Role of intra articular injection of autologous platelet rich plasma in osteoarthrosis of the knee joint

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Abstract
Osteoarthrosis (OA) represents a failure of the diarthrodial, synovial lined joint. Among the elderly, knee Osteoarthrosis is the most frequent cause of chronic disability [1]. Because of the increased life expectancy, the prevalence of osteoarthrosis is on the rise in the Indian population. Platelet rich plasma (PRP) is defined as a volume of plasma with a platelet concentration higher than average in peripheral blood. Many basic, preclinical and even clinical case studies and trials report PRP’s ability to improve musculoskeletal conditions including osteoarthrosis. Our study of platelet rich plasma has thrown up an exciting choice of treatment modality in knee osteoarthrosis, and it has proved efficient in observation period of one year.

Keywords: anti-inflammatory intra-articular therapies, clinical evidence, knee osteoarthrosis, platelet rich plasma

Introduction
Osteoarthrosis is age-related, affecting more than 80% of people over the age of 55 OA in weight-bearing joints is strongly linked to BMI (Body Mass Index). OA has a preference for knees, hips, shoulders, and the spine and phalanges. Occurrence in an atypical joint, such as an elbow, can usually be before the trauma, congenital joint abnormality, underlying systemic disease, or a chronic crystalline arthropathy. The heterogeneity of OA can be due to many factors that can contribute to cartilage damage. Symptomatic OA of the knee, which is having pain during most days of a month along with other evidence (e.g., radiological) of arthritis, has a prevalence of 30% to 40% in India [3, 4].

Osteoarthritis is a chronic disorder of synovial lined joints leading to progressive softening and disintegration of articular cartilage accompanied by the new growth of bone at the joint margins, cyst formation, and sclerosis at subchondral regions of bone, mild synovitis, and capsular fibrosis.

Aim of the study
Treatment of osteoarthrosis with NSAIDs is associated with Osteoarthritis is a clinically heterogenous degenerative condition characterized by the destruction of articular cartilage due to the uncoupling of a balance between cartilage degeneration and regeneration. The management of osteoarthrosis [13] has varied from conventional therapy with physical education, NSAIDS, intraarticular steroid injection increased the risk of GI disturbances along with the alarming rise in NSAID induced complications. Arthroplasty is usually reserved for advanced stages of OA.

The main aim of this study is to evaluate the effectiveness of Platelet Rich plasma in decreasing pain, stiffness, and improving function in patients with early osteoarthrosis knee, as Platelet Rich Plasma provides a cocktail of growth factors into the joint cavity. Platelet Rich Plasma is postulated to modify the disease process, unlike other methods of nonsurgical treatment which provide symptomatic relief. Platelet Rich Plasma is a cost-effective tool that could prevent the need for Total Joint Arthroplasty. Or at least reduce the number of surgeries.
Review of literature
Khosbin et al., in a systematic review with the quantitative synthesis in 2013, concluded that intraarticular PRP injections might have benefits in the treatment of adult patients with mild to moderate osteoarthritis. The study also reported an increased incidence of non-specific adverse events among patients treated with Platelet-rich plasma.

Kalbkhani et al. in 2014 studied the effect of PRP in experimentally induced OA in rabbits knee joint concluded that the PRP group had near-normal joint structure at 16-week post-op interval, and hence PRP could potentially be used for the treatment of osteoarthritis.

Giuseppe Filardo, in 2010, studied platelet-rich plasma intraarticular knee injections for the treatment of degenerative cartilage lesions, and osteoarthritis concluded that treatment with PRP could reduce pain and improve knee function and quality of life with short term efficacy.

Kon et al. Trial - the effectiveness of PRP injections were compared to hyaluronic acid (HA) intra-articular injection therapy. The primary outcomes of pain reduction function improvements were measured through the International Knee Document Committee (IKDC) and Visual Analogue Scale (EQ-VAS) scoring system.

Evaluation of the IKDC score in the PRP group showed a steady increase from (Baseline) to 62.7 and 64.0 at 2 and 6 months follow up, respectively.

