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ORIGINAL ARTICLE

Arthroscopic Debridement Versus Platelet Rich Plasma Injection in Treatment of Moderate knee Osteoarthritis

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ABSTRACT

Background: Knee osteoarthritis (OA) is considered the most common disease affecting knee joint. Various strategies are utilized to decrease the symptoms of knee OA, like analgesics, physiotherapy, intra-articular glucocorticoids and hyaluronic acid [HA] injection as well as arthroscopic debridement (AD). New studies have concentrated on new lines of treatment that stimulate damage improving and healing process of the cartilage, including mainly platelet-rich plasma (PRP) injection as growth factors complex.

Aim: Because of the high incidence of OA and its complications, this article aimed to study the effect of AD and PRP injection on patients with knee OA.

Methods: This controlled randomized clinical trial involved 20 patients with moderate knee OA. In the PRP group (n = 10), three intra-articular injections at 10-days interval were applied and compared to AD group (n = 10). All patients were prospectively evaluated before and after 6 months of the treatment by KOOS score.

Results: After at least 6-months follow-up, KOOS score was significantly improved in PRP group compared to the AD group ($P < 0.05$). All parameters were improved in the PRP group.

Conclusion: The study suggested that injection of PRP is more effective toward reducing pain and symptoms, with improvement of the daily living function, quality of life and function in sport and recreation. PRP is a method of choice in patients with mild to moderate knee OA, who not responding to classical treatment options.

Key words: Knee osteoarthritis (OA), intra-articular injection, platelet-rich plasma (PRP), Arthroscopic debridement (AD)

INTRODUCTION

Osteoarthritis (OA) is a joint disease resulting from cartilage and underlying bone breakdown in the joint [1]. Joint pain and stiffness are considered the most common complaints. Initially, symptoms may appear after exercise only, but by time, they might be persistent. Usually symptoms exaggerate over years with other symptoms comprising swelling of joint and limited motion range. Knee joint is among the most affected joints. Single body side is usually more affected than the other one. OA usually affects daily activities. Unlike other types of arthritis, such as Rheumatoid arthritis, OA only affects the joints [1]. Mechanical stress and low-grade inflammatory processes are supposed to induce joint osteoarthritis [2]. It progresses when cartilage is lost, and the bone becomes affected (e.g., multiple osteophytes, sclerosis and bony deformity). Muscle atrophy may arise as pain possibly will make exercise much difficult [3,4]. In contrast to rheumatoid arthritis, which is primarily an inflammatory condition, the joints in OA do not typically become hot or red [2]. OA is the most common form of arthritis in the knee and hip; and in 2010, the global age-standardized prevalence of knee OA represented 3.8% [5]. Among those, over 60 years old about 10% of males and 18% of females are affected. It is the cause of about 2% annual disability [6]. It becomes equal in both sexes as people become older [7]. To confirm the diagnosis; we need reliable medical history and clinical examination. X-rays are important to confirm the diagnosis. The main changes noticed on X-ray are; narrowing of the joint spaces, subchondral cyst, osteophytes, and subchondral sclerosis [8]. Plain x-rays are not necessarily in line with the physical examination findings or the pain degree. Other types of imaging show no significant role in OA diagnosis [9].

Lifestyle changes like weight reduction and exercise is the main line of management, while analgesics (NSAIDs) are the cornerstone of treatment. Glucocorticoids injection (such as hydrocortisone) directly in the joint leads to short-term relief of the pain that may last between a few weeks to a few months. Although these therapies only improve the inflammatory state and the pain, they are used widely because the patient quality of life is much enhanced with these methods of treatment [10]. However, these methods of treatment are associated with many problems including gastric and renal disturbances related to long-term using NSAIDs. Many studies found that hyaluronic acid injection have not been found to lead to significant improvement [11]. Although injection of steroids relives the pain on short term, it causes long-term complications such as increasing the osteoarthritis [12]Infusions of platelet-rich plasma and arthroscopic surgery are additionally two lines of treatment of knee osteoarthritis. The PRP injection has begun to get attention as a regenerative method of treatment of cartilage. The researches now are focusing on the PRP effects on cartilage lesions [13]. OA is exaggerated by an imbalance of ant-inflammatory and pro-inflammatory cytokines; this imbalance stimulates proteolytic enzymes and cause cartilage destruction [14]. The new lines of treatments of OA are focusing on ending these cytokine imbalances [15].Platelet alpha bodies have several growth factors stored in it will be considered a promising method when PRP injections into the joint results in proficient delivery, high level concentrations, and promotes remodeling [16]. The PRP inhibition of articular cartilage catabolism hypothesis has emerged recently [17]. PRP injection after ACL reconstruction could prevent secondary OA and this progress was confirmed experimentally [18].

