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Original Research Article

Platelet Rich Plasma Intraarticular Injections for Knee Osteoarthritis: A Prospective Study

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Conflict of interest: Nil

Abstract

Background: Around 10% of the global population is suffering from osteoarthritis which leads to moderate to severe long-term pain and disability. Tissue regenerative therapy like platelet rich plasma have shown a considerable potential to alleviate the symptoms & improve physical function.

Aims & Objectives: This prospective study was designed to evaluate the efficacy and safety of Platelet Rich Plasma intraarticular injections in patients affected by knee osteoarthritis.

Material & Methods: The present prospective randomized study was conducted in our tertiary care hospital from September 22 till Jan 2023. The study recruited 60 patients with early bilateral knee OA with Ahlback grade 1 or 2 knees without any significant deformity in patients. The patients were randomized into 3 groups: Group A – patients were given a single injection of PRP, Group B - patients were given a two injections of PRP at an interval of three weeks & Group C – patients were given a single injection of normal saline (placebo). The sociodemographic parameters like age, sex, weight, height, body mass index (BMI) were noted. WOMAC scores & pain on VAS scale at baseline, 6 weeks, 3 months & 6 months were recorded. Results – Intra group comparison showed statistically significant reduction in VAS & WOMAC scores in Group I & Group II at 6 weeks, 3 months & 6 months. Intergroup comparison between Group I & Group II showed no statistically significant reduction in VAS & WOMAC scores.

Conclusion: PRP shows a great potential in reduction of pain relief & improving the quality of life of patients with osteoarthritis with benefits extending even at 6 months followup.

Keywords: Platelet rich plasma, Knee osteoarthritis, WOMAC scores, Degenerative joint disease.

Introduction

Osteoarthritis (OA) of the knee is a common degenerative joint disease which affects the quality of life of the patients. The mechanism of OA involves complex interaction of various growth factors required in joint homeostasis and cartilage metabolism. Management includes patient education, weight reduction, orthotics, therapeutic exercise, dietary supplement,

medication. [1] The articular cartilage has a limited potential to repair, thus the effectivenss of current therapies remains a challenge. Thus alternative biological and regenerative treatment options like intraarticular injection of corticosteroid, hyaluronic acid (HA) or platelet-rich plasma (PRP), physical therapies,and surgery are coming in use. Recently, the therapies are targeted on the use of growth factors as therapeutic proteins for cartilage repair. [2]

Autologous platelet-rich plasma (PRP), is an ideal requisite material containing numerous growth factors like fibroblast growth factor, vascular endothelial growth factor, platelet-derived growth factor ,epidermal growth factor & transforming growth factor-β promoting tissue repair. [3] It has anti-nociceptive and anti-inflammatory effects which reduce pain & modulates the OA process. Some studies have also suggested its role as chondroprotective by the stimulation of endogenous hyaluronic acid production & synthesis of cartilage matrix. [4,5] Guillibert C et al 2019 suggested the role of growth factors & cytokines, in modulating the inflammatory processes contributing in tissue regeneration. [6] It is best technique to slow down the progress of OA. Intraarticular PRP is now considered as an effective and safe therapy for knee OA [9,10].But still the correct dosage & number of PRP injection remain dubious , with variations from every week to every 3–4 weeks & with single to multiple injections. [7]

This prospective study was designed to evaluate the efficacy and safety of Platelet Rich Plasma injections in patients affected by knee osteoarthritis.

Materials and Methods

The present prospective randomized study was conducted in our tertiary care hospital from September 22 till Jan 2023. The study recruited 60 patients with early bilateral knee OA with Ahlback grade 1 or 2 knees without any significant deformity in patients. Patients with generalized OA , metabolic diseases of the bone , joint inflammatory diseases, ,received intra-articular injections within 3 months , arthroscopic lavage in the previous 1 year ,on anticoagulant therapy & other comorbidities were excluded. A prior written informed consent was taken from all the patients priorly. Ethical clearance taken from institutional ethical committee.A standard study protocol was followed for each patient & the patient & observer were both blinded.

By using computer randomization, the patients were divided into 3 groups:

Group A – patients were given a single injection of PRP (n=20)

Group B - patients were given a two injections of PRP at an interval of three weeks (n=20)

Group C – patients were given a single injection of normal saline (placebo) (n=20).

The sociodemographic parameters like age, sex, weight, height, body mass index (BMI), and preinjection WOMAC scores were recorded by blinded observer.100mL of venous blood was drawn under aseptic precautions from the anticubital vein & collected in a bag anticoagulant .This was sent to laboratory where it was transfereed to tubes & centrifuged for 15 minutes at 1500 rpm in a centrifugation machine. Blood separated into PRP and residual red blood cells with the buffy coat. Using a leucocyte filter, leucocytes were filtered & PRP thus obtained was received in a 10 mL syringe. In placebo group, 5 mL of blood was collected. The patients in the three groups did not know how much blood was extracted, as they were made to look other way during blood collection.

