

## Original Research Article

# Comparative evaluation of efficacy of autogenous platelet rich plasma versus visco supplementation in treatment of early osteoarthritis of knee

Kumar Shantanu, Shailendra Singh\*, Mahesh Kumar Navadaya, Brijmohan Patel

Department of Orthopaedic Surgery, King George Medical University, Lucknow, Uttar Pradesh, India

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### \*Correspondence:

Dr. Shailendra Singh,

E-mail: [shailendra81mamc@gmail.com](mailto:shailendra81mamc@gmail.com)

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## ABSTRACT

**Background:** Osteoarthritis is a very common chronic degenerative disease most commonly affecting the knee joints. In present study we compared the efficacy of autogenous platelet rich plasma (PRP) versus visco supplementation in treatment of early osteoarthritis of knees.

**Methods:** 30 patients (56 knees) were registered and divided into two groups. Out of which PRP in 28 knees and visco supplementation in 28 knees injected during. Visual analogue scale (VAS) and Western Ontario and McMaster Universities Arthritis Index (WOMAC) scores were measured. These scores were measured at first visit, 6 weeks, 12 weeks and at 24 weeks.

**Results:** All registered patients were randomized in two groups. Group I (total 16 patients and 28 knees) for intraarticular PRP injection and group II (total 14 patients and 28 knees) for intraarticular viscosupplement injection. Out of 28 knees of group I; 12 (42.85%) knees belonged to grade II and 16 (57.15%) of grade III. Out of 28 knees of group II; 15 (53.57%) knees of grade II and 13 (46.45%) of grade III. None of the knees belonged to grade I and grade 0. There was significant difference in outcome of two treatment groups ( $p < 0.05$ ) at 24 weeks.

**Conclusions:** Treatment with PRP showed a significantly better clinical outcome compared with viscosupplementation at 24 weeks follow up. Although patients achieved lower WOMAC and VAS scores in PRP group at 6 and 12 weeks follow up that was statistically insignificant. We conclude that long term results of PRP are better than viscosupplementation.

**Keywords:** Osteoarthritis knee, Platelets rich plasma, Hyaluronic acid, WOMAC scale and VAS scale

## INTRODUCTION

Osteoarthritis (OA) refers to a clinical syndrome of joint pain with multifactorial etiopathogenesis that is characterized by the gradual loss of articular cartilage, osteophyte formation, subchondral bone remodelling and inflammation of the joint.<sup>1</sup> OA is a major source of disability owing to pain and loss of function. There are various conservative modalities for the treatment of OA knee which are recommended by clinical guidelines.<sup>2-4</sup> The non-pharmacological modalities are patient

education, exercises, weight reduction, walking supports (crutches), bracing, shoe and insoles modification, local cooling/heating. Pharmacologic therapies can be summarized as paracetamol, non-steroidal anti-inflammatory drugs, opioids, and slow-acting drugs (glucosamine and chondroitin sulfate). If orally administered drugs are ineffective, intraarticular (IA) injection (blood derived products, corticosteroids, viscosupplements) is the last non operative modality that can be preferred.<sup>5,6</sup> The major contraindication for IA injections is septic arthritis. Platelet-rich plasma (PRP)