Objectives
To evaluate the role of Autologous Platelet Rich Plasma (PRP) in treating patients presenting with early osteoarthritis knee and analyze whether it could be a cost-effective disease-modifying the measure.

Study Design
A prospective study was done in 150 patients in which standardized injection protocol was given and was assessed on variables such as pain, physical function using the WOMAC scale, and for depression using a visual analog scale at pre-injection, 6 weeks post-injection, 3 months and 6 months and 1yr post-injection.

Materials and Methods
Patients attending the outpatient department of Orthopaedics at NRI Medical College with complaints of bilateral knee pain and stiffness were screened, and those diagnosed as bilateral Knee Osteoarthritis were chosen for the study. The Patients, classified either grade 0 to 4 on the Kellgren-Lawrence grading scale or grade 1 to 4 on the Ahlback scale, were included in the study after prior well informed written consent.

150 Patients were chosen and were given an intraarticular injection of protein-rich plasma

Inclusion Criteria
1. Kellgren–Lawrence Grade 1, Grade 2, Grade 3A
2. Age of more than 35 years.
3. A patient who gave consent for the study.
4. Platelet count (minimum 2 lakhs per microliter)
5. Random blood sugar <160 mg/dl
6. haemoglobin >10 gm%

Exclusion Criteria
1. Platelet dysfunction syndrome.
2. Critical thrombocytopenia (<105/mL).
3. Hypofibrinogenemia.
4. Septicemia.
5. Coagulopathies.
6. Presence of tumors or metastasis.
7. Active infection.
8. Pregnancy or breast-feeding.
9. Immune deficiencies.
10. Patients with vascular injuries.

Kellgren Lawrence grading of osteoarthritis10
Grade 0: no radiographic features of OA are present
Grade 1: doubtful narrowing of joint space with possible osteophytes Lipping
Grade 2: definite osteophytes, definite narrowing of joint space
Grade 3: moderate multiple osteophytes, definite narrowing of joints space, some sclerosis and possible deformity of bone contour
Grade 4: large osteophytes, marked narrowing of joint space, severe sclerosis and definite deformity of bone contour

Ahlback radiological criteria1
Grade 1: Joint Space Narrowing (Less Than 3 Mm)
Grade 2: Joint Space Obliteration
Grade 3: Minor Bone Attrition (0-5 Mm)
Grade 4: Moderate Bone Attrition (5-10 Mm)
Grade 5: Severe Bone Attrition (More Than 10 Mm)

Autologous Platelet Rich Plasma (PRP) was prepared in the NRI medical college orthopedics department. The process of separating Platelet Rich Plasma was done under strict aseptic conditions. The Patients baseline platelet count and leukocyte count were determined, and Platelet Rich Plasma was quantified as having eight to ten times the baseline value of platelets. The Concentration of Platelets in the final product was corroborated by the Department of the pathology of NRI medical college on a periodic basis.

We in this study did not use leukocyte filter, and the final Platelet Rich Plasma contained minute traces of leucocytes.

Injection protocol
The Injection procedure was performed in the emergency operation theatre. The patient was placed supine on the operation table. Parts scrubbed, painted, and draped. Under sterile aseptic precautions, 3ml of Platelet Rich Plasma was injected into the joint cavity from a medial approach sterile bandaging given. Cycling of the knee is done 10 times for the distribution of PRP in the joint cavity. The Patient has advised analgesics and ice fomentation for pain after the procedure.

The Patients were advised to carry on with their regular work from Day 1.

Outcome analysis
The patients were advised to follow up at 6 weeks, 3 months, and 6 months and 12 months. Outcome analysis was done for the reduction in pain, decrease in stiffness, and improvement in physical function using the WOMAC scale. The Patients were also assessed for reduction in pain using Visual analog scale both at pre-injection and at 12 months post-injection.
**Fig 1:** Procedure

- take two 20 ml syringe with each 3 ml ACDA and 17 ml venous blood (overall 34 ml blood)
- remove needles, cover the tip of barrels with insulin caps.
- cut the edges of syringe (cut the plunger and overhangs of the barrel).
- place it in centrifuge with pre-set spin of 1500 RPM for 15 mins place two syringes in the opposite direction.
- aspirate plasma and buffy coat through three way stopcock into another syringe, as a result, 20 ml will be collected.
- take another 20 ml of normal saline as a counterweight.
- Place two syringes in opposite direction in the centrifuge.
- set the spin for 3500 RPM for 7 mins.
- Discard plasma except for 1-2 ml.
- Collect buffy coat with 1-2 ml of plasma.