The usage of extracted cell elements and other bio-modulators resulting from inflammatory tissue response is a new method for OA treatment. Therefore, the platelet rich plasma PRP has been used as a new line of treatment that improves signs and symptoms by introducing high number of growth factors, which induce cartilage remodeling and healing. It shows great results in vivo and vitro studies, while its efficiency in OA patients is not yet confirmed [19]. Baltzer [20] stated that PRP injection is a better treatment method than injection of hyaluronic acid in the treatment of OA. When there is no response of conservative treatment, the operative treatments can be introduced for OA which may include osteo-chondral transplantation, chondrocyte implantation and stimulation of bone marrow (micro-fracture) [21]. Arthroscopic debridement (AD) used for removing damaged bone and cartilage surgically. The procedure is a washout or lavage as the doctor use instruments to deliver high-pressured fluid to wash and remove all joint debris [22].

METHODS

This prospective study took places in Armed Forces Hospital in Alexandria (Mostafa Kamel Hospital) on twenty patients with moderate knee OA. Both genders; female and male, aged from 40 to 65 years complaining of moderate knee osteoarthritis grade 2 and 3 (with osteophytes formation, joint space narrowing and sclerosis) were included. Over-weighted patients, ages older than 65 years, intra-articular injected steroid, hyaluronic acid or PRP recently (last 6 months), recent history of severe trauma in the targeted knee, active infection, inflammation, or tumor existence around the targeted knee were excluded. Also, any patient with history of severe cardiovascular disorders, diabetes mellitus, coagulopathy, immune-compromised, collagen vascular or autoimmune disorder or patients receiving anticoagulant or antiplatelet medications or systemic corticosteroids ten days before injection, or using NSAIDs five days before injection, genu-varum or genu-valgus (more than 5 degrees), pregnant or breastfeeding, all were excluded. Sampling was simple random; the sample included 20 cases using OPEN-EPI (Open-Source Epidemiologic Statistics for Public Health, Version. 2.3) and divided into two groups (10 cases in each group); one group used PRP injection and the other one used arthroscopic debridement. The Power of study was 80% at CI 95%. After receiving the approval of the Hospital's Ethics Committee, the patients presented with a written form that declares the aims and methods of AD and PRP therapy, in addition to the benefits and the possible unwanted effects of the study. Only the participants who signed a written consent form were included in the study. The study was approved by the research ethical committee of Faculty of Medicine, Zagazig University. The study was done according to The Code of Ethics of the World Medical Association (Declaration of Helsinki) for studies involving humans. The study participants attended a screening visit that included recording of medical history, physical examination, and a survey of medication use. Patient's age, target leg, Sex, and KOOS-score were recorded pre-operative. After taking patient consent, 40 ml blood was collected in 2x20 ml sterile falcon tubes each containing 2 ml anticoagulant citrate dextrose. Thereafter, the tubes were centrifuged at 200xg for 10 min, and plasma (containing platelets) was separated in 4 plain sterile tubes using sterile pipettes with around 5 ml collected in each tube. After that, the 4 tubes containing the plasma underwent a second

centrifugation at 1200xg for 10 min. The supernatant containing platelet-poor plasma was discarded using pipette, keeping only 1.0 ml plasma in the bottom of each tube, and platelet pellet was mixed with this 1.0 ml plasma left. Finally, 4.0 ml of PRP was collected using sterile syringe from the 4 tubes and directly injected into the target knee, Then Ca gluconate is injected to enhance the platelets rupture. the cutoff level of platelets needed to produce significant improvement was 1000×10^9 platelets/L in 4 ml. Patients were injected 3 times, 10 days apart.

Follow up:Each patient has been followed-up for a minimum six months. After either the injection or arthroscopic debridement, there was a visit every 14 days/for two months, followed by monthly visit for the following four months. In each visit, depending on KOOS score, the patient underwent a comprehensive clinical examination. Though, because there were no expected major changes in X-ray images on short term follow up, X-ray pre-images, at 3rd month and at 6th month of follow up to decrease the radiation exposure to as possible.

