e-ISSN: 0975-5160, p-ISSN: 2820-2651

Available online on www.ijtpr.com

International Journal of Toxicological and Pharmacological Research 2022; 12 (6); 196-202

Original Research Article

Effectiveness of Intra-Articular Methylprednisolone along with Platelet Rich Plasma Vs. Platelet Rich Plasma in Early Osteoarthritis

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Received: 15-04-2022 / Revised: 18-05-2022 / Accepted: 01-06-2022

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Conflict of interest: Nil

Abstract

Background: Osteoarthritis (OA) is a slowly progressive chronic disease characterized by pain, loss of function, and deformity of the affected joints. In the past, OA was considered a normal sign of aging and it was described as a degenerative disorder that mainly causes cartilage loss. The use of platelet rich plasma in treatment of degenerative osteoarthritis of knee is more safe, can be easily produced and administered with relative ease. Present study was done to study the efficacy of intra-articular methylprednisolone therapy along with platelet rich plasma when compared with only platelet rich plasma in treatment of early osteoarthritis.

Material and Methods: Present cross-sectional hospital-based study was designed to include 200 patients with initial stages of osteoarthritis of knee who were diagnosed as per the Kellgren-Lawrence classification. Selected patients were then categorized into; group I: It comprised of 100 subjects who were treated with intra-articular injections of platelet rich plasma in combination with methylprednisolone and group II: This group was comprised of 100 patients who were treated with intra-articular injection of platelet rich plasma alone. Clinical data pertaining to medical history, VAS and KOOS scores were collected. Statistical analysis was performed using the student's t test.

Results: The differences in the VAS scores at one and three month intervals when compared with baseline scores demonstrated no statistically significant differences. It was noted that differences in KOOS-QOL scores and ADL between baseline; 3 and 6 months was found to increase significantly in PRP group when compared to the methylprednisolone group.

Conclusion: Treatment of osteoarthritis of knee joint in initial stages has not been studied in detail though there are studies related to treatment in advanced stages. Our study has analyzed combination therapy using PRP and methylprednisolone than compared to PRP alone.

Keywords: Knee joint, Methylprednisolone, Osteoarthritis, Platelet Rich Plasma

Introduction

Osteoarthritis (OA) is a slowly progressive chronic disease characterized by pain, loss of function, and deformity of the affected joints. In the past, OA was considered a normal sign of aging and it was described as a degenerative disorder that mainly causes cartilage loss [1]. However, more recent studies have shown that OA occurs and evolves due to the interaction of multiple risk factors affecting the whole joint including the cartilage, subchondral bone, synovium, ligaments, and menisci [2]. Currently, no disease-modifying treatment has been approved, which makes joint replacement the only viable solution for these patients. Non-pharmacological treatments include patient education and self-management, exercises, weight reduction, walking supports (crutches), bracing, shoe and insole modification, local cooling/ heating, acupuncture, and electromagnetic therapy [3,4]. Pharmacological treatments include topical and oral NSAID [5], intra-articular (IA) injections of corticosteroids, visco-supplements, and blood-derived products, including platelet-rich-plasma (PRP) [6].

Presence of requisite growth factors cause an increase in synthesis of chondrocytic matrix and causes stimulation of chondrogenous cellular proliferation [7].It causes reduction in nuclear factor kappa B activation that plays a significant function in pathogenesis of osteoarthritis by causing inhibitory action over inflammatory processes which are induced by interleukin-1β [8]. alpha granules found with platelets comprise of significant amounts of Growth Factors [9]. Hence, application of autologous platelet rich plasma or PRP has emerged as valid treatment modality for osteoarthritis. It also contains plasma proteins which function similar to mesenchymal cellular adhesion molecules such as-fibrin, fibronectin, vitronectin among others. These molecules are seen during process of recovery after episode of trauma within human body [10]. Platelet rich plasma or PRP has been found to contain mean of three-to-five times higher platelet numbers when compared with that in whole blood. At present, there is no widely accepted or quantified value of platelet concentrations within Platelet Rich Plasma. The numbers of platelets existing within whole blood ranges between 1,50,000 per µl to 3,50,000 per µl. This maintains platelet concentration in Platelet Rich Plasma at a concentration of 200 % when compared to whole blood. The concentration of platelets within platelet rich plasma varies depending upon the method of preparation which ranges between 2.5 to 8 times higher when compared to that of whole blood. Due to this, the therapeutic potential of Platelet Rich Plasma varies due to difference in techniques of preparation [11,12].

The use of platelet rich plasma in treatment of degenerative osteoarthritis of knee is more safe, can be easily produced and administered with relative ease [13]. Present study was done to study the efficacy of intra-articular methylprednisolone therapy along with platelet rich plasma when compared with only platelet rich plasma in treatment of early osteoarthritis.

