Research Article

Comparative Effect Of Autologous Platelet Rich Plasma Versus Viscous Supplementation In Treatment Of Early Osteoarthritis Of Knee : A Prospective Randomized Controlled Trial

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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 remodeling, and inflammation of the joint. With aging of the population and increasing obesity, OA arises as a major public health problem and an important financial burden for the global economy.

AIMS: To compare the effectiveness of intra-articular injection of platelet-rich plasma compared to low molecular weight hyaluronic acid for the treatment of osteoarthritis of the knee.

MATERIAL AND METHODS: It was hospital based observational prospective cohort study on 100 patients of osteoarthritis with minimum 3 months of knee pain with radiological changes or a clinical presentation of osteoarthritis of knee was selected for the study. The cases were divided into two groups according to treatment given: Group A: Patients who were get inj. PRP. Group B: Patients who were get inj. viscosupplementation with hyaluronic acid (HA).

RESULTS: The mean age of osteoarthritis patients was 59.30 years with standard deviation [SD] 9.26 years; range from 43-75 years (32 years), with minimum age of 43 years and maximum 75 years. Group-I included total 50 patients, out of which 32 of KL grade-II and 53 of KL grade-III. Group-II included total 50 knees, out of which 68 of KL-grade –II and 34 of KL-grade-III. None of the knee of KL-grade 0 and grade-I. The most important patients’ complaint was injection site pain and its lasts up to 10 minutes after injection.

CONCLUSION: PRP provides a simple, cost effective option for patients with early osteoarthritis with a no risk of immunological reaction. Limitations of our study were the relatively small sample size. Another limitation was that we followed our patients for a minimum of only 6 months; long-term follow-up should also be carried out.
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 remodeling, and inflammation of the joint\(^1\). With aging of the population and increasing obesity, OA arises as a major public health problem and an important financial burden for the global economy\(^2\). For the knee OA, various conservative treatment modalities are recommended by clinical guidelines\(^3,4\).

The non-pharmacological modalities are patient education and self-management, exercises, weight reduction, walking supports (crutches), bracing, shoe and insoles modification, local cooling/heating, acupuncture, and electromagnetic therapy. 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 (corticosteroids, viscosupplements, blood-derived products) is the last nonoperative modality that can be preferred\(^4,5\).

Etiopathogenesis of OA: To refer OA as “degenerative joint disease” would be a misnomer because OA is not simply a process of “wear and tear” but rather a much more complex disease driven by inflammatory mediators within the affected joint\(^6-10\). Recent researches supports that, OA is a “whole joint” disease\(^6-8\). Although cartilage destruction is the hallmark of the disease; synovitis, subchondral bone remodeling (thickening, bone collapse, bone cysts), degeneration of ligaments and menisci, and hypertrophy of the joint capsule take parts in the pathogenesis of OA\(^1\). In OA, chondrocytes, which are responsive to mechanical (e.g., malalignment, articular cartilage incongruity) and inflammatory stimulation, become activated to produce inflammatory mediators, similar to an injury response\(^7,11\). Also, subchondral bone cells response in a similar way, and may take role in degradation of the deep layer of cartilage\(^12\). As articular cartilage matrix proteins are fragmented, these fragments feedback and stimulate further matrix destruction\(^7\). On the other hand, aging-related changes in chondrocytes (i.e., accumulation of advanced glycation end-products) make the cartilage more brittle and lead to increased production of cytokines and chemokines by aged chondrocytes\(^13\). Therefore, increased age also arises as an important risk factor for OA. Synovial inflammation plays a critical role in the symptoms and structural progression of OA. Soluble inflammatory mediators, such as cytokines and chemokines, are increased in synovial fluid (SF) in OA and promote synovitis\(^7\).

Kellgren and Lawrence system is a method of classifying the severity of knee osteoarthritis (OA) using five grades\(^22\)

- **Grade 0** – No radiographic findings of osteoarthritis.
- **Grade 1** – Minute osteophytes of doubtful clinical significance
- **Grade 2** – Definite osteophytes with unimpaired joint space
- **Grade 3** – Definite osteophytes with moderate joint space narrowing
- **Grade 4** – Definite osteophytes with severe joint space narrowing and subchondral sclerosis.