Statistical Analysis of Data :The collected data were encoded, analyzed using the Statistical Package for Social Sciences (SPSS) version 22 for Windows (SPSS Inc, Chicago, IL, USA). Qualitative data was presented as number (frequency) and Percent. In-between groups comparison was done using Chi-Square test ($\chi 2$). Kolmogorov-Smirnov test was used to test the normality of the quantitative data. Normally distributed data was presented as mean ± SD. To compare between two groups, Student t-test was used (t). Nonparametric data was presented as median (min – max). Finally, Mann-Whitney test (z) was used for comparison between groups. For each score (before and after intervention), comparison between items in each group was done using Paired-Samples t-test (t). With normally distributed data and Wilcoxon signed rank test with not-normally distributed data (expressed as z). $P < 0.05$ was statistically significant.

RESULTS

From 20 potential patients who were candidate for PRP injection and AD, 10 patients underwent AD while the other received PRP injection. Demographic data analysis and patient criteria (Table 1) showed that mean age of AD group was about 53 years, distributed as 5 males and 5 females while that of PRP group was 52 years, 3 males and 7 females, with 8 right legged and 2 left legged in each group, all with moderate knee osteoarthritis (Table 1).At the 6-month follow-up, KOOS including symptoms, pain, daily activities, sports and recreational activities, and quality of life significantly improved in PRP group. However, most AD cases showed mild or no improvement at all, and only 10% of cases showed deterioration. Results of total KOOS score in both groups represented as mean ± SD or median (depending on data availability) in figure 1 and table 1. Analysis of relation between pre- & post- intervention regarding each parameter of KOOS score in-between each group are represented in table 2.

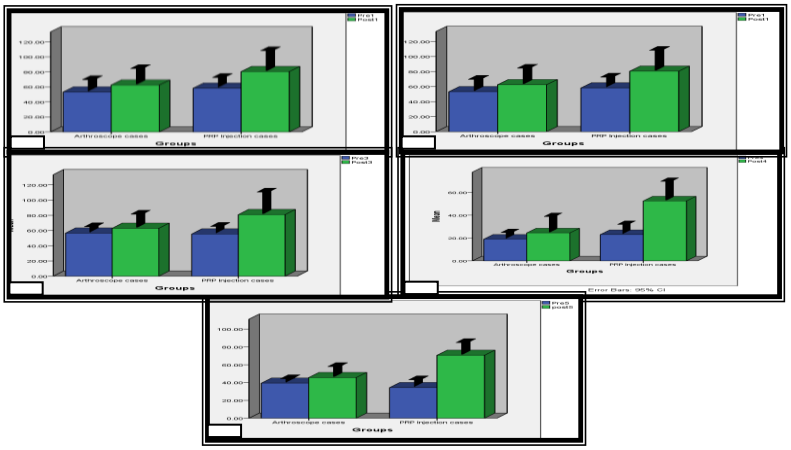

Fig. (1): Relation regarding symptoms (a), pain (b), daily activity (c), sports & recreational activities (d) and quality of life (e) between AD and PRP groups in addition to pre & post intervention in each group.

Table 1: Analysis of demographic data and all Koos score parameters between AD and PRP treated groups, represented as Mean ± SD or Median (depending on data availability).

Parameters		Group 1 (AD) (Mean ± S.D). or (Median)	Group 2 (PRP) (Mean ± S.D). or (Median)	Test of significance	P value
Demographic data and patient criteria					
Age		53.90± 6.574	52.90±5.971	t = 0.356	0.726
Sex	♂	5 (25%)	3 (15%)	$\chi 2$= 0.833	0.361
	♀	5 (25%)	7 (35%)		
Treated leg	Rt.	8 (40%)	8 (40%)	$\chi 2$= 0	1
	Lt.	2 (10%)	2 (10%)		
Symptoms					
Pre-intervention		53.19 ± 7.79	58.21 ± 6.74	t = -1.540	0.141
Post-Intervention		62.49 ±10.54	80.42 ±13.41	t = -3.322	0.004*
Difference (Post - Pre) (Median)		7.25 (-14.28 - 39.28)	23.22 (-14.29 -39.29)	z = -2.010	0.044*
Pain					
Pre-intervention		54.72±6.15	54.71±8.78	t = 0.001	0.999
Post-Intervention		61.39± 9.83	81.11±14.81	t = -3.508	0.003*
Difference (Post - Pre) (Median)		4.16 (-11.11 - 6.12)	29.16 (-13.89 - 50)	z = -2.347	0.019*
Daily activities					
Pre-intervention		56.61± 3.68	55.43± 4.49	t = .640	0.530
Post-Intervention		62.93± 8.84	80.88±14.39	t = -3.359	0.003*
Difference (Post - Pre) (Median)		4.41 (-8.83 - 3.53)	30.88 (-11.76 -41.18)	Z = -2.574	0.01*
Sports & recreational activities					
Pre-intervention		15 (10 – 35)	22.50 (10 - 45)	z = - 0.663	0.504
Post-Intervention		17.50 (10 - 60)	60 (10 - 75)	z = -2.068	0.039*
Difference (Post - Pre) (Median)		0 (-15 – 35)	35 (-15 – 50)	z = -2.174	0.03*
Quality of life					
Pre-intervention		39.37± 5.92	34.37±11.12	t = 1.255	0.226
Post-Intervention		43.75 (25 - 75)	75 (25 - 87.50)	z = -2.801	0.005*
Difference (Post - Pre) (Median)		0 (-12.50 - 37.50)	40.62 (-18.75 - 68.75)	z= -2.607	0.009*
= KOOS (Total score)					
Pre-intervention		49.93 ± 6.51	49.81 ± 4.87	t = 0.046	0.964
Post-Intervention		56.26±10.99	73.79 ±16.17	t = 2.835	0.011*
Difference (Post - Pre) (Median)		3.34 (-11.40 - 41.60)	27.65 (-13.10 - 45.50)	z= 2.212	0.034*