Procedure – Patients were instructed to lay in supine position & with knee in full extension. Under aspectic precautions, using an 18- gauge needle & supralateral

approach, 8 mL of PRP / Saline was injected into suprapatellar pouch. In Group I & II, 1 mL of CaCl2 (M/40) was injected in a ratio of 1:4 for every 4 mL of PRP. The knees were immobilized for 10 minutes after injection. For Group II , fresh PRP was prepared both times & cold storage was avoided. The patients were kept under observation for half an hour. Adverse events like dizziness or sweating were observed after injection. Patients were discharged after recovery. In case of any discomfort /pain Paracetamol 500mg tds was prescribed.

Parameters assessed (before injection and at 6 weeks, 3 months, and 6 months after injection) were:

1. Joint pain , Joint stiffness , Physical function - using the (Western Ontario and McMaster Universities Arthritis Index) WOMAC subscale [8]
2. Pain – Visual analogue scale)
3. Adverse effects - nature, time of onset, duration, and severity were recorded.

Statistical Analysis – The data was put in excel sheet, tabulated and analysed using statistical software (SPSS version 22, IBM, India). Data was expressed as mean & standard deviation. *P* value was noted at 95% confidence interval, $P < 0.05$ was considered significant. Group comparisons were made using student paired t test. Corelation between various parameters done using Pearson coefficient of correlation.

Results

This baseline characteristics age , sex, height, weight , BMI and WOMAC scores were comparable with no statistically significant difference (p >0.05). 4(20%) Patients in Group I , 12(60%) patients in Group II experienced adverse event in the form of dizziness, headache, syncope , nausea, sweating & tachycardia & no adverse events noted in Group III, which was statistically significant (p<0.05).

In Group I , there was a statistically significant decrease in the mean pain scores , joint stiffness physical function & total WOMAC score from baseline at followup visits(p <0.05). In Group II, there was a statistically significant decrease in the mean pain scores , joint stiffness , physical function & total WOMAC score from baseline at followup visits (p <0.05). In Group III, no statistically significant difference was observed in the mean pain scores , joint stiffness , physical function & total WOMAC score from baseline at followup visits .Intergroup comparison between Group I & Group II showed no statistically significant difference between the various parameters at all-time intervals (p >0.05).

There was a slight increase in mean pain score at 6 months which was significant (p<0.05). This was less than at the baseline. There was statistically significant decrease in VAS pain scores from baseline at 6 months in both Group I & II but in Group C no significant change was recorded(p>0.05). For knees with Ahlback grade 1 the scores were lower as compared to Ahlback grade 2 which was observed in both the groups I & II which was statistically significant. No significant correlation observed between the mean WOMAC scores with other sociodemographic parameters.

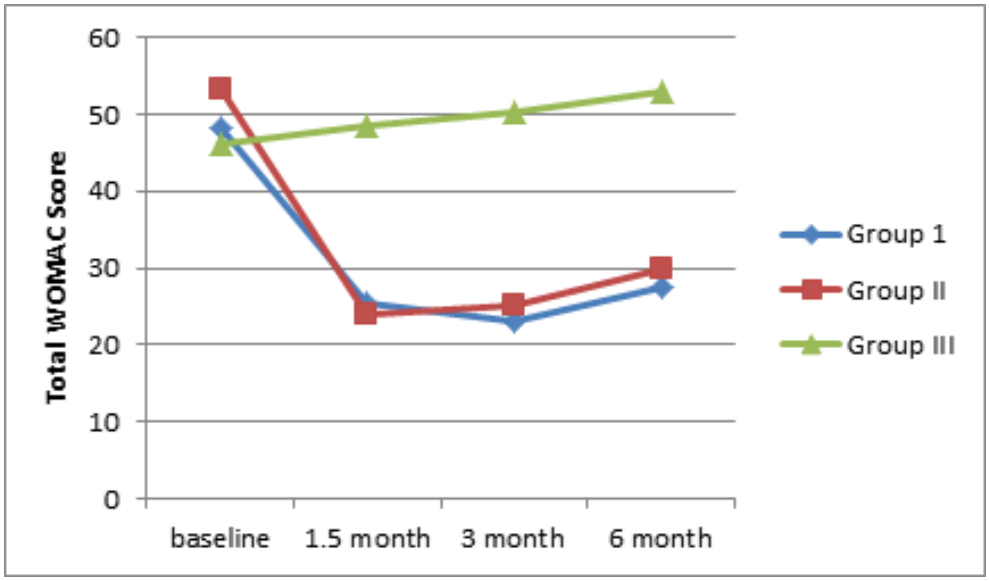
Table 1 Shows the WOMAC Scores of Group I , II & III at all time intervals

