

# **RESEARCH ARTICLE**

### INTRA-ARTICULAR PLATELET RICH PLASMA IN THE TREATMENT OF PATIENTS WITH KNEE **OSTEOARTHRITIS**

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#### Abstract

Introduction: Osteoarthritis of knee is the most common worldwide degenerative joint disease and is a common condition associated with pain and morbidity which significantly impacts the patient's mobility and quality of life. It is treated by use of exercises, weight reduction, walking supports, bracing, topical and oral NSAID, intra-articular (IA) injections of corticosteroids and blood-derived products, including platelet-rich-plasma. An autologous blood product containing a high percentage of various growth factors (GFs), cytokines and modulating factors as PRP has shown promising results in achieving this goal. The aim of this prospective study was to evaluate the efficacy and safety of Platelet Rich Plasma (PRP) injections in patients affected by knee osteoarthritis (KOA) of grades from 1 to 3 Kellgren-Lawrence (KL) grading.

Materials and Methods: In this study a total of 30 patients, radiologically confirmed with knee osteoarthritis. All patients were managed with intra-articular platelet rich plasma injection. The pain and function of the target knee were evaluated by the VAS, KSS and IKDC scales at the baseline, 1 week, 6 weeks, 12 weeks, 18 weeks, 24 weeks and 48 weeks after treatment.

**Results:** In this study, there was reduction of  $5 \pm 0.4$  and 4 in mean VAS from baseline was found after 24 and 48 weeks after treatment. A significant function improvements of 32.10±1.5 and 21.4±4.9 in mean KSS from baseline was seen after 24 and 48 weeks respectively after treatment. Similarly a significant function improvements of 47.1±3.9 and 32.1±4.6 in mean IKDC from baseline was seen after 24 and 48 weeks respectively after treatment.

Conclusion: Intra articular platelet rich plasma produce superior outcomes for symptomatic management in the treatment of patients with knee osteoarthritis grade I, II and III, including improved pain management, less joint stiffness and better participation in daily activity.

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## Introduction:-

Osteoarthritis (OA) is a chronic multifactorial degenerative condition defined by loss of articular cartilage, marginal bone hypertrophy (osteophytes) and a number of biochemical and morphological changes to the synovial membrane and joint capsule [1]. OA is the most common form of arthritis and often affects the hands, knees, feet, and hips. Knee osteoarthritis (OA) is a slowly progressive chronic disease characterized by pain, loss of function, and deformity of the affected joints. In the past, OA was considered a normal sign of aging and it was described as a degenerative disorder that mainly causes cartilage loss [2]. However, more recent studies have shown that OA occurs and evolves due to the interaction of multiple risk factors affecting the whole joint including the cartilage, subchondral bone, synovium, ligaments, and menisci[3].Adding to this, the burden of knee OA continues to grow [4], estimated to affect between 10 and 25% of patients over 60 [5], alongside a population that is increasingly comorbid and obese [6].Knee osteoarthritis is a common condition associated with pain and morbidity[7].It is also the second leading cause of disability and a heavy economic and social burden [8].

Management is directed to reduce pain, improve function and limit disease progression[9]. Non-pharmacological treatments include patient education, exercises, weight reduction, walking supports, bracing, acupuncture, and electromagnetic therapy [10]. Pharmacological treatments include topical and oral NSAID [11], intra-articular (IA) injections of corticosteroids and blood-derived products, including platelet-rich-plasma [12]. Analgesics and non-steroid anti-inflammatory drugs (NSAIDs) have suboptimal effectiveness. Surgical treatment can reduce pain and improve joint mobility and function; however, it is associated with significant cost and potential morbidity [13, 14]. Corticosteroids and hyaluronic acid injections provide short-term reduction in pain of OA [15]. Recently, placebo-controlled studies have shown that intra articular platelet-rich plasma can relieve pain, improving knee function and quality of life [16, 17]. Despite numerous studies and meta-analyses, the efficacy of intra articular platelet rich plasma in patients with knee OA remains debated and uncertain worldwide [18-20].

