



E-ISSN: 2395-1958
P-ISSN: 2706-6630
IJOS 2022; 8(1): 430-433
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www.orthopaper.com
Received: 21-11-2021
Accepted: 26-12-2021

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Effectiveness of platelet-rich plasma in the treatment of grade 1 osteoarthritis of knee

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DOI: <https://doi.org/10.22271/ortho.2022.v8.i1f.3052>

Abstract

Background: The most common cause of arthritis of the knee is degenerative osteoarthritis (OA) which is one of the leading causes of disability all over the world. Population which is at higher risk of osteoarthritis are elderly females, patients with obesity, and African Americans. This is a concerning factor for the advancement and different modalities of treatment for early diagnosis and early intervention in degenerative and progressive joint disease of the knee. As a recent advance in treatment platelet-rich plasma (PRP) infiltration has come to the limelight for its advantages over others.

Purpose: To determine the effectiveness of platelet rich plasma in the treatment of grade 1 osteoarthritis of the knee.

Methods: Patients at Vydehi institute of medical science and research centre, Bangalore with radiologically confirmed grade 1 osteoarthritis of the knee were included after adequate counseling and consent. They were evaluated and followed up with Visual Analogue Score (VAS) and International Knee Documentation Committee (IKDC) scores at the end of 6 months.

Results: In a study of 100 patients with grade 1 osteoarthritis evaluated with Visual Analogue Score and International Knee Documentation Committee scoring at the end of 6 months with a mean score of 3.34 and 76.14 respectively. The study shows there is a positive correlation for the effectiveness of PRP in the treatment of grade 1 OA of the knee.

Conclusion: PRP therapy is a simple, inexpensive, and minimally invasive intervention that is feasible to deliver in primary care to treat degenerative lesions of the articular cartilage of the knee. This therapy appears to have minimal associated adverse events and may have beneficial effects in terms of pain, health utility, patient satisfaction, and goal-orientated outcomes.

Keywords: Grade 1 osteoarthritis (OA), platelet rich plasma (PRP), intraarticular injection, hyaluronic acid (HA)

Introduction

The most common cause of arthritis of the knee is degenerative OA which is one of the leading causes of disability all over the world. Over 250 million people are affected by degenerative and progressive joint disease. Population which is at higher risk of OA (OA) are elderly females, patients with obesity, and African Americans^[1]. Increased life expectancy and changing trends of lifestyle modification have the likelihood of incidence of OA in upcoming years are expected to be high in numbers. This is a concerning factor for the advancement and different modalities of treatment for early diagnosis and early intervention in degenerative and progressive joint disease of the knee.

OA of the knee is mainly classified into primary and secondary where primary are due to idiopathic or non-traumatic and secondary is due to, usually traumatic or mechanical misalignment. The severity of the disease has been graded using radiological findings by Kellgren-Lawrence (KL) classification in 1957^[2,3].

As the disease is common, progressive, and increasing in incidence in recent times, it is important to diagnose and intervene in early stages. The treatment options for grade 1 OA have been growing from pharmacological methods which include analgesia, oral diacerein, glucosamine, chondroitin collagens etc. and non-pharmacological methods are using orthotics, physical therapy, or lifestyle modifications^[3]. These modes of treatment have been vastly used, but have given short-term success, not treating the etiology or have shown minimal results.

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The new trend in treatment are the intra-articular injections which have been restricted to analgesics, steroids, hyaluronates, and some unproven alternative therapies which have given good results in a number of patients [4]. Hyaluronic acid and steroids have been the most common modes of treatment in intra-articular treatment options for the management of patients who fail to respond to non-pharmacological therapy and oral drugs. As a recent advance in treatment platelet-rich plasma infiltration has come to the limelight for its own advantages over others.

Platelet-rich plasma is prepared from autologous blood which is centrifuged in a way to obtain the concentration of platelets to a level above that normally found in serum, the PRP is a type of local cell therapy that is complex and comprises a large number of chemical mediators which interact with endogenous cells inside the joint [4] and initiates immune responses for healing of the damaged cartilage.

Materials and Methods

This is a prospective study of 100 patients who were diagnosed with grade 1 OA according to Kellgren-Lawrence classification. All the patients involved in the study were picked among the outpatient department in Vydehi Institute of Medical Sciences and Research Centre, Bangalore. The study was conducted between June 2019-December 2020 with a follow-up of 6 months. The outcome data were analyzed on the follow-up and was documented. The mean age of the patients, gender, BMI, and side involved are enumerated in Table-1.

The patients who were diagnosed with grade 1 degenerative and progressive joint disease of the knee were counseled regarding the study and consent was taken. A detailed history was taken with reference to knee joint OA and an examination of the knee was done. Plain Radiographs of the knee were taken as the criteria for diagnosis and grading of the disease was made.

Inclusion criteria

1. History of pain for a minimum of 4 months and not responding to NSAIDs or physical therapy.
2. Radiographic diagnosis of grade 1 OA.

