth factor beta, vascular endothelial growth factors), endostatins, platelet factor 4, angiopoietins, and thrombospondin 1 are secreted upon activation of platelets, and these are involved in the healing process.[7]

Moreover, platelets have been identified to have analgesic properties by releasing protease- activated receptor 4 peptides.[8]

However, PRP contains not only platelets but also plasma with fibrin and other growth factors that influence healing. The 'therapeutic dose' of PRP is considered at a range of at least 2–6 times higher than the normal platelet count.[9]

Corticosteroids have both anti-inflammatory and immunosuppressive effect, but their mechanism of action is complex. Corticosteroids act directly on nuclear steroid receptors and interrupt the inflammatory and immune cascade at several levels. By this means, they reduce vascular permeability and inhibit accumulation of inflammatory cells, phagocytosis, production of neutrophil superoxide, metalloprotease, and metalloprotease activator, and prevent the synthesis and secretion of several inflammatory mediators such as prostaglandin and leukotrienes.[10]

The clinical anti-inflammatory reflections of these actions are decreases in erythema, swelling, heat, and tenderness of the inflamed joints and an increase in relative viscosity with an increase in hyaluronic acid (HA) concentration.[11] The initial recommended treatments for OA are the various non-pharmacological modalities (patient education, various self-management programmes, diet, and other therapies) and pharmacological therapies (involving non-opiate oral analgesics as well as the application of topical agents).

The use of intraarticular (IA) corticosteroid can be considered in patients that are unresponsive to these treatments, and is recommended when signs of local inflammation with joint effusion are present.[12] IA CS injections are frequently used to treat acute and chronic inflammatory conditions. Especially during the OA flare, when there is evidence of inflammation and joint effusion, CS injections decrease acute episodes of pain and increase joint mobility.[13]

Therefore, in this study, we aimed to assess whether PRP is an effective treatment for knee OA, and compare its efficacy with corticosteroid treatment in terms of pain control, physical function, and quality of life.

METHODOLOGY

Type of study: The study was a randomized prospective study.

Source: Patients with symptomatic OA of the knees of age of 40 - 65 years, at Narayan Medical College and Hospital, Jamuhar, were the subjects of the study.

Sampling methods: The randomized prospective method was used in this study.

Inclusion criteria

1. Patients with symptomatic OA of the knees between the ages of 40 - 65 years.
2. Patients having severe pain without relief with anti-inflammatory agents and physiotherapy even after 3 months.

Exclusion criteria

1. Patients diagnosed with any form of arthritis except OA,
2. concomitant severe hip OA were not included in the study.
3. A previous surgery on the knee
4. Blood disorders, systemic metabolic disorders, immunodeficiency, Hepatitis B or C, HIV positive status.
5. Local or systemic infection and ingestion of anti-platelet medications within 7 days prior to the injection

Sample size: 60 cases. 30 in each group

Duration of study: 2 years DECEMBER 2019 to NOVEMBER 2021

Patient was divided into 2 groups randomly (30 in each group).one group was administered intra-

articular corticosteroid injection (1 ml of Triamcinolone Acetonide with 1ml of 2% Lignocaine without epinephrine). And the other group was administered intra-articular PRP injection into the affected knee (5 ml of PRP).

During the study, the patients received no other intra-articular injections or oral medications for the knee with the exception of acetaminophen on an 'as required' basis.

Patients were questioned regarding analgesic consumption and alternative treatments at each follow-up.

All patients will be advised physiotherapy, with the same protocol after the injection to improve quadriceps muscle strength and range of motion.

Pre-treatment Investigations

Radiographic evaluation anteroposterior/lateral views of the knees.

Routine blood investigations were carried out before treatment, including complete blood count, profile ESR, RA Factor, Uric acid, Blood Urea, Creatinine, RBS and screening for transmittable diseases (HIV, HBsAg,HcV), ultrasound of the knee for synovial effusion.

WOMAC and VAS scores were recorded pre-treatment.

PRP injection technique

The procedure for collection of PRP was done under sterile condition using a double spin technique 30 ml of venous blood samples were collected, from every patient belonging to this group in sterilized sodium citrated tubes. The tubes with citrated blood were centrifuged at 1800 rpm for 15 min to separate erythrocytes, and at 3500rpm for 10 min to concentrate platelets.