An autologous blood product containing a high percentage of various growth factors (GFs), cytokines and modulating factors as PRP has shown promising results in achieving this goal. The aim of this prospective study was to evaluate the efficacy and safety of Platelet Rich Plasma (PRP) injections in patients affected by knee osteoarthritis (KOA) of grades from 1 to 3 Kellgren-Lawrence (KL) grading.

### Materials and Methods:-

This prospective observational study was conducted in the department of Orthopaedics, SDH Bijbahara from June 2020 to May 2022. Patients who met the inclusion criteria were included. In this study we enrolled 30 patients, radiologically confirmed with knee osteoarthritis (Kellgren-Lawrence grade I, II and III).

The inclusion criteria were patients with clinical and radiological diagnosis of knee OA either KL Grades 1, 2 and 3 without knee deformity, symptomatic for at least 6 months with pain of >40 mm on a 100 mm as per VAS pain despite, above the age of 50 years and swelling or reduced range of motion in the knee joint. The patients with KL Grade 4, severe mechanical deformity or received IA injection of HA in the past 6 months, patients who had received either oral, injectable steroid during the 3 months before the study, patients with uncontrolled diabetes mellitus, post-traumatic knee osteoarthritiswere excluded from the study.

Demographic variables such as age, sex and the degree of radiological involvement were collected. The use of analgesics, physiotherapy was not restricted during the study period.

#### Interventional procedure:

The patients were placed in the supine position with theknee in full extension. Under aseptic conditions, in all patients intra articular platelet rich plasma 6 ml was injected to knee joint. The intra-articular knee injection was performed under sterile conditions, without any local or general anesthesia, with 18G needle using an anterolateral approach. Echographic control allowed the correctneedle positioning by direct visualization. 0.5 mlof CaCl2 (M/40) was injected for every 6 ml of PRP toactivate platelets. The knees were immobilized for 10 minafter injection. After this manipulation, an aseptic cool bandage was applied for 15 minutes for local compression. The patients were observed for half an hour for some common complaints as dizziness orsweating and were discharged.

During the follow-up period, patients carried on their ordinary lives without any specific treatments or restrictions. The pain and function of the target knee were evaluated by the VAS, KSS and IKDC scales at the baseline, 1 week,

6 weeks, 12 weeks, 18 weeks, 24 weeks and 48 weeks after treatment. Descriptive statistics were calculated using the mean standard deviation for quantitative continuous data and frequencies with percentages for qualitative categorical data.

### **Results:-**

The mean age of the study population was 64.40 (range 52-67) years. Out of 30 patients, 11 (36.67 %) were males and 19 (63.33%) were females. There were 14 (46.67 %) patients with grade I of osteoarthritis (KL grade of knee OA), 11 (36.67 %)patients had grade II(KL grade of knee OA) osteoarthritis and 5 (16.66 %) patients had grade III(KL grade of knee OA) osteoarthritis. The mean BMI of study population was  $29.23\pm 3.60$  (range 22.60-32.10) Kg/M2 and mean duration of KOA was  $6.7\pm 1.30$  (range 2-11) years (Table 1).

**Table 1:-** Baseline characteristics of the study groups.

Age in years	
Mean ± SD	64.40±6.70
Range	52-67
Gender	
Male (%)	11 (36.67 %)
Female (%)	19 (63.33 %)
BMI (Kg/M2)	
Mean $\pm$ SD	$29.23 \pm 3.60$
Range	22.60-32.10
Duration of osteoarthritis in years	
Mean $\pm$ SD	$6.7 \pm 1.30$
Range	2-11
Kellgren and Lawrence grade of knee OA	
Grade I (%)	14 (46.67 %)
Grade II (%)	11 (36.67 %)
Grade III (%)	5 (16.66 %)

All patients showed effective reduction in pain, and they improved the knee function after the first week of treatment. A significant reduction of  $5 \pm 0.4$  and 4 in mean VAS from baseline was found after 24 and 48 weeks after treatment (p < 0.0001).