Material and Methods

Present cross-sectional hospital-based study was designed to include 200 patients with initial stages of osteoarthritis of knee who were diagnosed as per the Kellgren-Lawrence classification. Patients were aged between 48 to 85 years. Selected patients were then categorized into; group I: It comprised of 100

subjects who were treated with intra-articular injections of platelet rich plasma in combination with methylprednisolone and group II: This group was comprised of 100 patients who were treated with intra-articular injection of platelet rich plasma alone. Complete history, clinical examination, complete blood count thrombocytopenia-related details and radiographic features were accessed from medical records of the patients who visited the tertiary care Institute of hospital of Gujarat OPD for the duration of 1 year. Pain levels were evaluated after treatment by using the visual analog scale (VAS) while clinical outcome was performed by using "knee injury and osteoarthritis outcome score or KOOS" at 0, 1, 3, and 6 months following treatment. All patients were asked to stop use of non-steroidal antiinflammatory drugs one week prior to initiating either of the therapy protocols.

The patient's exclusion criteria were post-traumatic knee osteoarthritis, pregnancy, breastfeeding, oncological diseases, endocrine diseases (gout, diabetes), autoimmune diseases acute/chronic infectious disease, blood clotting disorders, previous interventions on the knee joint (i.e., punctures, blockades, arthroscopy), and previous consistent hormonal therapy or non-steroidal antiinflammatory drugs (NSAIDs) treatment.

20 ml of venous blood was collected from patient and transferred to a test-tube which were coated with an anticoagulant (sodium citrate) for preparation of 4 to 6 ml of platelet rich plasma containing concentration of platelets which was 3 to 6 times greater average normal parameters. The test tubes were then centrifuged at a speed of 3500 rpm for duration of 10 minutes which separated plasma in top layer which was separated from packed red blood cells which collected at bottom layer. Collected red blood cell layer was discarded. Then, the test tubes were centrifuged for second time at 4000 rpm for duration of 7 minutes. Thus, obtaining platelet rich plasma. Following this, approximately, 4 to 6 ml of prepared PR product was dispensed within a sterile syringe for the purpose of injection

For both the study groups, intra-articular injections were given to patients in a supine position. After disinfection of overlying skin by using betadine, the medicaments were injected. 2 ml of local anesthesthetic solution was injected first, followed by injection of platelet rich plasma or combination of PRP with methylprednisolone by using either antero-medial or antero-lateral approach. Following an observation rest period of approximately 20 minutes, patients were then instructed to perform flexing and extension of injected knees, so as to enable even spread of PRP across joint space. After this, the concerned patient was discharged.

After receiving either of the injections, all patients were given following instructions; avoidance of running or any other high impact activities for a total duration of ten days; Ice application over the injected area for controlling pain thrice daily for approximately 10 minutes; use paracetamol as analgesic agent and avoid any NSAIDs with salicylate group throughout the follow-up period.

Statistical analysis

The recorded data was compiled and entered in a spreadsheet computer program (Microsoft Excel 2007) and then exported to data editor page of SPSS version 15 (SPSS Inc., Chicago, Illinois, USA). For all tests, confidence level and level of significance were set at 95% and 5% respectively.

Results

Majority of patients who were selected for study belonged to female gender. All patients belonged to upper middle socioeconomic status.

VAS scores were found to decrease for both the study groups with no statistically

significant difference. The differences in the VAS scores at one and three month intervals when compared with baseline scores demonstrated no statistically significant differences ($p \leq 0.05$) between the study groups. Although, this difference was found to be of statistical significance between the groups at six months ($p \leq 0.05$) (Table 1).

The statistical difference between both the study groups following injection at 3 months was found to be significant with respect to pain and active daily life (ADL) ($p \leq 0.05$) while at the 6th month interval, it was found to be significant with respect to pain, ADL and quality of life. It was noted that differences in KOOS-QOL scores and ADL between baseline; 3 and 6 months was found to increase significantly in PRP group when compared to the methylprednisolone group. For symptoms assessment at 1 month, mean±SD were: 11.9±10.1 for group I and 12.6±1.3 for group II; three months 12.94±6.5 for group I and 0.10±0.1 for group II, respectively. The differences in KOOS–QOL scores and ADL scores at baseline; 3 and 6 months were found to increase significantly in PRP group than the methylprednisolone group (Table 2).

Table 1: Differences in visual analogue scale scores at baseline, 1, 3, and 6 month duration

Visual analogue scale	Platelet rich plasma with methylprednisolone (group I)	Platelet rich plasma (group II)	P value
Baseline (Mean)	56.5±12.8	56.1±11.2	0.5
1 month (Mean)	37.2±15.4	37.05±17.3	0.07
3 month (Mean)	36.10±15.2	36.80±18.4	0.09
6 month (Mean)	30.9±14.4	40.9±13.20	0.02*

* indicates statistically significance at $p \leq 0.05$

Table 2: Differences in knee injury and osteoarthritis outcome scores in both the study groups following injections at baseline, 1, 3 and 6 months