The study was conducted to compare the effectiveness of intra-articular injection of platelet-rich plasma compared to low molecular weight hyaluronic acid for the treatment of osteoarthritis of the knee.

MATERIAL AND METHODS
The present study was conducted in the department of Orthopaedics, MLB Medical College, Jhansi. It was hospital based observational prospective cohort study. The hundred (100) patients of osteoarthritis with minimum 3 months of knee pain with radiological changes or a clinical presentation of osteoarthritis of knee was selected for the study.

**Inclusion criteria**
1. Any patient with a history of unilateral or bilateral knee pain for at least three months duration with radiological changes of
osteoarthritis and do not responding to other non-interventional treatments.

2. Patients with X-ray findings of moderate OA (Kellgren Lawrence grade II).

3. Patients’ compliance to complete the treatment regime with requisite follow-ups and prescribed exercise programs.

**Exclusion criteria**

1. Age greater than 80 years or under 25 years,
2. Kellgren Lawrence score of more than 2, major axial deviation, non-OA knee joint pain, inflammatory arthropathy,
3. Hematological diseases, cardiovascular disease or systemic infection and
4. Use of NSAIDs in the last 5 days before treatment and hemoglobin count less than 11 g/dL and platelet count lower than 150000/mm³.

The cases were divided into two groups according to treatment given:

Group A: Patients who were get inj. PRP.

Group B: Patients who were get inj. viscosupplementation with hyaluronic acid (HA).

**PREPARATION OF AUTOGENOUS PLATELET RICH PLASMA**

60 ml of Peripheral blood of the patient was collected by transfusion medicine department maintaining the standardised sterility protocol. The procedure consisted of a 60-ml venous blood sample for every knee treated. Then, 2 centrifugations (the first at 1480 rpm for 6 minutes to separate erythrocytes, and a second at 3400 rpm for 15 minutes to concentrate platelets) produced a unit (5-10ml) of PRP. thus ensuring a controlled not contaminated intra-articular delivery of the product.

The collected blood was undergo series of centrifugation process ultimately delivering the desired platelet rich plasma with resultant increase in platelet concentration of five to ten folds.
FOLLOW UP
During the follow-up period, nonsteroidal anti-inflammatory drugs were not be allowed, and paracetamol (dosage, 500 mg tds) will be prescribed in case of discomfort. Clinical outcome will be evaluated using the western ontario and McMaster universities arthritis index (womac) questionnaire and by visual analog scale for pain at 6 weeks, 12 weeks and 24 weeks after treatment. Overall satisfaction with the procedure and complications was noted.

RESULTS

Table-1 : Gender Distribution Of The Patients

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>43</td>
<td>43.0</td>
</tr>
<tr>
<td>Female</td>
<td>57</td>
<td>57.0</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

Table -1 shows that total 100 patients were included in this study out of which 43 (43.0%) were males and 57(57%) were females.

Table-2 : Age Distribution Of The Patients

<table>
<thead>
<tr>
<th>Age</th>
<th>59.30</th>
<th>9.26</th>
<th>43</th>
<th>75</th>
<th>32</th>
</tr>
</thead>
</table>

Table-2 show that the mean age of osteoarthritis patients was 59.30 years with standard deviation [SD] 9.26 years; range from 43-75years(32years), with minimum age of 43 years and maximum 75 years.