The PRP aspirated (5ml) into a syringe and intra-articular infiltration by a superolateral approach under sterile aseptic precautions.

Corticosteroid injection technique

Inj. Triamcinolone Acetonide 40 mg/ml along with 1ml of Lignocaine (2%) was injected using a 5cc syringe intra -articular infiltration by a superolateral approach using sterile aseptic precautions.

Post-treatment

After treatment, compression bandage was applied for 48hrs, along with local ice packs application for 20 mins, every 3-4 hours for 48 hours. Patients were allowed weight bearing, Vigorous activities of the knee was not recommended for 48 hrs. A follow up was done after 48 hrs and the compression bandage was removed.

Following treatment they were assessed using McMaster Universities Arthritis Index (WOMAC)[31], Visual Analogue Scale (VAS) (0 = no pain to 10 = worst possible pain) [32], scoring systems which was recorded through questionnaires prior to the injection to record baseline scores and post injection then at 6weeks,3,6 and 12 months follow-up.

RESULTS

Data was analyzed using Statistical Package for Social Sciences (SPSS) version 21, IBM Inc. Descriptive data was reported for each variable. Descriptive statistics such as mean and standard deviation for continuous variables was calculated.

Summarized data was presented using Tables and Graphs. Shapiro Wilk test was used to check the normality of the data. As the data was found to be normally distributed bivariate analyses was performed using Independent t test. Chi square test was used for categorical data. Level of statistical significance was set at p-value less than 0.05 and was denoted as "S".

Table No.1: Age wise distribution of patients

Age in years	Group A		Group B		Total	
	No.	%	No.	%	No.	%
40-50	9	30.0	11	36.7	20	33.3
51-60	15	50.0	15	50.0	30	50.0
61-70	6	20.0	4	13.3	10	16.7
Total	30	100.0	30	100.0	60	100.0
Mean ± SD	55.03 ± 6.01		52.97 ± 6.54		54 ± 6.3	
t-test value P-value	t = 1.27		P = 0.208 NS			

NS= not significant, S=significant, HS=highly significant, VHS=very highly significant Study observes that, maximum number of patients in both the groups 15 (50.0%) belong to the age group of 51-60 followed by 40-50 years age group. But there was no statistical significant difference in mean age between groups A and B when compared using Independent t test.

Table No.2: Gender wise distribution of patients

Gender	Group A		Group B		Total	
	No.	%	No.	%	No.	%
Females	16	53.3	17	56.7	33	55.0
Males	14	46.7	13	43.3	27	45.0
Total	30	100.0	30	100.0	60	100.0

X^2-test value P-value	X^2 = 0.795	P = 0.500	NS

Study observes that, Female patients were more 16 (53.3 %) in groups A and 17 (56.7%) in group B. But there was no statistical significant difference of gender between the groups A and B when compared using Chi square test.

