A Prospective Observational Study of Platelet Rich Plasma as a Modality of Treatment for Primary Knee Osteoarthritis

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Abstract
Introduction: Osteoarthritis (OA) of the knee is one of the main causes of musculoskeletal disability. Osteoarthritis is a common, debilitating disease which is associated with a large societal and economic burden, in addition to the physical and psychological sequelae, it often manifests in the affected individual. Osteoarthritis is the fourth leading cause of “years lived with disability” (YLD), accounting for 3.0% of total global YLD’s. As per WHO by 2030, the demand for total knee arthroplasties will increase up to 670%.

Materials and Methods: This is a prospective observational study, conducted among 50 patients (selected at conveniences) with knee osteoarthritis who were studied in the outpatient department of Orthopaedics, Dr Lals Hospital, Kadru, Ranchi. An informed written consent was taken from all the participants. Patients were diagnosed using. The American College of Rheumatology (ACR) classification criteria of osteoarthritis. All patients were treated with 3 monthly intra-articular injections of autologous platelet-rich plasma into the knee joint, under local anesthesia on an outpatient basis. All these cases were treated from January 2019 to December 2019. A detailed history was taken. A preliminary general and physical examination were done. Build and nourishment noted.

Results: After 6 months, all patients were re-evaluated according to Age, Sex, BMI (Body mass index), Side involved, Severity (Grade) of osteoarthritis, Pre and post-PRP injection comparison of crepitus, local temperature, Joint line tenderness, Effusion, Range of motion, Visual Analog Scale for pain, International Knee Documentation Committee (IKDC) score(Table 2). The maximum and minimum age in this study was found to be 41 years and 70 years. The average age of the patients was calculated as the total age of patients/ no. Of patients = 52.68 yrs. Out of 50 patients, 32 were females, and 28 were males Out of 50 knee joints treated, 28 were the right side and 22 were the left side. 32 patients were found to be overweight, 12 were obese, and 6 were normal weight. The grading of osteoarthritis of the knee.

Conclusion: PRP procedure showed a higher degree of efficacy as well as significant findings of more and longer pain reduction, improved function, and patient satisfaction. This was particularly noticeable in the treatment of younger patients with less severe articular cartilage degeneration. It could be utilized as a reasonable treatment option when other therapies fail or are inappropriate for the particular patient. However, more number of observations should be done to come to a conclusion.

Key Words: Osteoarthritis, BMI, IKDC

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I. Introduction

Osteoarthritis (OA) of the knee is one of the main causes of musculoskeletal disability. Osteoarthritis is a common, debilitating disease which is associated with a large societal and economic burden, in addition to the physical and psychological sequelae, it often manifests in the affected individual. Osteoarthritis is the fourth leading cause of “years lived with disability” (YLD), accounting for 3.0% of total global YLD’s. As per WHO by 2030, the demand for total knee arthroplasties will increase up to 670%.

Pathogenesis: Osteoarthritis (OA) is a degenerative condition involving cartilage, bone, synovium, ligamentous capsular structures, and surrounding muscles. It is characterized structurally by synovial inflammation, degradation of articular cartilage, loss of joint function, active bone remodeling and angular deformity or malalignment. Although a variety of synovial fluid markers provide insight into the biological response of joints to injury, no chemical or anatomic (imaging) biomarkers have been identified that monitor the development and progression of OA or the response to therapy. OA is thought to be highly cytokine-driven, and is associated with mechanical stress resulting from overloading of subchondral bone from dysplasia, malalignment, and trauma. The small protein mediators (cytokines) provide chemical signaling or “cross-talk”
among involved tissues. These signaling molecules incite inflammation in the synovium, remodeling subchondral bone, and enzyme activation and extracellular matrix degradation in the articular cartilage.6

