Cartilage regeneration following PRP administration in patients of osteoarthritis of knee: A novel technique

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Abstract

Background: Most of the current treatments for osteoarthritis are palliative and attack the symptoms rather than influencing the biochemical environment of the joint. Platelet-rich plasma (PRP) therapy is a simple, low-cost and minimally invasive method that provides a natural concentrate of autologous blood growth factors (GFs) that can be used to enhance tissue regeneration.

Objective: A longitudinal study was conducted with an aim to evaluate cartilage regeneration following PRP administration in patients of knee osteoarthritis.

Material and Methods: Thirty patients of knee osteoarthritis were selected as per our inclusion criteria and were subjected to PRP administration and were evaluated objectively through ultrasonography at 9 months of follow-up

Results: There has been significant improvement in cartilage thickness of Grade 1 and Grade 2 osteoarthritis patients following PRP administration at nine months with p value < 0.05

Conclusions: Platelet rich plasma injection is safe and effective modality for treatment in knee osteoarthritis.

Keywords: Knee osteoarthritis, Platelet rich plasma (PRP)

Introduction

The term osteoarthritis is currently used to define an idiopathic slowly progressive disease of diarthrodial (synovial) joints occurring late in life and characterized pathologically by focal degeneration of articular cartilage, subchondral bone thickening (sclerosis), marginal osteochondral outgrowths (osteophytes), and joint deformity; clinically by recurring episodes of pain, synovitis with effusion, stiffness, and progressive limitation of motion; and roentographically by narrowing of joint interval, increased density and thickening of subchondral bone, subchondral cysts, and marginal bony excrescence [1]. There are various predisposing factors:- increased age [2], female sex, inherited metabolic condition [3, 5], inflammatory diseases [4], obesity etc.

Pain is the usual presenting symptom [6]. It is aggravated by exertion and relieved by rest, although with time relief is less and less common Non operative method of treatment work on Principles of 1: Maintain movement and muscle strength 2: Protect the joint from overload 3: Relieve pain 4: Modify daily activities. Operative methods include 1: Joint debridement either by arthroscopy or by open operation 2: Realignment osteotomy 3: Joint replacement 4: Arthrodesis Best management include combination of pharmacological and non pharmacological methods Recently Platelet rich plasma has been proposed as a useful modality in treatment of osteoarthritis knee joint.

Broadly Platelet concentrates are of 4 types:- 1. Pure PRP 2. Leukocyte rich PRP 3. Pure platelet-rich fibrin (PRF) 4. Leukocyte-rich PRF Dense granules of platelet contain important factors that help in cartilage regeneration. The plasma itself contains important molecules involved in the healing mechanism of connective tissues, also contributing to the platelet stimulus in tissue regeneration. [8,10]

The logic behind PRP is that platelets are the first to arrive at the site of tissue injury, and thus have the potential to release growth factors that play a critical role in mediating healing.
Role of Specific Growth Factors

PDGF Encourages proliferation of fibroblasts, enhances collagen synthesis TFG-β Stimulates fibroblast proliferation, formation of collagen, and extracellular matrix components IGF Mediates growth and repair of skeletal muscle EGF Stimulates cellular proliferation VEGF Promotes angiogenesis Platelet-rich plasma (PRP) is a regenerative therapy that is thought to promote healing by augmenting and accelerating the natural healing cascade. The effects of intra-articular injections of PRP can be objectively assessed through USG imaging. USG helps us to critically monitor the course of osteoarthritis and injury progression, and to evaluate the success of treatment to patients with the early stages of osteoarthritis. USG is an cost effective modality can help to assess articular cartilage thickness in normal to moderately damaged cartilage using 5 to 12 MHZ Probe

Materials and Methods
This prospective study had been conducted in the department of orthopedic surgery, G SVM Medical college & Associated Hospitals, Kanpur, UP, India

The study included patient admitted through orthopedic OPD of this Institution. Total 30 patients included in the study out of which 18 were females and 12 were males. Follow-ups were done at 9 month and 12 month. At 9 month USG was done to evaluate cartilage regeneration and at 12 month various scoring done to evaluate functional outcome.

Study Design:- Prospective longitudinal Study

Statistical Analysis:-Analysis of data was done using the INStat software. The results were expressed as mean ± SD. A p value of 0.05 or less is considered significant.

The following selection criteria was used:-

Inclusion criteria
1. Unilateral or bilateral primary osteoarthritis knee
2. Age more than 35 years
3. History of pain and swelling more than 4 months

Exclusion Criteria
1. Age more than 75 years
2. Kellgren Lawrence Grade 4
3. Systemic disease such as rheumatoid arthritis, hematological diseases (coagulopathy), infections, immunodepression, patients in therapy with anticoagulants or anti-platelet aggressants
4. Use of NSAIDs within a week before procedure
5. Patients with Hb values < 10gm/dl and platelet values<150000/mm3

Radiological Investigations:
1. Ultrasound Imaging for cartilage thickness(Pre injection and Post injection)

USG Equipment and Technique
The Ultrasonography machine used in our setting was Micromax ultrasonography system, Sono Site Inc. The probe used had frequency range of 5 – 12 Mhz.