**Fig 2:** The process of separating Platelet Rich Plasma was done under strict aseptic conditions.
Womac (western ontario and mcmaster universities) index of osteoarthritis 5, 17

The WOMAC index is used to assess patients with osteoarthrosis of the hip or knee using 24 parameters. It can be used to monitor the course of the disease or to determine the effectiveness of Therapy.

Circle one number for each activity

**Pain**

Scale of difficulty: 0 = None, 1 = Slight, 2 = Moderate, 3 = Very, 4 = Extremely

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<td>Walking</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
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<tr>
<td>2</td>
<td>Climbing stairs</td>
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<td>1</td>
<td>2</td>
<td>3</td>
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<tr>
<td>3</td>
<td>Nocturnal</td>
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<td>4</td>
<td>Rest</td>
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<td>1</td>
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<td>3</td>
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<tr>
<td>5</td>
<td>Weight bearing</td>
<td>0</td>
<td>1</td>
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**Stiffness**

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<tr>
<td>1</td>
<td>Morning stiffness</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
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<td>2</td>
<td>Stiffness occurring later in the day</td>
<td>0</td>
<td>1</td>
<td>2</td>
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**Physical function**

1. Descending stairs | 0 | 1 | 2 | 3 | 4
2. Ascending stairs | 0 | 1 | 2 | 3 | 4
3. Rising from sitting | 0 | 1 | 2 | 3 | 4
4. Standing | 0 | 1 | 2 | 3 | 4
5. Bending to floor | 0 | 1 | 2 | 3 | 4
6. Walking on flat surface | 0 | 1 | 2 | 3 | 4
7. Getting in / out of car | 0 | 1 | 2 | 3 | 4
8. Going shopping | 0 | 1 | 2 | 3 | 4
9. Putting on socks | 0 | 1 | 2 | 3 | 4
10. Lying in bed | 0 | 1 | 2 | 3 | 4
11. Taking off socks | 0 | 1 | 2 | 3 | 4
12. Rising from bed | 0 | 1 | 2 | 3 | 4
13. Getting in and out of bath | 0 | 1 | 2 | 3 | 4
14. Sitting | 0 | 1 | 2 | 3 | 4
15. Getting on and off toilet | 0 | 1 | 2 | 3 | 4
16. Heavy domestic duties | 0 | 1 | 2 | 3 | 4
17. Light domestic duties | 0 | 1 | 2 | 3 | 4

Total Score: ___ / 96 = ____%

**Visual analog scale for pain**
The Pain, the Patient, perceives is graded on a visual scale and the score calculated.

Ask patients about their:

1. Intensity
2. Location
3. Duration
4. Onset
5. Variation
6. Quality
Pain Score

Fig 7: Mean Pain score

Stiffness score

Physical function score

Fig 8: Mean Stiffness score

Fig 9: Mean Physical function score

Visual Analog Score

Fig 10: Mean visual analog score

Discussion

Osteoarthrosis is a synovial joints disorder caused mainly by the uncoupling of balance between cartilage regeneration and degeneration due to focal loss of hyaline cartilage leading to proliferation of cells and the formation of new bone and remodeling of joint surfaces. Osteoarthrosis is a dynamic repair process of synovial joints that may be triggered by a variety of causes. The use of biological agents, including PRP and mesenchymal stem cells (MSCs) in orthopedics, has increased exponentially over the last few years due to its autologous nature, lack of side-effects, and supposed effectiveness. Platelet-rich plasma is an autologous blood product with platelet concentrations above baseline.