can be defined as the volume of the plasma fraction from autologous blood with a platelet concentration above baseline count (200 000 platelets/ $\mu$ l).<sup>7</sup> Platelets contain many important bioactive proteins and growth factors (GFs). These factors regulate key processes in tissue repair, including cell proliferation, chemotaxis, migration, cellular differentiation, and extracellular matrix synthesis.<sup>8</sup> The rationale for the use of PRP is to stimulate the natural healing cascade and tissue regeneration by a “supra-physiologic” release of platelet-derived factors directly at the site of treatment. When PRP solutions are injected directly for topical treatment, platelets are activated by endogenous thrombin and/or intra-articular collagen.<sup>9</sup> GFs have a half-life from minutes to hours. Studies have shown that the clinical efficacy of PRP products is expected to increase, at minimum, 2 to 6 fold of platelets count from baseline value.<sup>10</sup> Platelets  $\alpha$ -granules contain a variety of GFs, including transforming GFs, platelet-derived GFs, hepatocyte GFs, basic fibroblast GFs, epidermal GF, vascular endothelial GFs, and insulin-like GF. GFs mediate the biological processes necessary for repair of soft tissues, such as muscle, tendon, and ligament, following acute traumatic or overuse injury. In vitro studies in animal and human chondrocytes have demonstrated that PRP secreted GFs stimulate proliferation and collagen synthesis. More interesting, their positive effect in OA-affected animal joints, by stimulating cartilage matrix metabolism, has been reported. Recent studies showed promising preliminary clinical results in the treatment of knee OA. Viscosupplementation includes hyaluronic acid (HA) derivatives.<sup>11,12</sup> HA is produced either from harvested rooster combs or via bacterial fermentation in vitro.<sup>13</sup> The injectable hyaluronan products include sodium hyaluronate, Hylan G-F 20, and high-molecular weight hyaluronan that are approved by FDA. Injection schedules vary from 1 to 5 injections and patients that are satisfied with this schedule course, advised to repeat the same schedule every 6 monthly. Although the basic science evidence studies suggest that the use of both low molecular weight hyaluronic acid and high molecular weight hyaluronic acid (HMWHA) have disease modifying effects, comparative clinical studies and meta-analyses tends to favour the efficacy of HMWHA for knee OA.<sup>14-18</sup> HA is occurring naturally as a component of synovial fluid (SF) and cartilage matrix. Synovial cells, fibroblasts and chondrocytes synthesize HA and secrete into the knee joint. HA increases the viscosity and the elasticity of the joint. SF with normal HA concentration acts as a viscous lubricant during slow joint movements and as an elastic shock absorber during rapid joint movements.<sup>19</sup> This ability of SF decreases stress and friction on the cartilage.<sup>20</sup> HA acts through anti-inflammatory, anabolic, analgesic, and chondro protective mechanisms.<sup>21</sup> In an osteoarthritic joint, synovial inflammation leads to increase permeability of the synovial membrane for HA and it also increased the levels of free radicals, inflammatory cytokines, and proteolytic enzyme. Synovial inflammation and

inflammatory mediator leads to progression of osteoarthritis.<sup>22,23</sup> The IA injection of HA is thought to restore normal viscoelastic properties of the pathologically derange SF, which explains the term of the approach: “viscosupplementation”. It is thought that HA not only temporarily restores the lubricating and shock-absorbing property of SF as well as it act like a disease modifying effect by reducing inflammation, protection against cartilage erosion, and promotion of IA HA production.<sup>24-32</sup> Overall, HA have indirect as well as direct analgesic activity within the joints. Indirect effect is via the anti-inflammatory properties of HA. Direct effect is by the direct inhibition of nociceptors and the decreased synthesis of bradykinin and substance P. Viscosupplementation is mostly used to improve biomechanical function by increasing the level of HA in osteoarthritic knee and pain management based mainly on potentially therapeutic physicochemical properties.<sup>33</sup>

Objective of present study was to compare the efficacy of intra articular injection of hyaluronic acid and autogenous platelet rich plasma in treatment of early osteoarthritis of knee.

## METHODS

A prospective study was conducted on patients with early stage osteoarthritis knee enrolled on OPD basis during the year 2015 -2016 (study period 1 year) in the Department of Orthopaedic Surgery King George Medical University, Lucknow, UP. Effective sample size was 30 patients with 56 knees. Out of which intraarticular PRP injection was given in 28 knees and intraarticular HA injection in 28 knees. Patients randomized according to random table generator. Odd number patients classified under group-I and even number patients classified under group-II; group-I in which intraarticular PRP injected and group-II in which intraarticular viscosupplement was injected.