In this study a significant function improvements of  $32.10\pm1.5$  and  $21.4\pm4.9$  in mean KSS from baseline was seen after 24 and 48 weeks respectively after treatment. Similarly a significant function improvements of  $47.1\pm3.9$  and  $32.1\pm4.6$  in mean IKDC from baseline was seen after 24 and 48 weeks respectively after treatment.

In the study, highest change of  $5.0 \pm 1.3$  in the mean VAS score from the baseline was at 24 weeks and a sustained improvement in pain relief up to 30 weeks, showing a small increase in pain in the 1-year evaluation follow-up. Primary and secondary outcomes in per-protocol population during the follow-up of the study are summarized in table 2. No adverse effects were noted during or after the PRP procedure.

<b>Table 2:-</b> Distribution of VAS, KSS and TKDC scores during the patient follow-up.				
Weeks	VAS Mean	KSS Mean	IKDC Mean	
Baseline	$6.8 \pm 1.4$	$62.8\pm6.9$	39. 1 ± 11.2	
1 Week	$3.9 \pm 2.2$	$86.3 \pm 11.4$	63.9 v 13.7	
6 Weeks	$3.0 \pm 1.9$	$90.7 \pm 9.8$	$71.5 \pm 13.9$	
12 Weeks	$2.1 \pm 1.3$	$93.8\pm7.9$	$81.4 \pm 14.3$	
24 Weeks	$1.8 \pm 1.0$	$94.9 \pm 8.4$	$86.1 \pm 15.1$	
48 Weeks	$2.8 \pm 1.4$	$84.2 \pm 11.8$	$71.2 \pm 15.8$	

Table 2:- Distribution of VAS, KSS and IKDC scores during the patient follow-up.

Data presented in Mean  $\pm$  SD, {% change from the baseline} is given within parenthesis. Friedman Test used to compare the VAS, KSS and IKDC score between different time points. The significant Friedman test was followed by Post hoc test (PHT) for the multiple comparisons, showing the significant change in score from baseline to 1, 6,

12, 24 and 48 weeks. Percent (%) changes (using mean score) are calculated at the time points of 1, 6, 12, 24 and 48 weeks respectively with respect to baseline (Figure 1, 2 and 3).



Figure 1:- VAS score at baseline and different time points.



Figure 2:- KSS and IKDC scores at baseline and different time points.

## **Discussion:-**

Primary knee osteoarthritis (OA) continues to be a hard-to-control degenerative disease. With the increase in average life expectancy and the prevalence of obesity, OA is creating a rising economic and physical burden [21]. Knee OA is a chronic musculoskeletal condition that can eventually require surgical intervention. Thus, patients continue to search for potential non-operative therapies, such as platelet-rich plasma (PRP) injections into the affected knee [22]. Multiple studies have reported the use of PRP among other agents in the non-operative treatment of knee osteoarthritis. According to Jayaram et al., PRP is an emergent therapeutic approach for the treatment of OA; however, there remains a lack of clinical evidence for its effectiveness, and its mechanisms of action are indeterminate [23]. Despite promising outcomes reported with regard to PRP utilization in knee OA, crucial issues such as conclusive evidence about its effectiveness, standard dose, and good preparation techniques remain unknown [24]

In this prospective study, we use Platelet Rich Plasma (PRP) injections to evaluate the efficacy and safety in the patients affected by knee osteoarthritis (KOA) of grades from 1 to 3 Kellgren-Lawrence (KL) grading. The use of PRP in the treatment of degenerative knee OA has increased in recent years given its apparent high margin of safety and ease of production and administration. Contrasting scientific evidence exists regarding PRP injections for knee OA, with the efficacy of PRP injections widely reported. PRP use has been advocated as a treatment option in all stages of knee OA. Intra-articular PRP injections in active patients with knee OA show significant improvements in pain reduction, improved symptoms and QoL. This could be due to the immediate and sustained release of growth factors over a prolonged period, which enhances healing resulting in sustained clinical effects.