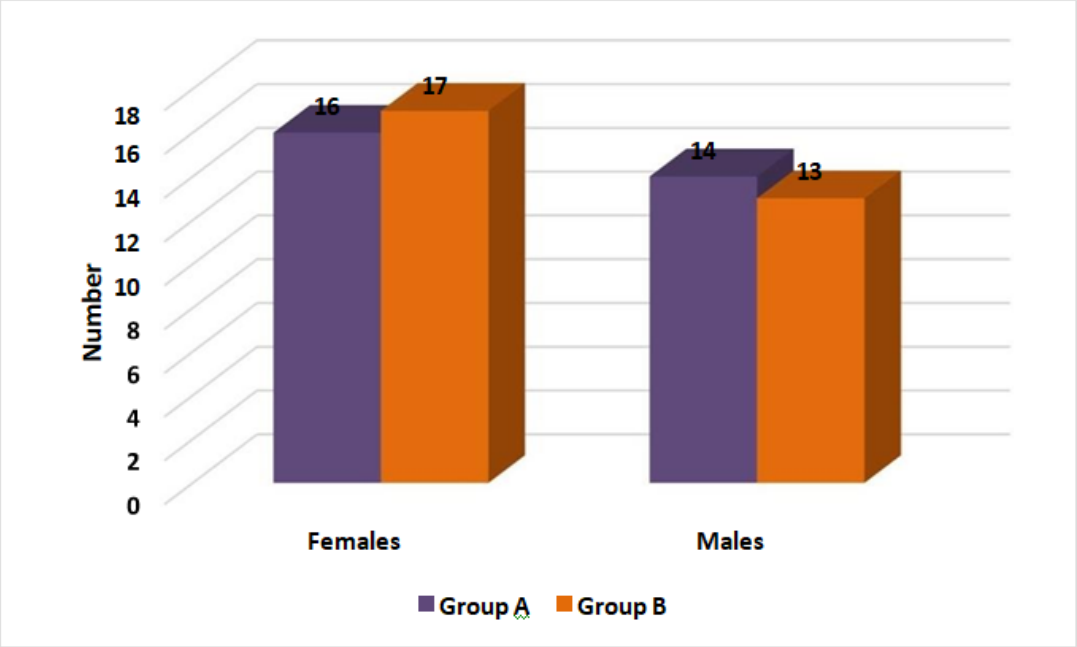


Table no 3: Diagnosis wise distribution of patients

Diagnosis	Group A		Group B		Total	
	No.	%	No.	%	No.	%
OA of B/L knee	12	40.0	13	43.3	25	41.7
OA of Right Knee	8	26.7	9	30.0	17	28.3
OA of Left Knee	10	33.3	8	26.7	18	30.0
Total	30	100.0	30	100.0	60	100.0
X^2-test value P-value	X^2 = 0.32		P = 0.852		NS	

Present study observes that, OA of B/L Knee diagnosed cases were more 25 (41.7 0%), OA of Right Knee and OA of Left Knee patients were 17 (28.3%) and 18 (30%) respectively. And there was no statistical significant difference of diagnosis between the groups A and B.

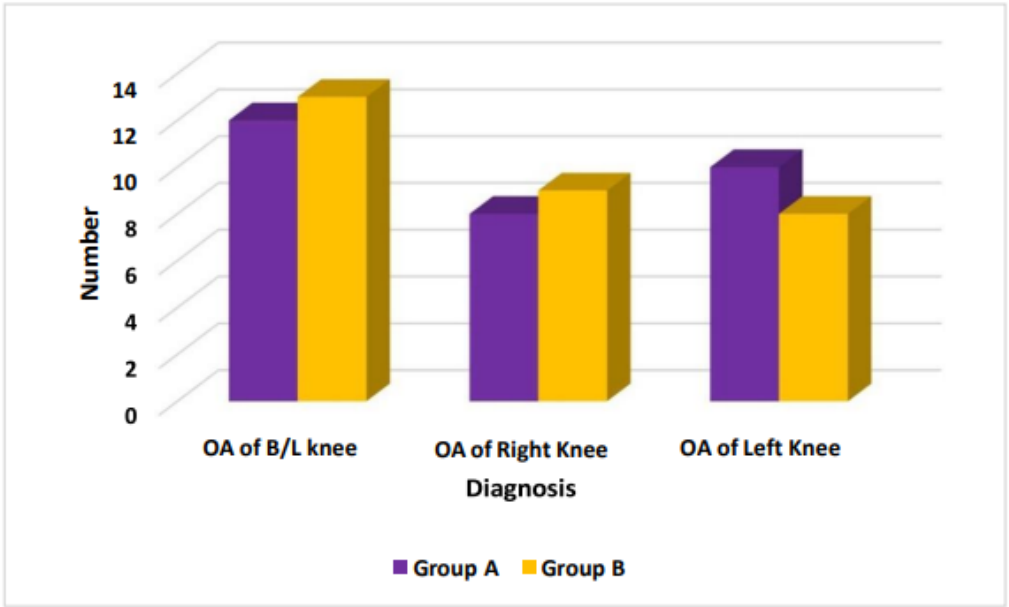


Table No.4: Distribution of patients according to duration of symptoms

Duration in months	Group A		Group B		Total	
	No.	%	No.	%	No.	%
< 6	1.00	5	3	10.0	8	13.3
6--12	2.00	7	11	36.7	18	30.0
12--24	3.00	18	13	43.3	31	51.7
>24	0	0.00	3	10.0	3	5.0
Total	30	100	30	100.0	60	100.0
Mean ± SD	**13.90 ± 6.20**		**14.33 ± 7.77**		**14.12 ± 6.99**	
t-test value P-value	**t = -0.238**				**P = 0.813**	**NS**

Study reveals that, 31 (51.7%) of patients had the 12- 24 months duration of symptoms. And there was no statistical significant difference of duration of symptoms in months between the groups A and B