### Methodology

We enrolled patients of early stage osteoarthritis knee of either sex with inclusion criteria such as: Kellgren Lawrence grade 0–III with knee pain, patients with age more than 40 years, history of pain and swelling more than 4 months, symptoms and physical examination results consistent with osteoarthritis, patients who has persistent pain despite standard non operative treatment (physical therapy, NSAIDs, activity modification) and patient wished to pursue alternative to conservative treatment

All the patients who do not fulfilled the above criteria and not willing for this type of treatment were excluded from the study such as: Kellgren Lawrence grade more than III, BMI more than 30, patients with systemic diseases such as uncontrolled diabetes and hypertension, those who have rheumatoid arthritis, haematological disease

(coagulopathy, anticoagulant therapy) and patient with Hb values <11 gm/dl and platelet value <150,000/mm<sup>3</sup>.

After recording the demographic data, all the enrolled patients were subjected to clinico-radiological assessment. Visual analog scale (VAS) scores eastern Ontario and McMaster Universities Arthritis Index (WOMAC) scores were measured.

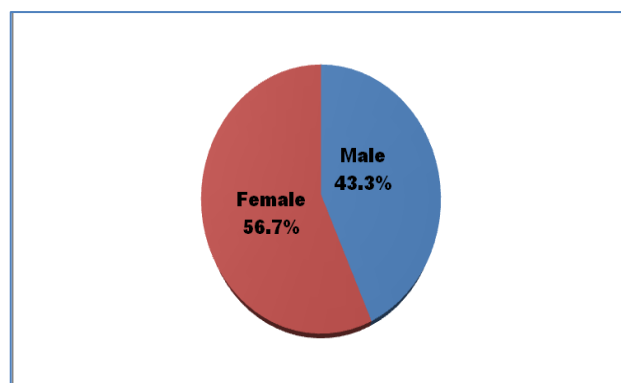
**Procedure**

Peripheral blood of the patient was collected and underwent series of centrifugation process ultimately delivering the desired platelet rich plasma with resultant increase in platelet concentration of four to six folds by transfusion medicine department maintaining the standardised sterility protocol. Different brands of HA injection available in the market. One of them is synviscone 48 mg/6 ml intra-articular syringe. After taking history of allergy patient placed in a supine position with the knee in full extension. Under aseptic conditions, 4 ml of platelet concentrate or HA was injected into a supra- patellar pouch through a superolateral approach with a 21-gauge needle without local anaesthetic and discharged after 30 minutes of observation. Immediately after the injection, passive flexion and extension of the affected knee was performed three times, followed by 10 mins of resting supine. Patients were given acetaminophen for pain on sos basis and antibiotic for three days and were instructed to limit the use of their affected knee for 24 hrs post injection, after which normal activities were resumed. During the follow-up period, nonsteroidal anti-inflammatory drugs were not allowed, and paracetamol (dosage, 500 mg tds) was pre- scribed in case of discomfort; all patients were asked to stop medications 48 hours before follow-up assessment.

Statistical analysis of data was done by using SPSS software and Mann-Whitney U test for significance was applied.

**RESULTS**

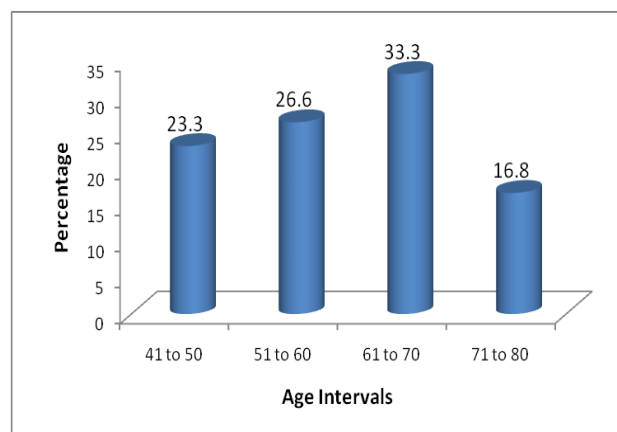
Total 30 patients were included in this study out of which 13 (43.3%) were male and 17 (56.7%) were female (Figure 1).