Table 2: Analysis of relation between pre- & post- intervention regarding each parameter of Koos score in-between each group, represented as Mean ± SD or Median (depending on data availability).

	Pre-intervention (Mean ± S.D)	Post-intervention (Mean ± S.D)	Test of significance	P value
Symptoms				
Group 1 (AD)	53.19 ± 7.79	62.49 ±10.54	t =-2.253	0.051
Group 2 (PRP)	58.21 ± 6.74	80.42 ±13.41	t = -4.173	0.004
Pain				

	Pre-intervention (Mean ± S.D)	Post-intervention (Mean ± S.D)	Test of significance	P value
Group 1 (AD)	54.72±6.15	61.39± 9.83	t = -1.563	0.153
Group 2 (PRP)	54.71±8.78	81.11±14.81	t = -4.483	0.002*
Daily activities				
Group 1 (AD)	56.61± 3.68	62.93± 8.84	t = -2.109	0.064
Group 2 (PRP)	55.43± 4.49	80.88±14.39	t = -4.754	0.001*
Sports & recreational activities				
Group 1 (AD)	15 (10 – 35)	22.50 (10 - 45)	z = -1.051	0.293
Group 2 (PRP)	17.50 (10 - 60)	60 (10 - 75)	z = -2.507	0.012*
Quality of life				
Group 1 (AD)	40.62 (25 - 43.75)	43.75 (25 - 75)	z = -1.289	0.197
Group 2 (PRP)	34.37 (18.75 - 50)	75 (25 - 87.50)	z = -2.599	0.009*
= KOOS (Total score)				
Group 1 (AD)	49.93 ± 6.51	56.26±10.99	t =-1.194	0.318
Group 2 (PRP)	49.81 ± 4.87	73.79 ±16.17	t = -4.207	0.002*

DISCUSSION

This study included 20 patients. 10 patients underwent arthroscopic treatment and 10 patients received PRP injection. KOOS scoring systems was used to evaluate the patients in both groups. We found that, only 20 % of cases that treated with knee arthroscopy showed significant improvement regarding all aspects of KOOS score (pain, symptoms, daily activity, sports, and quality of life). Most cases (70%) showed mild or no improvement at all, and only 10% of cases showed deterioration. There are many studies supporting these results. Moseley et al in a randomized controlled trial (RCT) found knee arthroscopy has no benefit for moderate to severe knee OA [23].