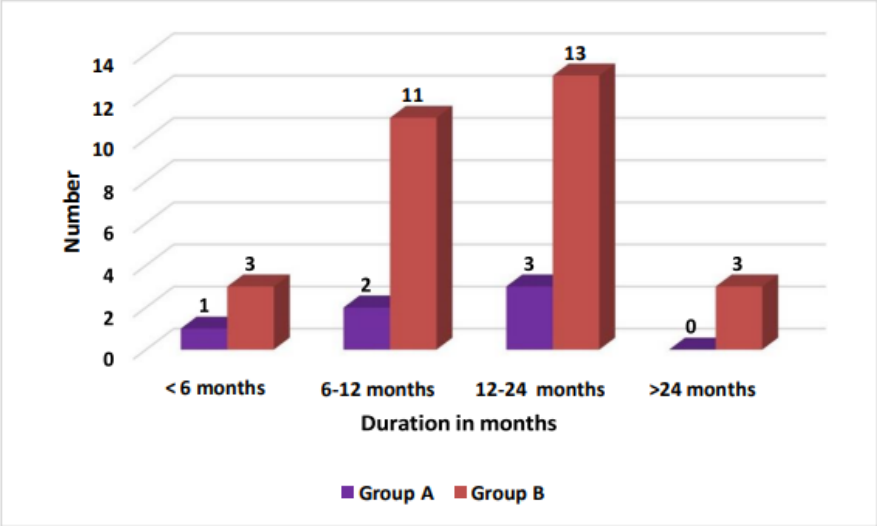


Table No.5: Distribution of patients according to clinical grading (K-L GRADE)

Clinical grading	Group A		Group B		Total	
	No.	%	No.	%	No.	%
Grade I	10	33.3	10	33.3	20	33.3
Grade II	20	66.7	20	66.7	40	66.7
Total	30	100.0	30	100.0	60	100.0
X^2-test value P-value	X2 = 0.000		P = 0.608		NS	

Study observes that, Grade I patients were less in the both the groups 10 (33.30%) and 10 (33.3%) respectively group A and B, Grade II patients were 20 (66.70%) and 20 66.7%) in the group A and B respectively, but there was no statistical significant difference of clinical grading between the groups A and B

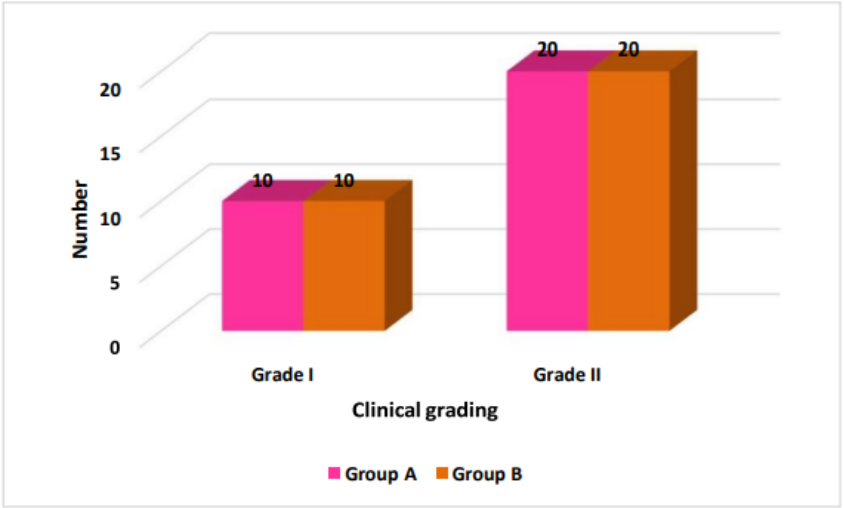


Table No.6: Comparison of mean WOMAC scores between the groups A and B

Time period	WOMAC scores		t– test value	P- value and Significance
	Group A	Group B		
	Mean ± SD	Mean ± SD		
Baseline	60.03 ± 16.84	55.93 ± 17.89	t = 0.914	P = 0.365 NS
1 week	53.20 ± 16.94	14.97 ± 7.07	t = 11.40	P = 0.0001 S
4 weeks	48.63 ± 15.94	16.67 ± 6.89	t = 10.07	P = 0.0001 S
8 weeks	44.13 ± 15.79	19.67 ± 8.21	t = 7.52	P = 0.0001 S
12 weeks	38.87 ± 16.20	24.73 ± 11.14	t = 3.93	P = 0.0001 S
6 months	31.10 ±14.88	38.27 ± 16.69	t = -1.75	P = 0.085 N S
12 months	29.57 ± 14.38	44.93 ± 18.28	t=-3.61	P = 0.0001 S

Significant difference was seen in mean WOMAC scores in Group A and Group B at 1 week, 4weeks, 8 weeks, 12 weeks and 12 months but no significant differences were observed at 6 months.