Table-3 : Age Interval Of The Patients

<table>
<thead>
<tr>
<th>Age Intervals</th>
<th>No. of cases</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>41 - 50</td>
<td>22</td>
<td>22.0</td>
</tr>
<tr>
<td>51 - 60</td>
<td>30</td>
<td>30.0</td>
</tr>
<tr>
<td>61 - 70</td>
<td>30</td>
<td>30.0</td>
</tr>
<tr>
<td>71 - 80</td>
<td>18</td>
<td>18.0</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

Table-3 show that majority of the patients30 (30.0%) belong to 51 – 60 years and 61- 70 years of age group followed by 22(22.0%) patients in 41 to 50 years age group.
Table-4: number of knees --kll grading:

<table>
<thead>
<tr>
<th>KLL Grade</th>
<th>Group-I (PRP)</th>
<th>Group-II (VISCO)</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade-2</td>
<td>Count 32</td>
<td>Count 68</td>
<td>100</td>
</tr>
<tr>
<td></td>
<td>% within group 37.64%</td>
<td>66.67%</td>
<td>53.48%</td>
</tr>
<tr>
<td>Grade-3</td>
<td>Count 53</td>
<td>Count 34</td>
<td>87</td>
</tr>
<tr>
<td></td>
<td>% within group 62.35%</td>
<td>33.33%</td>
<td>46.52</td>
</tr>
<tr>
<td>Total</td>
<td>Count 85</td>
<td>Count 102</td>
<td>187</td>
</tr>
<tr>
<td></td>
<td>% within group 100.0%</td>
<td>100.0%</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Table-4 show that patients were randomized in two groups. Group-I for PRP and group-II for Viscosupplementation intraarticular injection. Group-I included total 50 patients, out of which 32 of KL grade-II and 53 of KL grade-III. Group-II included total 50 knees, out of which 68 of KL-grade-II and 34 of KL-grade-III. None of the knee of KL-grade 0 and grade-I.

TABLE-5: RESULTS OF PRP and VISCO COMPARE FOR KL-GRADE-II

<table>
<thead>
<tr>
<th>KL-GRADE-II for PRP</th>
<th>KL-GRADE-II for VISCO</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>Std. Deviation</td>
<td>Mean</td>
</tr>
<tr>
<td>WOMAC-B</td>
<td>53</td>
<td>8.577</td>
</tr>
<tr>
<td>VAS-B</td>
<td>6.27</td>
<td>1.1</td>
</tr>
<tr>
<td>WOMAC-6</td>
<td>12.93</td>
<td>5.612</td>
</tr>
<tr>
<td>VAS-6</td>
<td>1.53</td>
<td>0.834</td>
</tr>
<tr>
<td>WOMAC-12</td>
<td>20.2</td>
<td>5.467</td>
</tr>
<tr>
<td>VAS-12</td>
<td>2.73</td>
<td>0.704</td>
</tr>
<tr>
<td>WOMAC-24</td>
<td>30.33</td>
<td>4.701</td>
</tr>
<tr>
<td>VAS-24</td>
<td>3.73</td>
<td>0.704</td>
</tr>
</tbody>
</table>

Table-5 show that WOMAC mean value for KL-grade-II in which PRP were injected, at baseline(B) 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 (SD;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 mean value for KL-grade-II in which viscosupplement were injected ,at baseline(B) 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 mean value for KL grade –II in which viscosupplement were injected at baseline (B) 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). There Is Only Significant Difference (P-VALUE <0.05) AT 24 weeks of KL- Grade-II In Which PRP And Viscosupplement Were Injected.
Figure -1; Diagrammatic representation of mean at subsequent follow up in grade-II knees

![Diagram](image.png)

**TABLE-6 : Results Of PRP and Visco Compare For KL-Grade-III**

<table>
<thead>
<tr>
<th>SCORE</th>
<th>KL-GRADE-III for PRP</th>
<th>KL-GRADE-III for VISCO</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>Std. Deviation</td>
<td>Mean</td>
</tr>
<tr>
<td>WOMAC-B</td>
<td>61.67</td>
<td>6.553</td>
<td>66.08</td>
</tr>
<tr>
<td>VAS-B</td>
<td>7.33</td>
<td>0.97</td>
<td>7.38</td>
</tr>
<tr>
<td>WOMAC-6</td>
<td>16.28</td>
<td>4.336</td>
<td>15.62</td>
</tr>
<tr>
<td>VAS-6</td>
<td>2.11</td>
<td>0.832</td>
<td>2</td>
</tr>
<tr>
<td>WOMAC-12</td>
<td>24.17</td>
<td>4.018</td>
<td>27.77</td>
</tr>
<tr>
<td>VAS-12</td>
<td>3.22</td>
<td>0.647</td>
<td>3.23</td>
</tr>
<tr>
<td>WOMAC-24</td>
<td>33.5</td>
<td>4.462</td>
<td>38.38</td>
</tr>
<tr>
<td>VAS-24</td>
<td>3.72</td>
<td>0.669</td>
<td>4.85</td>
</tr>
</tbody>
</table>