Parameters	WOMAC Scores		
Pain	Group 1	Group II	Group III
baseline	10.2	10.6	9.01
1.5 month	4.5	4.7	9.31
3 month	3.7	4.2	10.4
6 month	4.1	5.6	10.8

P value	<0.05	<0.05	>0.05
Stiffness	Group 1	Group II	Group III
baseline	3.5	3.7	3.6
1.5 month	2.4	2.6	3.7
3 month	1.6	2.3	3.9
6 month	2.1	1.92	4.12
	<0.05	<0.05	>0.05
Physical function	Group 1	Group II	Group III
baseline	37.21	38.61	33.62
1.5 month	18.24	17.29	35.28
3 month	17.94	17.83	37.51
6 month	20.14	20.91	41.62
	<0.05	<0.05	>0.05
Total WOMAC Score	Group 1	Group II	Group III
baseline	48.29	53.27	46.21
1.5 month	25.42	24.03	48.53
3 month	22.93	25.26	50.41
6 month	27.64	29.91	52.84
P value	<0.05	<0.05	>0.05

Table 2 Shows the VAS score of Group I , II & III at baseline & 6 months

VAS score	Group I (mean±SD)	Group II (mean±SD)	Group III (mean±SD)
Baseline	5.12±0.21	4.87±0.44	4.92±1.32
6 months	2.23±1.02	2.54±1.15	4.83±1.03
P value	<0.05	<0.05	>0.05



Graph 1 Shows the Total WOMAC Score of Group I , II & III at all time intervals

Discussion

No standard protocol exists on the preparation of PRP and diversity arises in the study designs of various previous studies on the treatment of knee OA. A meta-analysis by Sheth et al 2012 concluded insufficient evidence on the role of PRP in many cases. [9] Futher more

studies by Patel et al 2013 [8] , Huang P.H et al 2017 [10] , Buendía-López D 2018 [11] noted improvement in knee OA with the use of PRP injections. Bansal et al 2021 concluded the PRP injections with 10 billion platelets count in a volume of 8 ml results in significant chondro-protection with redcutioni in pain scores as compared to placebo in knee OA. [12]

The baseline parameters were comparable. No correlation was observed between WOMAC scores & other sociodemogarphic parameters at the baseline. At followup visits the WOMAC scores decreased in Group I & II with no significant correlation with respect to all parameters. Similar findings were noted by Patel et al 2013 study. [8] In contrast Kon et al 2010 [12] observed better improvement in young males & patients with low BMI. In theis study , mean BMI was comparable to that in Patel et al 2013 [8] & Kon et al 2010 [13] study with lesser number of overweight patients.

In Group I & II , a statistically significant correlation was observed in relation to Ahlback grading. With grade 1 , lower mean pain & WOMAC scores were observed than grade 2 knees($p<0.05$). The mean pain scores significantly decreased at 6 weeks & 3 months in both the groups receiving PRP, however, a small increase was noted at 6 months. Similar observations were noted by Patel et al 2013 [8] & Kon et al 2010 [13] with a slight worsening of subjective symptoms from 3 months to 6 months which was not statistically significant. This improvement deteriorates over time for further 2 yrs of followup. This indicates no significant sustained long term effects & waning of improved treatment outcomes after a short period of time. Thus further study designs should incorporate PRP injections at baseline 6 months & one year to assess the treatment outcome in knee OA. [14]

Also , the Group I patients receiving single injections have nearly similar improvement in mean scores & other WOMAC score as compared to Group II indicating no added advantage of injecting two PRP injections. Sanchez et al 2008 observed 33.3% of patients had significant imorovement at 5 weeks. [1] In the present study , 67% were satisfied in Group I , 69% in Group II & 3.5% in Group III. Similarly, Kon et al 2010 [13] observed 80% patient satisfaction. Patel et al [8] study noted 67.3% & 64% patient satisfaction in PRP groups at the

In the present study , few adverse effects were noted which were short duration lasting 30 minutes.The number of adverse effects in Group II were higher as higher number of platelets were injected in this group.Calcium chloride used as an activating agent may be a contributing Factor. [15]

The suggested mechanism of PRP induced improved treatment outcome may be its overall effect on joint homeostasis by reducing synovial membrane hyperplasia and cytokine modulation .Thus , further studies should be conducted to evaluate the longevity of treatment of knee OA by PRP injection & understand the mechanism of its action & disease-modifying properties.

Conclusion

The study concludes the efficacy of the PRP injections on the knee osteoarthritis with results achieved as early as 6 weeks with sustained effects at 6 months. The joint pain, stiffness reduced & physical functions improved in early osteoarthritis. The effects of intraarticular PRP injections wane over a period of time which should be further evaluated.

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