**Figure 1: Gender distribution.**

The mean age of osteoarthritis patients was 59.20 years with standard deviation (SD) 9.29 years; range from 43-75 years (32 years).

Majority of the patients, 10 (33.33%) belong to 61–70 years age group followed by 8 (26.70%) patients in 51 to 60 years age group (Figure 2).



**Figure 2: Percentage of age intervals.**

Group I included total 28 patients, out of which 12 of KL grade II and 16 of KL grade III. Group II included total 28 knees, out of which 15 of KL grade II and 13 of KL grade III (Table 1). None of the knee of KL grade 0 and grade I.

**Table 1: Number of knees- KLL grading.**

		Group		Total	
		Group-I (PRP)		Group-II (VISCO)	
<b>KLL grade</b>	Grade-2	Count	12	15	27
		% within group	42.85%	53.57%	48.21%
	Grade-3	Count	16	13	29
		% within group	57.15%	46.43%	51.79%
<b>Total knees</b>	Count	28	28	56	
		% within group	100.0%	100.0%	100.0%

Mean WOMAC and VAS score of both groups for KLL grade 2 is detailed in Table 2 and Figure 3 at subsequent follow up at 6, 12 and 24 weeks. There was no significant difference in mean WOMAC and VAS score at baseline, 6 weeks, and 12 weeks. There was only significant difference (p value <0.05) in WOMAC and VAS score at 24 weeks follow up of KL grade-II in which PRP and

viscosupplement were injected (Table 2). Mean WOMAC and VAS score of both groups for KLL grade 3 is shown in Table 2 and Figure 4 at subsequent follow up at 6, 12 and 24 weeks. Table 3 shows that there was only significant difference (p value <0.05) in WOMAC and VAS score at 24 weeks of KL grade-III in which PRP and viscosupplement were injected.

**Table 2: Results of PRP and viscosupplementation for KL-grade-II.**

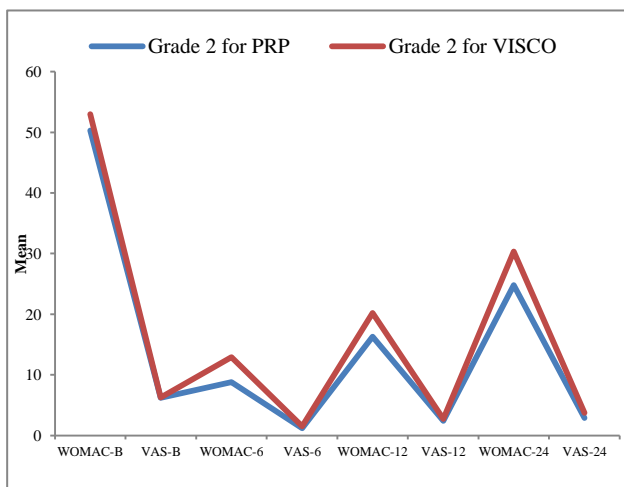
	KL-Grade-II for PRP		KL-Grade-II for VISCO		P value
	Mean	Std. deviation	Mean	Std. deviation	
<b>WOMAC-B</b>	53	8.577	50.3	5.539	0.389
<b>VAS-B</b>	6.27	1.1	6.2	0.789	0.87
<b>WOMAC-6</b>	12.93	5.612	8.8	2.044	0.054
<b>VAS-6</b>	1.53	0.834	1.2	0.422	0.257
<b>WOMAC-12</b>	20.2	5.467	16.3	4.084	0.067
<b>VAS-12</b>	2.73	0.704	2.4	0.516	0.213
<b>WOMAC-24</b>	30.33	4.701	24.8	7.177	0.028*
<b>VAS-24</b>	3.73	0.704	2.9	0.876	0.015*

Applied Mann-Whitney U test for significance. \* Significant.