Table-6 show following finding- 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). There is only significant difference (P-VALUE <0.05) at 24 weeks of KL-GRADE-III in which prp and viscosupplement were injected.
DISCUSSION
The present study was conducted on patients of osteoarthritis knee attending OPD of department of orthopaedic, MLB Medical College, Jhansi. The aim of this study is to compare the efficacy platelet rich plasma and viscosupplementation in early osteoarthritis knee. For this we registered 100 patients and 187 knees. Out of which we injected PRP in 85 knees and viscosupplementation in 102 knees during my study period. The mean age of osteoarthritis patients attending OPD of department of orthopaedic, MLB Medical College, Jhansi was 59.30 years with standard deviation [SD] 9.26years ; range from 43-75years(32years) .Majority of the patients 30.0% belong to 51 – 60 years age group and 61-70 year of age followed by 22.00% patients in 41 to 50 years age group . Seyed Ahmad Raeissadat et al[54] in his studies had the mean age of participants 56.90 ± 8.8 years. Cerza et al[55] consisted of 25 men and 35 women, with a mean age of 66.5 years range, 31-90 years; standard deviation [SD], 11.3 years. In the present study females outnumbered males . There were 43 (43.0%) male and 57 (57.0%) female patients of osteoarthritis knee. Seyed Ahmad Raeissadat et al[54] in his studies enrolled 60 patients in the final analysis including 52 women (93.3%) and 4 men (6.7%). All patients were randomized in two groups. Group-I for intraarticular PRP injection and group-II for intraarticular viscosupplement injection. Group-I included total 50 patient and 100 knees, out of which 21 (42.0%) were male and 29(58.0%) female. Group-II included total 50 patients and 87 knees, out of which 22(44.0%) were male and 26(52.0%) female. Seyed Ahmad Raeissadat et al[54] included total of 87 subjects were randomized to the PRP group and 73 subjects to HA group. Out of 187 knees in which intraarticular injections were given, 85 (45.45 %) of the knees belonged to group I , 102 (54.54%) of the knees were of group-II. Out of 85

Figure -2 Diagrammatic representation of mean at subsequent follow up in grade-III knees
knees of group-I; 32 (37.64%) knees belonged to grade-II and 53 (62.35%) of grade-III. None of the knees belonged to grade I and grade 0. Seyed Ahmad Raeissadat et al. [54] 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%). Cerza et al. [55] 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.

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)

There Is Only Significant Difference (P- VALUE <0.05) AT 24 weeks of KL- grade-III in which PRP and viscosupplement were injected.

Cerza et al,2012 [55] 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 patientstreated with ACP (P<0.001).

Chang et al, 2014 [56] reviewed the effects of intra-articular PRP injection in knee OA compared to HA in a systematic review performed in 2014. 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[57] found the PRP injection more efficient than HA and normal saline in mild-to-moderate OA in 2013. 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. Seyed Ahmad Raeissadat et al, 2014[54] like others proposed the effectiveness of PRP in short term. 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 addition, the data indicated that this difference is greater in grade II and grade III osteoarthritis. 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. Treatment with viscosupplementation seem to be less effective in the patients with grade II and grade III osteoarthritis knee.

PRP provides a simple, cost effective option for patients with early osteoarthritis with a no risk of immunological reaction.

**BIBLIOGRAPHY**


How To Cite This Article:

Source of Support: Nil
Conflict of Interest: None declared

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