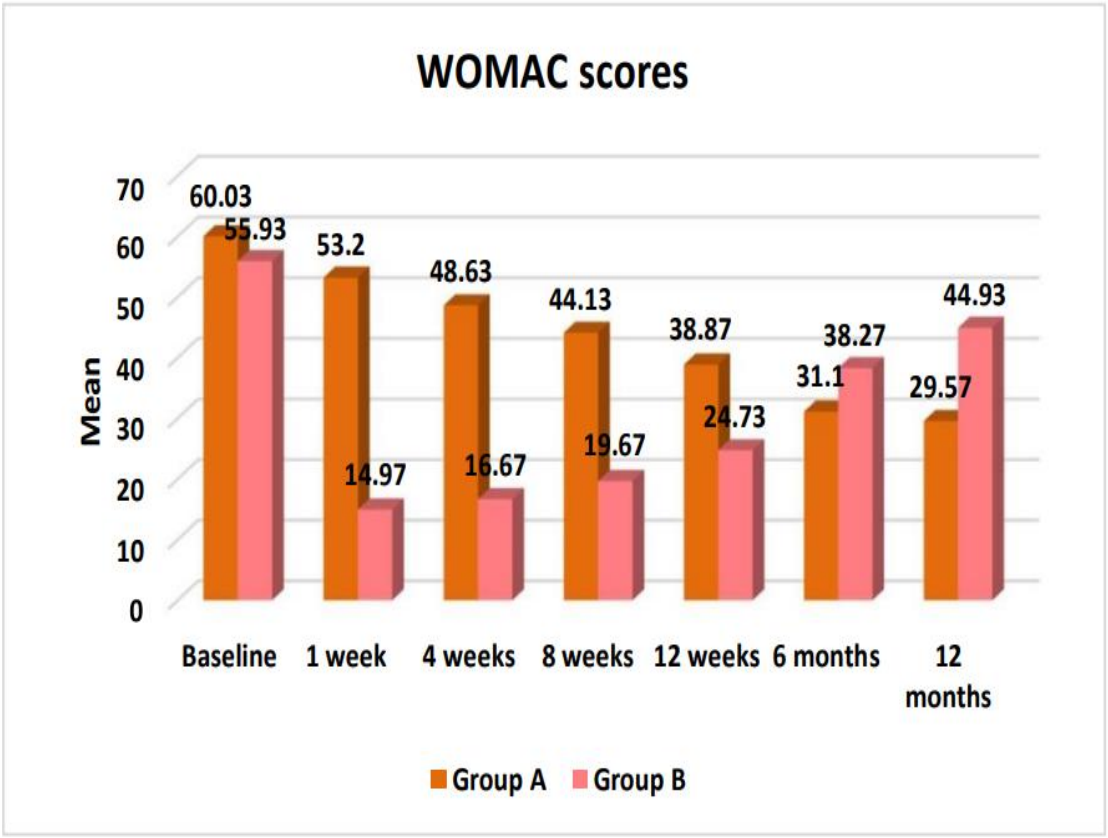
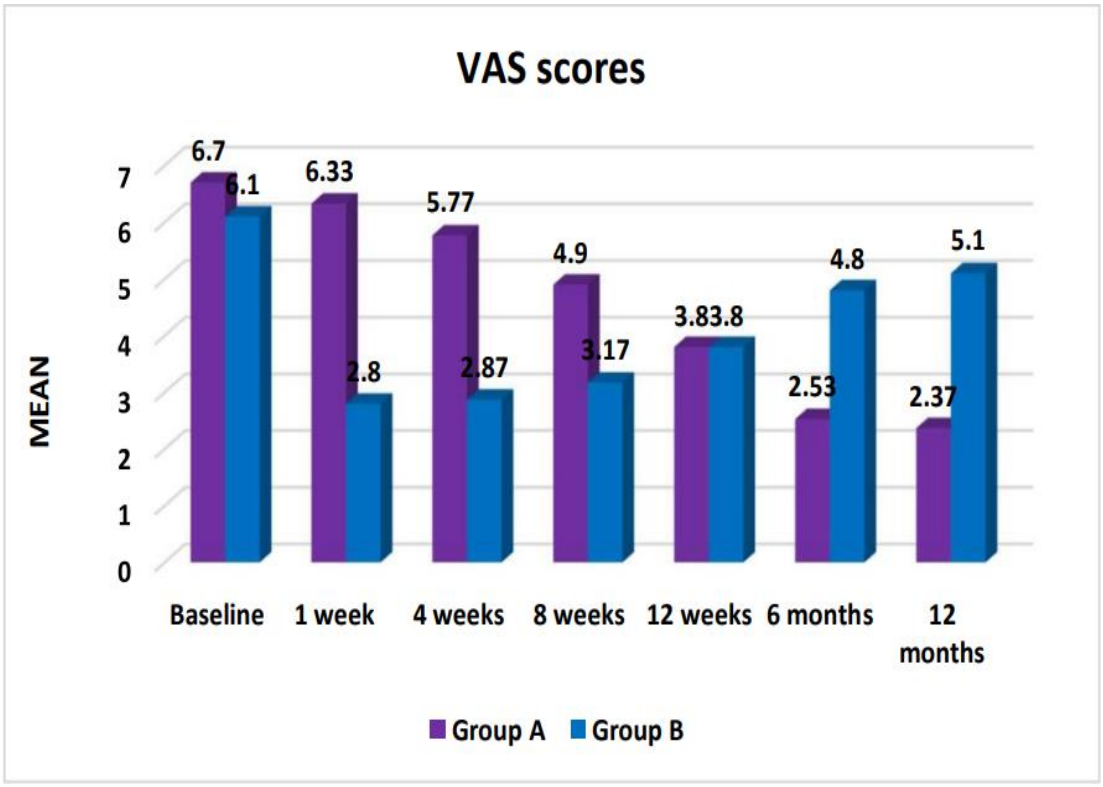