II. Materials And Methods

This is a prospective observational study, conducted among 50 patients (selected at conveniences) with knee osteoarthritis who were studied in the outpatient department of Orthopaedics, Dr Lals Hospital, Kadru Ranchi. An informed written consent was taken from all the participants. Patients were diagnosed using the American College of Rheumatology (ACR) classification criteria of osteoarthritis. All patients were treated with 3 monthly intra-articular injections of autologous platelet-rich plasma into the knee joint, under local anesthesia on an outpatient basis. All these cases were treated from January 2019 to December 2019. A detailed history was taken. A preliminary general and physical examination were done. Build and nourishment noted. Systemic examination of the cardiovascular, respiratory, gastrointestinal and genitourinary examination was followed as routine. A detailed local examination of the knee joint was done. Data was entered in MS Excel 2007 and analysed. Preparation of autologous platelet-rich plasma (PRP)- 30 ml of venous blood was taken from every patient and collected in sterile sodium citrated tubes. The tubes with citrated blood were centrifuged at 1800 rpm for 15 min to separate erythrocytes, and at 3500 rpm for 10 min to concentrate platelets. By this method, 3 - 5 ml of platelet-rich plasma were obtained and injected immediately without storage. It has been stated that using freshly harvested PRP might preserve all the platelet functions better.

PRP knee intra-articular injection technique- The injection was given in the supine position and with all aseptic precautions. The affected side was exposed up to the thigh and cleaned with betadine scrub (7.5%) and spirit. Then painted with 5% betadine solution and draped with linen towels. The knee joint was palpatated, and good understanding of anatomical configuration was made. 2% Xylocaine injection was given in the skin and soft tissues of the lateral aspect of knee joint. The leg was held firm in neutral rotation, and intra-articular injection of autologous platelet-rich plasma was given by the lateral approach with knee in complete extension using a 23-gauge needle. After injection, patients were instructed not to use the injected leg for 24 h, use ice packs over the injected joint and not to use NSAIDs during this period.

Inclusion Criteria

Patients with history of chronic pain (of at least 4 months duration) or swelling of the knee, not responding to NSAIDs and/or physical therapy with radiographic findings of grade 1 (definite osteophyte, unimpaired joint space) and grade 2 (moderate diminution of joint space osteoarthritis of the knee joint) according to Kellgren-Lawrence scale were included in the study.

Exclusion Criteria

Patients with diabetes, rheumatoid arthritis, major axial deviation (varus of more than 5 deg/valgus more than 5 deg), haematological diseases (coagulopathies), severe cardiovascular diseases, infections, immunosuppression, patients on therapy with anticoagulants–anti aggregants or nonsteroidal anti-inflammatory drugs within 5 days before blood donation, were excluded from the study.

Follow up Assessment

After 6 months, all patients were re-evaluated by physical examination, assessment of visual analog scale for pain, international knee documentation committee (IKDC) score.

Statistical Analysis

Chi-square test was used to assess differences between quantitative and qualitative data at baseline and after 3 PRP injections. Spearman’s correlation coefficient analysis was performed to identify factors associated with better functional outcomes. The clinical features were evaluated using the chi-square test. The VAS scale and IKDC score were assessed using chi square test. A statistically significant cut-off value was set at p < 0.05.

III. Results

After 6 months, all patients were re-evaluated according to Age, Sex, BMI (Body mass index), Side involved, Severity (Grade) of osteoarthritis, Pre and post-PRP injection comparison of crepitus, local temperature, Joint line tenderness, Effusion, Range of motion, Visual Analog Scale for pain, International Knee Documentation Committee (IKDC) score(Table 2). The maximum and minimum age in this study was found to be 41 years and 70 years. The average age of the patients was calculated as the total age of patients/ no. Of patients = 52.68 yrs. Out of 50 patients, 32 were females, and 28 were males Out of 50 knee joints treated, 28 were the right side and 22 were the left side. 32 patients were found to be overweight, 12 were obese, and 6 were normal weight. The grading of osteoarthritis of the knee.
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Kellgren and Lawrence Classification:
Grade 1 (Doubtful):
Minute osteophyte, doubtful significance.
Grade 2 (Mild):
Definite osteophyte, unimpaired joint space.
Grade 3 (Moderate):
Moderate diminution of joint space.
Grade 4 (Severe):
Joint space greatly impaired with sclerosis of subchondral bone.

Out of 50 study patients, 24 patients had grade 1 osteoarthritis, and 26 patients had grade 2 osteoarthritis. The clinical features were evaluated using the chi-square test. The VAS12 scale and IKDC13 score were assessed using the chi square test.