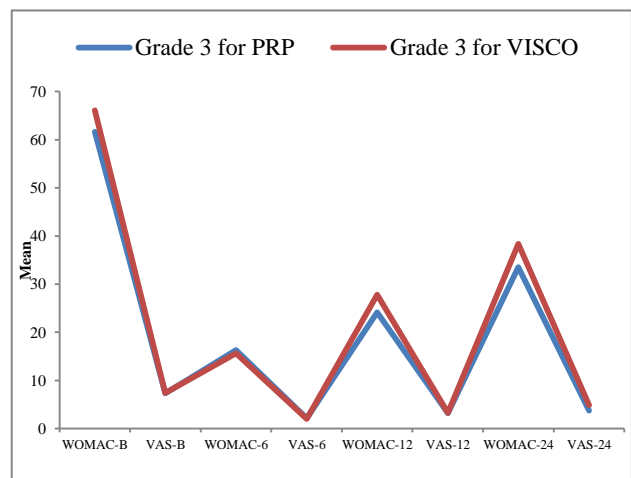
**Table 3: Results of PRP and Visco compare for KL-grade-III.**

SCORE	KL-grade-III for PRP	KL-grade-III for VISCO	P value		
	Mean	Std. deviation	Mean	Std. deviation	
<b>WOMAC-B</b>	61.67	6.553	66.08	6.422	0.072
<b>VAS-B</b>	7.33	0.97	7.38	1.044	0.889
<b>WOMAC-6</b>	16.28	4.336	15.62	5.91	0.721
<b>VAS-6</b>	2.11	0.832	2	0.816	0.714
<b>WOMAC-12</b>	24.17	4.018	27.77	8.054	0.111
<b>VAS-12</b>	3.22	0.647	3.23	0.832	0.975
<b>WOMAC-24</b>	33.5	4.462	38.38	4.35	0.037*
<b>VAS-24</b>	3.72	0.669	4.85	1.068	0.043*

Applied Mann-Whitney U test for significance. \* Significant.



**Figure 3: Mean WOMAC and VAS score at subsequent follow up in grade II knees.**



**Figure 4: Mean at subsequent follow up in grade III knees.**

## DISCUSSION

The present study was conducted on patients of osteoarthritis knee attending OPD of department of Orthopaedic Surgery KGMU Lucknow. For this 30 patients and 56 knees were registered. Out of which PRP in 28 knees and viscosupplementation in 28 knees was injected during study period. The mean age was 59.20 years (standard deviation 9.29 years); range from 43-75 years (32 years). Majority of the patients 33.33% belong to 61–70 years age group followed by 26.70% patients in 51 to 60 years age group. Raeissadat et al in his studies had the mean age of participants  $56.90 \pm 8.8$  years.<sup>2</sup> Cerza et al consisted of 25 men and 35 women, with a mean age of 66.5 years range, 31-90 years; standard deviation of 11.3 years.<sup>34</sup> All patients were randomized in two groups. Group I for intraarticular PRP injection and group-II for intraarticular viscosupplement injection. Group I included total 16 patient and 28 knees, out of which 7 (43.8%) were male and 9 (56.2%) female. Group II included total 14 patients and 28 knees, out of which 6 (42.9%) were male and 8 (57.1%) female. Raeissadat et al conducted a study in which total of 87 subjects were randomized to the PRP group and 73 subjects to HA group.<sup>2</sup> Out of 28 knees of group I; 12 (42.85%) knees belonged to grade II and 16 (57.15%) of grade III. Out of 28 knees of group II; 15 (53.57%) knees of grade II and 13 (46.45%) of grade III. None of the knees belonged to grade I and grade 0. Raeissadat et al in his studies had patients of Grade of tibiofemoral osteoarthritis Grade 1-3 (5%) Grade 2 -25 (41.7%) Grade 3- 22 (36.7%) Grade 4- 10 (16.7%).<sup>2</sup> Cerza et al done another study in which patients were graded according to the Kellgren-Lawrence radiographic classification: 21 patients had grade I gonarthrosis, 24 had grade II, and 15 had grade III.<sup>3</sup> During follow up there was reduction in mean of WOMAC and VAS score for KL-II and KL-III in which intraarticular PRP and viscosupplementation were injected. WOMAC mean value for KL grade-II in which PRP were injected, at baseline 53.00 (SD;8.5) at 6 week 12.93 (SD;5.60); at 12 week 20.20 (SD;5.40) and at 24 week 30.33 (4.70). VAS mean value for KL grade-II in which PRP were injected at baseline 6.27 (standard deviation (SD);1.1); at 6 week 1.53 (SD;0.8); at 12 week 2.73 (SD;0.7); at 24 week 3.73 (SD;0.7) WOMAC score mean value for KL grade-II in which viscosupplement were injected, at baseline 50.30 (SD;5.5); at 6 week 8.80 (SD;2.0); at 12 week 16.30 (SD;4.0); 24 week 24.8 (SD;7.18). VAS score mean value for KL grade-II in which viscosupplement were injected at baseline 6.20 (SD;0.78); at 6 week 1.20 (SD;0.42); 12 week 2.40 (SD;0.5); and at 24 week 2.9 (SD;0.87) WOMAC mean value for KL grade- III in which PRP were injected ; at baseline 61.67 (SD;6.5) at 6 week 16.20 (SD;4.33); at 12 week 24.17 (SD;4.0) and at 24 week 33.50 (SD;4.5). VAS mean value for KL grade-III in which PRP were injected ; at baseline 7.33 (SD;0.97); at 6 week 2.11 (SD;0.83); at 12 week 3.22 (SD;0.64) and at 24 week 3.72 (SD;0.67). WOMAC mean value for KL grade- III in which viscosupplement were injected; at baseline 66.08 (SD;6.4); at 6 week 15.62