Table No.7: Comparison of mean VAS scores between the groups A and B

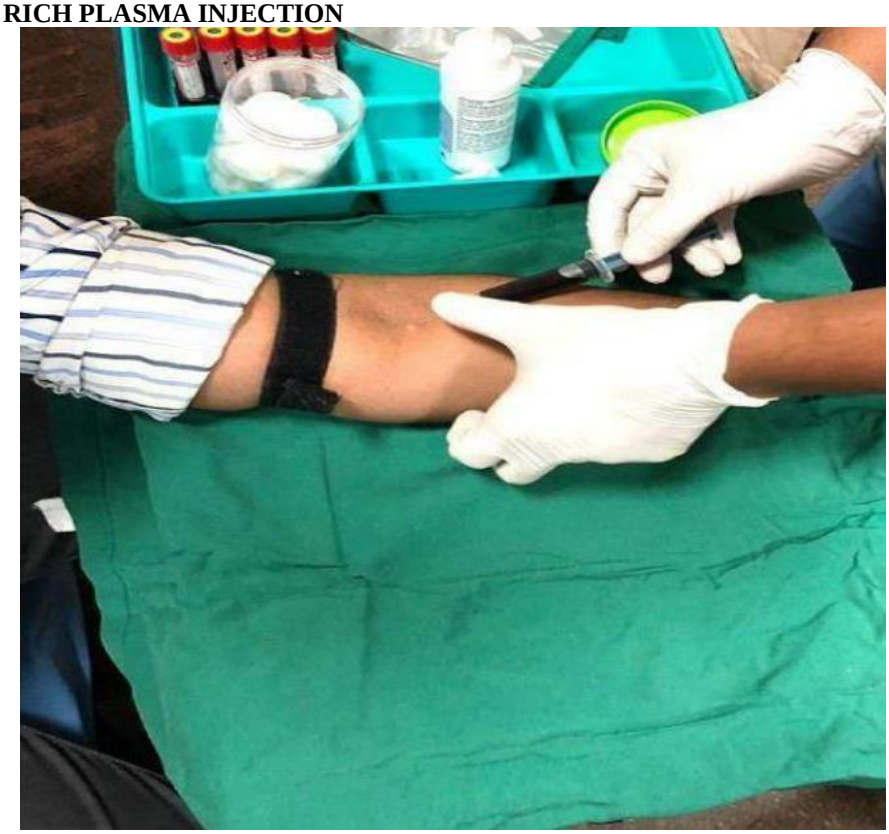
Time period	Group A	Group B	t– test value	P- value and Significance
	Mean ± SD	Mean ± SD		
Baseline	6.70±1.368	6.10±2.537	t = 1.14	P = 0.259 NS
1 week	6.33±1.241	2.80±1.883	t = 8.58	P = 0.0001 S
4 weeks	5.77±1.135	2.87±1.676	t = 7.84	P = 0.0001 S
8 weeks	4.90±1.561	3.17±1.206	t = 4.81	P = 0.0001 S
12 weeks	3.80±1.562	3.80±1.472	t = 0.000	P = 1.000 NS
6 months	2.53±1.502	4.80±1.648	t = -5.56	P = 0.0001 S
12 months	2.37±1.542	5.10±1.668	t=-6.59	P = 0.0001 S