Exclusion criteria

1. Higher grades of OA.
2. Non-degenerative arthritis of the knee.
3. Major axial deviation.
4. Haematological diseases.
5. Infections.
6. Immunosuppression.

Injection of intra articular PRP in knee joint technique [4]

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 palpated and a good understanding of anatomical configuration was made.

2% Xylocaine injection was given in the skin and soft tissues of the lateral aspect of the knee joint. The leg was held firm in neutral rotation and intra-articular injection of autologous PRP (platelet-rich plasma) was given by the lateral approach with knee incomplete extension using a 16 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.

Preparation of autologous platelet-rich plasma (PRP) [4]

The procedure consisted of 30 ml of venous blood samples taken from every patient and collected in sterile sodium citrated tubes. Platelet concentrates rich in growth factors were obtained by the following technique: 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, 5 ml of PRP were obtained and injected immediately without storage. It has been stated that using freshly-harvested PRP might preserve all the platelet functions better.

The severity of pain was assessed by using the Visual Analogue Score (VAS) score and the international knee documentation committee (IKDC) score. The functional outcome was tabulated for each individual and the patterns of change were observed.

Statistics

Each patient has been evaluated thoroughly VAS and IKDC scores were documented at the time prior to the procedure and similarly evaluated at the end of 6 months. The values were combined to form a mean score at each time interval and The VAS score and IKDC were evaluated using paired T-test to know the statistical significance among them.

Results

Table 1: Demographic data.

Total number of patients		100
Gender	Male	64
	Female	36
Age	Range	41-70
	Average	31.6
BMI	18-24.9	24%
	25-29.9	66%
	Above 30	10%
Side	Right	64
	Left	36

Table 1 depicts demographic data. A total of 100 grade 1 OA patients were taken up for study out of which males were 64 in number and females were 36 in number. Age distribution ranges from 41 to 70 years with a mean age of 31.6 years. Patients with BMI of normal weight were 24% in number, overweight were 66% and obese were 10% of them. The study population showed right-sided dominance of 64 patients and 36 patients with left-sided involvement.

Table 2: Results.

Scores	Baseline	6 Month follow up	P-value
VAS	5.97 +/- 0.79	3.34	<0.001
IKDC	38.56	76.14	<0.001

Table 2 depicts the functional outcome of 100 patients at a minimum follow-up of 6 months. Baseline scores of VAS and IKDC are 5.97 +/- 0.79 and 38.56 and at the end of 6 months, the score improved to 3.34 and 76.14 respectively (Figure-1) which is statistically significant.

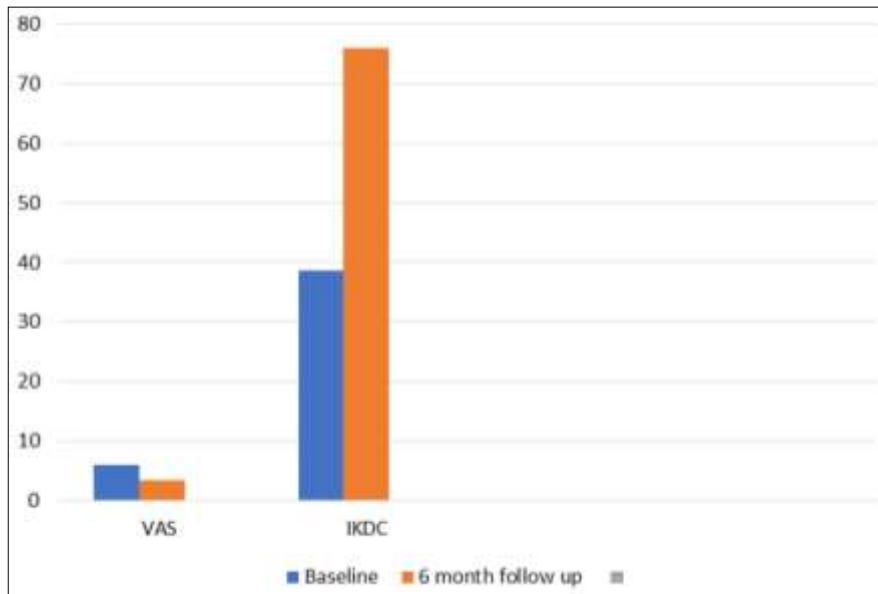


Fig 1: Mean scores of VAS score and IKDC at baseline and at 6 months follow up.

Discussion

In this study, it is demonstrated that PRP therapy in primary care of grade 1 OA is feasible and safe. Follow-up and outcome measures were completed by all the patients. In our study, it has been shown that the primary measure of outcome i.e., pain, is significantly improved at the end of 6 months.

The treatment modalities for grade 1 OA of knee referred to the conservative treatment, includes NSAIDs, analgesics, intra-articular hyaluronic acid injection, corticosteroid injection, weight loss, strengthening exercises.