In this study obtained results demonstrated that intra articular platelet rich plasma shows greater overall efficacy 12 months of follow-up. This effect becomes statistically significant from 3 months onwards, and is most pronounced from 6 to 9 months, with the strongest evidence of benefit at 6 months post-injection. Mean changes in the scales and subscales from baseline to 24 weeks was statistically significant. Significant difference from baseline was seen as early as 6 weeks for all the outcome parameters in study population. Pain and stiffness scores in the PRP group continue to improve until 9 months post-injection, with statistical significance from three months onwards. This is supported by previous evidence by Shen et al. [25] and Filardo et al. [26], who suggested a sustained effect following PRP injections of up to 12 and even 24 months. The former study was a systematic review and metaanalysis investigating the temporal effect of PRP injections compared to control (including HA, CS, placebo and ozone) which reported superior treatment effects from PRP at 3, 6 and 12 months; the latter was a single arm study investigating whether beneficial effects from PRP persist. At 24 months, patient scores were still improved compared to baseline, but the median duration of effect was 9 months. Our study showed that 6-9 months was the time point when patients observed the greatest treatment effect from IA-PRP injections. In a review by Meheux et al. [27] comparing PRP to HA and placebo for knee OA, PRP was recommended to be reserved for patients with KL 1–3. This may be due to the ability of PRP to restore and protect cartilage [28], as this may be more effective where there is more pre-existing joint cartilage. Gobbi et al. tried to determine the effectiveness of intra-articular PRP injections in active patients with knee OA and to evaluate clinical outcomes in patients with and without previous surgical treatment for cartilage lesions [29]. The PRP treatment showed positive effects in patients with knee OA. Operated and non-operated patients showed significant improvement by means of pain reduction and improved symptoms and quality of life. This recommendation is based on ranges used in the studies included in this review.

Most of the studies of PRP commonly perform the first assessment of patients 1 month after treatment, making impossible the determination of the evolution in the first few days [30]. Based on this remark and on our personal experience that we have observed from this study, we evaluated the clinical outcome of the patients in the very short term (1 week). From our knowledge, this is the first PRP clinical study for early-stage knee OA that incorporated outcome assessment by means of this approach. The rapid reduction in pain observed upon treatment with PRP might be attributed to a combined effect, mainly due to the induction of endogenous cell endocannabinoids[31] together with the anti-inflammatory activity effect of PRP on chondrocytes [32].

We hypothesized that the improvement of both parameters (pain and function) were mainly due to control of the inflammation of the knee rather than the trophic effect of PRP on cartilage. This rationale is due to the fact that it has not yet been demonstrated that the improvement of knee function after PRP treatment correlates with a volume increase of the articular cartilage [33]. Even though the mechanism of action on improving cartilage repair remains unclear, it has been reported in the literature that PRP can induce tissue maturation characterized by increased cell proliferation and tissue stiffness [34]. These cells, in turn, produce more superficial zone protein that functions as a

boundary lubricant that helps reduce friction and wear. Moreover, it has been reported that PRP can enhance HA secretion from synovial fibroblasts in arthritic patients, producing a lubricating effect that could reduce the shear stress of the joint [35].Intra-articular PRP infiltrations have been widely used for the treatment of knee OA with many beneficial results. In this study, intra-articular PRP injections were well tolerated. Treatment with PRP injections can be considered safe since no severe adverse events or complications have been reported. We consider that the safety of PRP is mainly due to two factors: the administration of the PRP done through minimally invasive procedures and non-existent risk of transmission of infectious diseases (because it is an autologous procedure).

## **Conclusion:-**

Intra articular platelet rich plasma produce superior outcomes for symptomatic management in the treatment of patients with knee osteoarthritis grade I, II and III, including improved pain management, less joint stiffness and better participation in daily activity.

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