Significant differences were seen in the VAS score for Group A and Group B subjects at 1 week, 4 weeks, 8 weeks, 12 weeks, 6 months and 12 months when compared using Independent t test as $p<0.05$.

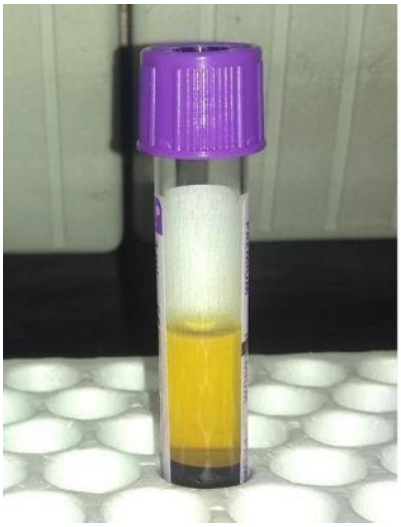


CASE ILLUSTRATIONS

PLATELET RICH PLASMA INJECTION



Blood drawing under sterile precautions.

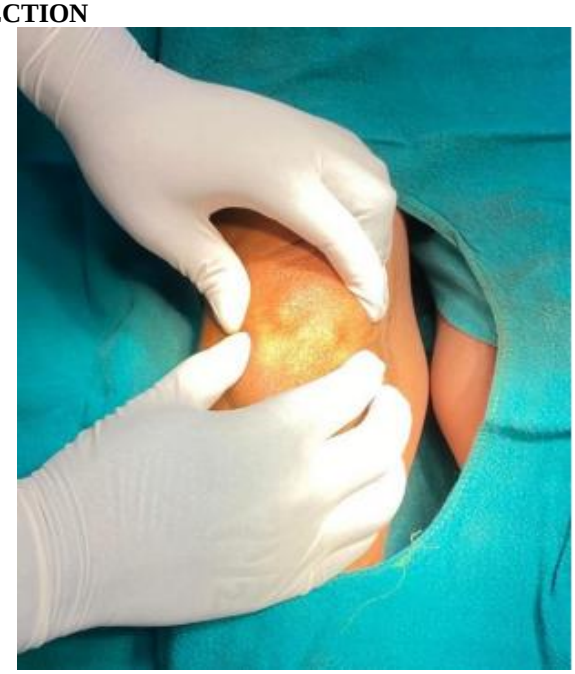


PRP

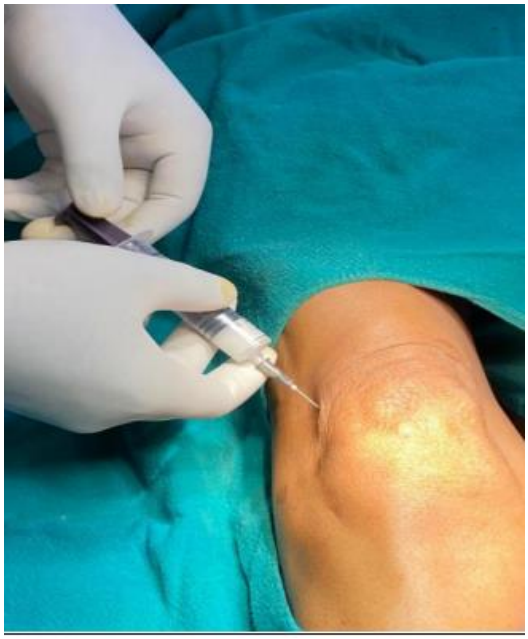
PRP is taken in syringe for injection.