(SD;5.9); at 12 week 27.77 (SD;8.0) and at 24 week 38.38 (SD;4.3) VAS mean value for KL grade-III in which viscosupplement were injected; at baseline 7.38 (SD;1.0); at 6 week 2.00 (SD;0.8); at 12 week 3.23 (SD;0.83) and at 24 week 4.85 (SD;1.06). Thus there was only significant difference (p value <0.05) at 24 weeks of KL grade-II and III in which PRP and viscosupplement were injected. Cerza et al did a study in which statistically significant difference between grade III gonarthrosis treated with ACP and that treated with HA was observed at week 12 as well as at week 24, with a noticeable improvement that was greater in the patients treated with ACP (P value 0.001).<sup>34</sup> Chang et al reviewed the effects of intra-articular PRP injection in knee OA compared to HA in a systematic review study.<sup>35</sup> The study demonstrated that PRP led to significant functional improvement in patients with knee cartilage pathology, whose effects last at least 12 months. Compared to patients receiving HA, patients in the PRP group had more and longer improvement. There were also better results among those patients with milder forms of OA than advanced ones. Similar results were obtained in another meta-analysis. Khoshbin et al found the PRP injection more efficient than HA and normal saline in mild-to-moderate OA in 2013.<sup>36</sup> The most important patients' complaint was injection site pain. In some cases, pain lasted up to 10 minutes after injection, decreased gradually, and continued as a dull pain at the injection site. Some patients complained of transient knee stiffness and feeling of swelling. Pain in most of them was improved by following the instructions and acetaminophen consumption. No significant complication was observed except for transient increase in local pain and swelling. Raeissadat et al like others proposed the effectiveness of PRP in short term.<sup>2</sup> In our study, we tried first to evaluate the safety of our therapeutic protocol. Except for 10 minute pain at the site of injection and dull pain up to one week maximally, no other complication such as infection, atrophy, deep vein thrombosis, fever, hematoma, and tissue hypertrophy was observed (just like other studies).

## CONCLUSION

Treatment with PRP showed a significantly better clinical outcome compared with viscosupplement treatment; patients achieved lower WOMAC scores, which were subsequently maintained during follow up. In fact, in grade II and grade III patients, treatment with viscosupplement seemed decidedly less effective than treatment with PRP. Despite the relatively low number of patients in the subgroups, statistical analysis confirms the better result of the PRP. Limitations of our study were the relatively small sample size.

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