As this finding was so different to current practice, the authors' conclusion was not accepted widely. Arthroscopic debridement surgery still be used for moderate to severe knee osteoarthritis [24]. Certainly, The American Academy of Orthopedic Surgeons (AAOS) guidelines stated in 2008 that "partial meniscectomy by arthroscopy or removal of loose body is a line of treatment in patients with symptomatic knee OA who also have signs and symptoms of a meniscus tear and/or a loose body" [25]. However, these guidelines do not enclose any evidence from the Kirkley et al study [26].*Kirkley et al* introduced a non-blinded RCT of 188 patients complaining from moderate to severe knee OA; they excluded those with mal-alignment, large meniscal tears, severe bi-compartmental arthritis, or previous arthroscopic surgery. The control group has received best physical and medical therapy, which was a one hour of physical therapy per week, exercises twice daily, and stepwise use of acetaminophen, (NSAIDs), and intra-articular injections with hyaluronic acid. The other group had arthroscopic surgery (menisci and articular cartilage debridement, loose bodies removal and osteophytes excision), and received physical and medical therapy. The validated Western Ontario and McMaster Universities Arthritis Index (WOMAC) score was the principal outcome measure. (The range is 0 to 2400, which more severe symptoms indicated by higher scores). Two years later, slight difference founded by the researchers in the WOMAC scores of the control group (897±583) and the surgery group (874±624); the absolute difference was –23±605 (95% confidence interval, –208 to 161; P=.22). They found no difference in the secondary outcomes of pain, quality of life and function. surgery didn't provide any advantage to the subgroup of patients with mechanical problems [26].These findings were in line with those of Moseley et al single-blinded RCT, as the researchers assigned 180 patients to either arthroscopic surgery or sham surgery and concluded that the surgery has no benefit. The researchers used a not valid outcome measure and the patients who has malalignment and advanced disease did not exclude, and that affected the surgery outcome that is why this study was criticized. The study by Kirkley et al in 2008 excluded such methodological faults and, in retrospect, it appears that these apparent faults did not account for the negative outcomes of the 2002 study.The new RCT evidence confirms the results of the 2002 trial. It obviously shows that there are

no benefits from arthroscopic surgery for knee OA, even in patients having mechanical symptoms. Kirkley's study excluded the earlier study criticism by using a validated outcome measure, avoiding malalignment patients, and the patients with mechanical symptoms were performed in subgroups. Now we have two studies showed that arthroscopic knee surgery has no benefit in patients with OA, whether they have or do not have mechanical problems. That is like our study, as no significant difference between pre and post arthroscopic debridement by KOOS score.

In the other approach, according to KOOS score, 70% of cases that treated with PRP injection showed noticeable improvement regarding the symptoms, sports, pain, daily activities, and quality of life. 20% of cases showed mild or no improvement while only 10% showed deterioration. In line with our results, *Sanchez* [27] suggested that in football players who has avulsion fractures of the articular cartilage, treatment with PRP might improve symptoms and enhance healing. In degenerative OA, PRP is more efficient than hyaluronic acid injections in both improvement of function and pain management. Moreover, 100 patients having knee OA evaluated by Kon treated with PRP injection, and reported pain relief and clinical improvement of joint function [28]. In this study, we also found that the pain improved significantly after PRP injection while there was no significant improvement after arthroscopic debridement. *Soo-Jin Jang, et al* reported that some patients complained from mild pain and a temporary joint effusion post injection last for less than 2 days. They suggested that the mild inflammatory response after the PRP injection is the cause of mild knee pain and heating, and the PRP injection volume should be carefully considered as it causes synovial joint space expansion [29]. The study showed major improvement post injections of PRP for 12 months follow up after treatment [29]. It is meaningful that this study reported the accurate time of knee pain recurring. The follow-up time in the study was narrow but was long enough to decide the tendency of recurrent pain with diminished potential of the effect of PRP and to assess the duration of PRP. They observed 20 people (30.8%) for 24 months. The PRP injections clinical effect remained for 2 years, but decreasing potential continuously was observed. This means that the effect of PRP injection treatment has minimal advantages when used as a management for advanced degenerative knee OA or even worse especially in older age. And their study reported that the intra-articular injections of PRP showed longer and more efficacy than injections of hyaluronic acid in younger patients [30]. OA is directly associated with degeneration of PFJ and might be included in this disease progression. Treatment of OA by using injection of PRP may be worse if the patient has degeneration of PFJ. So, when planning for PRP intra-articular injection, PFJ degeneration should be considered as a significant factor.

Duymus, et al [31] stated that PRP is acceptable method of treatment for mild - moderate and moderate knee OA and is an hopeful option of treatment, which became progressively widespread. Injection of PRP alone achieved at least 12 months of pain-free daily activities.

Abate et al study results reported that the association of PRP and HA injection is highly effective and safe as a method of treatment for patients complaining from mild-to-moderate knee OA. Indeed, at 6 months, the VAS pain score at rest and during activities, significantly diminished, whereas knee function (KOOS score) was clearly got better. The NSAIDs usage (number of patients and tablets/week) and inflammation of the joint were also decreased, while side effects were little and in a very small number of participants [32].

CONCLUSION

According to this study, considering the analgesic and anti-inflammatory medications side effects, injection of PRP can be considered as a useful and safe method of treatment in select patients with mild-to-moderate knee OA who have no response to present treatments like modification of ADL, therapeutic exercise, and physical methods.

Conflict of Interest

The authors of this manuscript declare no relevant conflicts of interest, and no relationships with any companies, whose products or services may be related to the subject matter of the article.

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