Tissue repair is a complex process comprising chemotaxis, angiogenesis, cell proliferation, and matrix formation. Platelets are involved in all of these functions by the release of growth factors. High concentrations of proteins such as platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), endothelial cell growth factor, and the fibroblast growth factor have led to suggestions that PRP may be useful in conditions requiring tissue healing. Conversely, the other protein in PRP, transforming growth factor (TGF-β), has an inhibitory effect and can lead to non-predictable results.

Preparation of PRP can result in four products

1. Pure PRP (P-PRP) with a low content of leucocytes. This can be injected as a liquid or a gel.
2. Leucocyte-rich PRP (L-PRP) has a higher concentration of platelets than P-PRP. Similarly to P-PRP, it can be used as an activated gel or in a liquid form to be injected intra-articular.
3. Pure platelet-rich fibrin (P-PRF). This is obtained by double-spinning centrifugation without adding anticoagulants. The end product is a platelet-rich fibrin scaffold, which is stiffer than the conventional PRP and takes the form of a gel and can be used for the healing of wounds.
4. Leucocyte- and platelet-rich fibrin (L-PRF), which is a leucocyte-rich gel which is non-injectable and is applied locally.

Platelets are regarded as the primary mediators of hemostasis. They contain alpha granules enriched with growth factors. Platelets also have anti-bacterial and fungicidal agents, which provoke the synthesis of interleukins and chemokine’s. When platelets get activated, this causes the release of growth factors. Among them, important ones include transforming growth factor-beta family (TGF-beta), platelet-derived growth factor (PDGF), insulin-like growth factor (IGF), and fibroblast growth factor (FGF), etc. In the presence of calcium chloride, the platelet concentrate is activated, which causes the release of these growth factors, eventually promoting healing. PRP has also been found to have anti-inflammatory actions. The inflammatory cascade generated by cyclooxygenase family can be inhibited by anti-inflammatory mediators present in PRP. PRP has an influence on all structures of joint. Chemotactic assays have revealed that the PRP stimulated the differentiation of type-II collagen cells and the production of prostaglandins along with the migration of corticospinous bone cells. We, in our study, had 150 patients with classic findings of Osteoarthritis. They were comparable to baseline characteristics of age, weight, and pre-injection, and post-injection WOMAC.
score. All the patients received intraarticular injections. The Efficacy of Platelet Rich Plasma (PRP) in decreasing pain, stiffness, physical function were assessed and scored on the WOMAC index.

Age distribution revealed a mean age in to be 49.92. Gender distributions were comparable in both groups, with 66.6% being male 33.3% being female. Thus the study of platelet-rich plasma ensured that all patients were comparable to baseline.

The Global WOMAC score showed a mean of 74.1 at the pre-injection period, which decreased to 62.45 at 6 weeks follow up and 47.68 at 3 months and declining to 33.40 at 6 months and 33.20 at one year.

Individual variables such as pain, physical function, etc. were assessed. The mean score for pain showed a decrease from 16.57 to 11.31 at 6 weeks post-injection. At the end of 1 year follow up, the mean was 5.34.

The mean of Physical function decreased from a pre-injection score of 51.11 to 24.62 at 6 months follow up and 24.50 at one year.

Conclusion

The Epidemic of Modernization, along with adequate health care delivery, has led to an expanded lifespan of human beings. The focus of health care providers is undergoing a drift towards noncommunicable and degenerative disorders. Osteoarthrosis represents a failure of the diarthrodial joint, characterized by degenerative changes in articular cartilage of joints. The management of Osteoarthrosis has undergone a sea change during the last century.

Our study of platelet-rich plasma relied on injecting a highly concentrated mix of platelets into the joint cavity and observing the patients for the decrease in symptoms of pain, stiffness, and improvement in physical function. Our study has revealed a consistent reduction in pain and stiffness and a definite improvement in lifestyle of the patients.

Our study of platelet-rich plasma has thrown up an exciting choice of treatment modality using Platelet Rich Plasma in the treatment of Knee Osteoarthrosis, and it has proved efficient in the observation period of one year.

Complications

There were no significant complications of infection in our patients.

Limitations

Long term follows up needed with magnetic resonance imaging to assess the Regeneration of cartilage.

References