Intra-articular PRP injection for symptomatic OA becomes the frequent mode of treatment. As it becomes a good promising agent of tissue repair and regeneration. Most studies involving PRP injection for OA shows improvement in pain and functional outcomes but lacks documentation. PRP-derived growth factors have been shown to promote cell recruitment, proliferation, and angiogenesis which results in the reduction of the critical regulators of the inflammatory process and results in decreased expression of inflammatory enzymes (Van Buul *et al.* 2011) [5]. Chondrogenesis and mesenchymal stem cell proliferation have been seen in PRP induced regenerative process of damaged tissue (Kabiri *et al.* 2014) [6]. In clinical practice, an appropriate scaffold is used along with autologous plasma and platelet-derived proteins to the desired location to assist in the repair of the injured tissue (Marx 2001) [7]. The rationale for use of scaffolds in PRP is to take advantage to promote cartilage regeneration by taking a huge amount of growth factors contained in platelets; however, the use of the PRP-augmented scaffolds is still in a preliminary state, which has a low scientific level of power (Kon *et al.* 2013) [8]. Growth factors promote matrix synthesis, migration and facilitate protein transcription and cell growth in chondrocytes application. The release of platelet-derived factors at the site of diseased cartilage directly, particularly in the case of knee OA. It may stimulate regenerative signaling cascade and enhance tissue healing with further anti-inflammatory response mediation (Mascarenhas *et al.* 2014) [9]. PRP showed to affect local and infiltrating cells, i.e. endothelial cells, those cells involved in innate immunity (such as macrophages) synovial cells, cartilage and bone cellular components (Mifune *et al.* 2013; Dhillon *et al.* 2017) [10, 11], in OA joints. PRP can affect inflammation, anabolic, angiogenic processes, and catabolic

balance in cartilage formation. Additionally, alter the existing microenvironment during the progression of disease (Andia and Maffulli 2013) [12].

Pilot and prospective studies investigating the clinical efficacy of intra-articular injections of PRP in patients with knee OA have demonstrated clinical improvement in self-reported pain and functional capacity with no major adverse effects [13].

A recent related systematic review included six randomized controlled trials comparing the effectiveness of PRP to other intra-articular injections, exercise, or analgesia for a minimum of 6 months. PRP injections were found to produce statistically significant improvements in overall WOMAC scores for patients with knee OA up to 12 months after intervention [14].

Research into the efficacy of PRP has focused on comparing the effects of intra-articular PRP injections to other injection therapies. In many studies, PRP injections have improved functional outcomes when compared to HA and placebo controls and appear more efficacious in reducing symptoms and improving QoL (Raissadat *et al.* 2015; Kanchanatawan *et al.* 2016) [15, 16].

Kon *et al.* (2011) [17] examined three homogenous groups of patients treated with three injections of PRP, low molecular weight HA, and high molecular weight HA and concluded that autologous PRP injections have longer efficacy than HA injections and enhance articular function. The results showed improved outcomes for the PRP group at 6 months with younger and more active patients achieving better results with a low degree of cartilage degeneration (Meheux *et al.* 2016) [18]. Conversely, PRP causes a significantly greater acute inflammatory response and an increase in synoviocyte cell death (Braun *et al.* 2014) and induces more transient reactions than HA (Riboh *et al.* 2016) [19].

The risk of adverse events in PRP-treated participants was not significantly increased in comparison with other knee OA treatment options [14]. These findings are consistent with much recently published research involving PRP as an intervention in knee OA [20]. The goal-oriented outcome approach used in this study has several advantages. It frames the discussion in terms of individually desired rather than universally applied health states; this approach simplifies decision making for patients with multiple conditions by focusing on outcomes

that span conditions and aligning treatments toward common goals; goal-oriented care prompts patients to articulate which health states are important to them and their relative priority; and finally, if they know what health states are most desired, patients and clinicians can agree on steps that can be taken to achieve these goals and monitor progress in reaching them^[21]. In essence, it allows the participant to co-design the outcomes based on their own individual preferences.

Despite the apparent positivity in the use of PRP for the treatment of knee OA, methodological concerns and considerable heterogeneity between studies are evident (Rodriguez-Merchan 2013b)^[22]. Large RCTs are needed to further assess the efficacy and duration of PRP treatment for patients with knee OA (Rodriguez-Merchan 2013a; Lai *et al.* 2015)^[23]. When planning or analyzing treatments, frequency and number of injections, as well as the activation methods (in the case of anti-coagulated PRP), storage aspects, time from plasma isolation, and accompanying therapy should be considered as at present they vary widely between groups. The greatest limiting factor for PRP use is the lack of standardization with further research required to investigate how leukocyte inclusion, activation, and platelet concentration affect therapeutic efficacy.

Conclusion

PRP therapy is a simple, inexpensive, and minimally invasive intervention that is feasible to deliver in primary care to treat degenerative lesions of the articular cartilage of the knee. This therapy appears to have minimal associated adverse events and may have beneficial effects in terms of pain, health utility, patient satisfaction, and goal-orientated outcomes.

Conflict of interest

The Authors declare no conflict of interest whatsoever arising out of the publication of this manuscript.

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