Injection of PRP into the knee joint under aseptic precautions.

CORTICOSTEROID INJECTION



Knee painted with betadine, wiped with sterile spirit swab and draped with hole towel.



Injection of Corticosteroid injection into the knee joint under aseptic precautions.

DISCUSSION

Osteoarthritis, being the most common disease of the joints in the elderly, frequently affects the knee joint causing a major source of disability owing to pain and deformity leading to significant loss of function.[14]

Current literature indicates that IA knee injection is a promising modality in managing pain associated with OA knee. It is a well tolerated, minimally invasive intervention, especially in patients with co-morbidities, who neither have the fitness for the surgery nor able to tolerate oral analgesics for a long-term period. Various IA injectables like corticosteroids, infliximab, hyaluronic acid, botulinum neurotoxin, PRP, and even stem cells are being used in the management of knee OA. [15]

Last few years, there is growing interest in exploring PRP as a treatment modality for OA knee. The platelet concentrate in PRP when activated results in the formation of platelet gel and the release of growth factors and bioactive molecules which effectively participate in the healing process.[16] Platelets contain significant amounts of cytokines and growth factors and are responsible for stimulating cellular growth, vascularization, proliferation, tissue regeneration, and collagen synthesis. A regenerative therapy that is believed to promote healing by augmenting and accelerating the natural healing cascade. The Injection of PRP to treat OA of the knee can be considered a relatively new therapeutic indication.[16]

PRP may be prepared by single spin or double spin technique. Studies suggest no clear advantage of double-spin technique over single-spin technique or vice-versa. A 2-stage centrifugation process/double spin technique in which the first (hard) spin separates low-platelet concentrated plasma from RBC and PRP. In the second (soft) spin, this mixture or RBC and PRP is separated and the PRP is collected at the bottom of the test tube because of its high specific gravity. [17]

PRP as a treatment modality in the OA knee. Sánchez et al.[97] were the first to describe the IA injection of plasma rich in growth factors for treating articular cartilage avulsion in a soccer player. The studies by Sampson et al.[18] Kon et al.[19] reported a favorable outcome with IA injections of PRP in most of the OA knee patients.

Traditionally IA steroids are used for OA knee pain. Steroids act on nuclear steroid receptors and heckle the inflammatory and immune cascade at several levels. Among the steroids, triamcinolone acetonide is one of the most commonly used drugs for IA injections. The studies by so many authors like, Chao et al[20] Beyaz et al,[22] have used triamcinolone acetonide as the steroid drug in the dose of 40 mg for IA injections in OA knee. The same was followed in our study.

The efficacy of intraarticular corticosteroid injection in knee OA has been confirmed in a Cochrane review done in 2006, and in a systematic review by Hepper et al[23] and meta-analysis by Bannuru et al[24] Chao J et al[20] found IA corticosteroids to be superior to placebo on WOMAC scores at four weeks.

This study was directed to assess the clinical implication of intraarticular injection of PRP and Triamcinolone acetonide in mild and moderate knee osteoarthritis and to compare the Clinical efficacy of Intra-articular injections of PRP and Triamcinolone acetonide using Visual Numeric Scale and Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores.

CONCLUSION

The present study conducted is to evaluate and compare the functional outcome of patients with

Kellegren Lawrence grade I and II osteoarthritis knee treated with a single intra-articular injection of platelet rich plasma and Triamcinolone acetonide**.**

Therefore single dose, intra-articular PRP injection is superior to that of Triamcinolone Acetonide. PRP holds a promising solution in the management in OA knee in the present state of knowledge. Though PRP has consistently been shown to be superior to other intra-articular agents. Our findings have shown that intraarticular PRP injections are more safe and effective treatment than intraarticular Triamcinolone Acetonide in 6 months follow-up study. Intraarticular steroid relieves knee pain rapidly up to 2 months and effect wears off in 6 month follow up. While effect of intra articular prp lasts longer on 6 month follow up.

So, for a long duration relief of symptoms and the functional outcome, intraarticular PRP is better than Triamcinolone acetonide injections.

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