KOOS	Baseline	P value	1 month	P value	3 month	P value	6 month	P value
Pain (mean±SD)								
PRP+methylprednisolone	44.2±11.2	0.62	46.1±14.5	0.2	43.1±12.5	0.002*	45.1±19.9	0.003*
Methylprednisolone	44.8±13.5		53.2±14.1		38.9±11.9		39.98±10.6	
Symptoms (mean±SD)								
PRP+methylprednisolone	32.9±11.4	0.24	11.9 ± 10.1	0.05*	12.94 ± 1.06	0.05*	13.64 ± 6	0.001*
Methylprednisolone	30.94±16.2		12.6 ± 1.3		0.10 ± 0.1		0.19 ± 0.2	
Quality of life (mean±SD)								
PRP+methylprednisolone	21.7±10.1	0.32	23.5±11.6	0.07	30.01±22.1	0.3	30.90±20.01	0.32
Methylprednisolone	23.02±12.2		24.41±13.6		26.6±11.9		24.9±11.2	

Discussion

PRP in knee OA has experienced a real boom in recent years, which can be seen both in clinical practice and in the scientifc literature. The experts have considered that PRP was an effective treatment for symptomatic early or moderate knee OA and might be used in severe forms of knee OA, particularly in cases of contraindications to surgery. They have acknowledged that the level of scientific evidence for end-stage OA was much lower and that PRP have probably a lower symptomatic effect than in earlier stages. Experts agreed that PRP should be only proposed after failure of well-conducted oral and topic symptomatic treatments and appropriate physiotherapy. Nevertheless, PRP is a treatment that remains, to date, costly for the patient and which is in "competition" with other injectable treatments whose symptomatic efficacy is at least partially recognized by many experts. Consequently, the use of PRP rather than injectable CS and HA should be discussed on a case-by-case basis, especially considering that CS injections should be preferred during an acute infammatory phase.

The main aim in managing osteoarthritis of knee joint is reduction of pain along with stiffness, to protect or regain entire range of movement and muscular strength and decreased dependence on daily activities of life. Therefore, in recent times, medications that support or improve cartilage health have been researched upon. Use of platelet rich plasma which contains growth factors is effective as well as easily available option for treatment option while treating and managing degenerative osteoarthritis. The growth factors which are released undergo binding with specific and high affinity trans-membranous receptors which leads to triggering of various intracellular signal pathways. Important growth factors that are involved are as follows- insulin-like growth factor (IGF)-1, transforming growth factor (TGF)-β, platelet-derived growth factor (PDGF), vascular endothelial growth factor (VEGF), basic fibroblast growth factor (bFGF), hepatocyte growth factor(HGF) and epidermal growth factor(EGF). Tavassoli *et al* in 2019 compared clinical outcomes of treatment with platelet rich plasma and hyaluronic acid injections in patients who were diagnosed with bilateral osteoarthritis affecting the knee joint in a randomized control trial by using the Western Ontario and McMaster Universities arthritis index (WOMAC).

Greatest efficaciousness of platelet rich plasma was noted in the 4^{th} week with approximately 50% reduction in the symptoms compared with 25% decrease in patients treated with hyaluronic acid [14]. Kurapati *et al* in their combination therapy following use of both platelet rich plasma and hyaluronic acid on patients suffering from initial stage of knee osteoarthritis reported statistically significant improvement in VAS scores. Significant improvement from values at 3.00±0.49 recorded at baseline level to 1.57±0.41 in grade I and Ismaiel in 2018 compared effects of intra-articular injections of platelet-rich plasma and corticosteroid in causing reduction of pain and improvement in function. Statistically significant differences between both the study groups were observed. Also, greater degree of improvement was seen in the study group treated with platelet rich plasma [15]. Calis *et al* evaluated the effectiveness of autologous platelet- rich plasma therapy on pain, functional status and cartilaginous regeneration in advanced osteoarthritis affecting knee. While comparing the mean visual analogue scale values before any treatment, it was noted that these values had undergone significant decrease ($p< 0.001$) after third and sixth months of treatment. Significant increase ($p< 0.05$) in cartilage thicknesses was observed following treatment at 3rd and 6th months

when compared with values before initiating treatment [16].

Intra-articular PRP infiltrations have been widely used for the treatment of knee OA with many beneficial results [17-19]. In this study, intra-articular PRP injections were well tolerated. The most common side effect being mild synovitis tended to resolve within the first week after treatment. Treatment with PRP injections can be considered safe since no severe adverse events or complications have been reported. We consider that the safety of PRP is mainly due to two factors: the administration of the PRP done through minimally invasive procedures and non-existent risk of transmission of infectious diseases. In addition, in this study, we used pure PRP to prevent possible inflammatory reactions in spite of the reported safety of using leucocyte-rich PRP [20-22].

Present study showed that treatment of initial stages of osteoarthritis can be treated more effectively by intraarticular injections of platelet rich plasma combined with methylprednisolone when compared with Platelet rich plasma alone. It is demonstrated by progressive increase in statistically significance on follow-up at 1 month, 3 momthsand 6months intervals using the KOOS (knee injury and osteoarthritis outcome score) and visual analogue scale (VAS) score values.

Conclusion

Treatment of osteoarthritis of knee joint in initial stages has not been studied in detail though there are studies related to treatment in advanced stages. Our study has analyzed combination therapy using PRP and methylprednisolone than compared to PRP alone. Using this combination can effectively reduce symptoms; improve an individual's daily life activities and quality of life.

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