Preparation of platelet rich plasma and intra articular injection-
The procedure consisted of a 40ml venous blood sample drawn under aseptic conditions in a 50ml dispovan syringe with 4ml CPD-A or 4ml as anticoagulant for every knee treated. Then, 2 centrifugations (the first at 1600 rpm for 6 minutes to separate erythrocytes and a second at 3400 rpm for 15 minutes to concentrate platelets) produced a unit (04 ml) of PRP. The unit of PRP was divided in to 2 small units of 1ml and 3ml. One ml was sent to the laboratory for analysis of platelet concentration and microbiological assessment. The remaining 3ml PRP group was injected in the knee, after that 0.2 ml of [M/40] of CaCl₂ was injected to activate the platelets. Followed by two more similar injection cycle of PRP at a interval of 4 weeks. In the case of PRP administration, the total no. of platelets per milliliter in the PRP represented an increase of at least 2.5 times compared with whole blood values. In the platelet concentrate the presence of leukocytes was also observed. After the injection, patients were sent home with instructions to restrict the use of leg for at least 24 hours and to use cold therapy/ice on affected area to relieve pain. During this period of 24 hours, the use of non-steroidal medication was forbidden. The effects of intra-articular injections of PRP was objectively assessed through USG. USG Can help to assess femoral articular cartilage thickness in normal to moderately damaged cartilage.

Pre Injection and Post Injection Evaluation of Patients by comparison of Femoral articular cartilage thickness of medial condyle in study subjects before and after PRP administration after 9 months follow-up

| Determinant | Pre Prp | Post Prp |
|-------------|---------|----------|
| Femoral articular cartilage thickness (Medial condyle) | Mean(cm) | SD | Mean(cm) | SD |
| 0.157 | 0.03 | 0.174 | 0.03 |
| P< 0.0001 |
| Femoral articular cartilage thickness (intercondylar notch) | Mean(cm) | SD | Mean(cm) | SD |
| 0.209 | 0.03 | 0.215 | 0.03 |
| P = 0.05 |
| Femoral articular cartilage thickness (lateral condyle) | Mean(cm) | SD | Mean(cm) | SD |
| 0.178 | 0.03 | 0.182 | 0.03 |
| P< 0.04 |
Discussion

Osteoarthritis is a chronic, degenerative disease characterized by progressive cartilage damage. Knee is the most commonly affected joint in OA. Platelet rich plasma is known to be used for the last 20 years. In our study, total 30 patients included in the study and the results are compared before and after PRP administration and only the cases of primary osteoarthritis were included. Sánchez et al. (2008) compared 60 patients treated with PRP intra-articular injections to 30 patients treated with hyaluronic acid injections for knee OA. Sampson S et al. (2010) conducted a study which included a total of 14 patients in which both primary and secondary osteoarthritis cases were included. Spakova’ T et al. (2012) conducted a study in which included a total of 120 patients were included in the study. Our study showed improvement in cartilage thickness in femoral condyles at 9 months of follow-up (p< 0.0001 in medial condyle). Kon et al. (2011) speculated that, additional biological mechanisms, not currently known, are responsible for the improvement of OA symptoms after PRP treatment. Naredo E et al. (2009) conducted study in which he proved Ultrasound validity in the measurement of knee cartilage thickness (p<0.05). Kwon et al. (2012) showed that PRP was efficient in all stages of degeneration; but PRP injections had stronger regenerative effects in mild-moderate stage OA. Sampson et al. (2010) conducted the study in which improvement in cartilage thickness happened but that improvement was not significant (P value= 1.0 in medial condyle). They attributed the insignificant statistical results to the limited number of patients. Hart et al. (2013) reported, no significant influence on cartilage was observed in magnetic resonance imaging (MRI). Çalis et al. (2015) conducted a study which showed significant improvement in cartilage thickness (p value< 0.05) at 3 months and 6 months follow-up. Moussa et al. (2017) reported PRP increased significantly the proliferation of chondrocytes, decreased apoptosis of chondrocytes. In our study VAS score, KOOS score and IKDC score showed improvement at 12 months of follow up. In our study to show the cartilage regenerative power of PRP. Concentration of chondroprotective anabolic cytokines is high in PRP compared to whole blood. They enhance synthesis of type II collagen and chondrocyte by stimulating the proliferation of chondrocytes and pluripotent mesenchymal stem cells. Based on potential benefits of these biological factors, it is hypothesized that PRP may have positive effects on cartilage regeneration.

Food and Drug Administration approved commercial PRP kits are used for some studies. In our study, we prepared PRP manually. To standardize this protocol, we ensured that platelet counts were 2-8 fold higher compared to whole blood. Thus, we managed a reliable and cost-effective application. There were no complication detected.

Conclusion

In our study it was found that PRP is a user friendly therapeutic application that is well tolerated. It shows encouraging Preliminary results in active patients with knee osteoarthritis. It is hoped that tendency of patients to undergo surgery will decrease. The future holds good promise for the directed regeneration of cartilage in osteoarthritis. Platelet rich plasma is useful in improving the symptoms and functions of the patients knee joint. It is minimally invasive approach and almost has no complications.

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