<table>
<thead>
<tr>
<th>Kellgren-lawrence Scale</th>
<th>No of Patients</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grade 1 (Doubtful)</td>
<td>24</td>
<td>48%</td>
</tr>
<tr>
<td>Grade 2 (Mild)</td>
<td>26</td>
<td>52%</td>
</tr>
<tr>
<td>Grade 3 (Moderate)</td>
<td>0</td>
<td>0%</td>
</tr>
<tr>
<td>Grade 4 (Severe)</td>
<td>0</td>
<td>0%</td>
</tr>
</tbody>
</table>

Table 1: Kellgren-Lawrence Grading of Patients with Primary Osteoarthritis

<table>
<thead>
<tr>
<th>Clinical Data</th>
<th>Baseline (No. Patients out of 50)</th>
<th>After 6 Months Follow Up (No. of Patients out of 50)</th>
<th>Chi-Square Value</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local Rise of temp</td>
<td>5</td>
<td>0</td>
<td>7.76</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Tender Joint line</td>
<td>33</td>
<td>15</td>
<td>12.98</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Crepitus</td>
<td>33</td>
<td>20</td>
<td>6.78</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Effusion</td>
<td>5</td>
<td>5</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Limited range of movements</td>
<td>18</td>
<td>5</td>
<td>9.54</td>
<td>&lt;0.002</td>
</tr>
</tbody>
</table>

Table 2: Clinical Evaluation of Patients with Primary Osteoarthritis after PRP Injection

IV. Discussion

Osteoarthritis is a major public health problem which causes pain and disability in one-third of all affected patients. The symptoms are often associated with notable functional impairment, as well as signs and symptoms of inflammation, including pain, stiffness, and loss of movement. Multiple factors are known to affect the progression of OA, including joint instability and/or malalignment, obesity, increasing age, associated intra-articular crystal deposition, muscle weakness, and peripheral neuropathy. Advances in molecular biology raise hopes that new therapeutic targets will be identified that will allow more than just symptomatic therapy. Joint replacement is still the unsurpassed therapy for advanced and incapacitating OA.

However, with increasing appreciation of the contribution of all three joint compartments to disease progression, research in OA pathogenesis, biomarkers, and treatment has broadened immensely, and many new potential therapeutic targets have emerged over the past years. The growing interests in the use of PRP in OA treatment, which might provide cellular and humoral mediators to promote tissue healing and repair have gained momentum in the past few years and led to several studies. Autologous plasma is a biological therapy approach with the goal of delivering concentrated platelets to accelerate and support the healing of injuries to hard and soft tissue without exposing the patient to major risks. Growth factors, an essential part of PRP, induce differentiation of mesenchymal stem cells into chondrocytes and thereby increase cell proliferation. They also suppress inflammatory mediators such as interleukin-1, encourage matrix deposition, and slow down catabolism. Hence, growth factors help stabilize cartilage homeostasis and possibly reverse articular degeneration. The use of autologous blood versus synthetic chemicals also eliminates the risk for allergic reaction or disease transfer in addition to limiting possible drug toxicity. The simple and efficient in-house preparation at the time of patient visit proves to be of advantage for the PRP procedure.
In our study 50 patients with Grade 1 or Grade 2 knee osteoarthritis treated with 3 monthly injections of platelet-rich plasma and following conclusion made after six months of follow up. The average age documented was 52.68 years. Osteoarthritis of the knee was common in 5th and 6th decade of life, the commonest in between 51- and 55-years age group. In this study, 41 patients were found to be below the age of 60 years. Also, results were found to be better in the younger patients when compared to the older. In this study 32 patients (64%) were females, and 18 (36%) patients were male. The baseline visual analog score in female patients was 5.93 and 3.45 at 6 months, and that in males was 5.98 (Baseline) and 3.36 (at 6 Months) thus showing that there is no notable difference in response to treatment between males and females. The value of IKDC score in males was 38.75 (Baseline) and 76.08 (at 6 Months) and that in females was 38.42 (Baseline) and 76.14 (at 6 Months) therefore showing no significant difference in response to treatment in between males and females.

V. Conclusion

PRP procedure showed a higher degree of efficacy as well as significant findings of more and longer pain reduction, improved function, and patient satisfaction. This was particularly noticeable in the treatment of younger patients with less severe articular cartilage degeneration. All of the comparative studies suggest that PRP injections are a useful approach and an alternative in the treatment of OA. This minimally invasive procedure appears to be safe and effective. It could be utilized as a reasonable treatment option when other therapies fail or are inappropriate for the particular patient.

References

[8]. Werner S, Grose R: Regulation of wound healing by growth factors and cytokines. Physiol Rev 2003; 83:835–70.