



Effect of Platelet Rich Plasma Injection Effect on Knee Osteoarthritis in Elderly: Single Dose versus Double Dose Randomized Clinical Trial

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Authors' contributions

This work was carried out in collaboration among all authors. Author HAUS designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors SSH, NHK and MAQ managed the analyses of the study. Authors NKV and SSN managed the literature searches. All authors read and approved the final manuscript.

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ABSTRACT

Objective: This study aims to evaluate the effect of platelet rich plasma (PRP) and compare between single and double dose regimens among patients diagnosed with osteoarthritis admitted to the orthopedic department of Al Qassimi Hospital Sharjah, United Arab Emirates.

Methods: 200 patients were allocated into two groups in this randomized clinical trial. Patients were chosen to participate in this study after an informed consent. The trial took place at the Al Qassimi Hospital Sharjah, United Arab Emirates from July 2019 to July 2020. All patients had knee osteoarthritis, half of them received single dose PRP (group A) and the other half received double dose PRP (group B). All patients were adults and older than 18 years of age. Patients were

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followed up using Western Ontario and McMaster Universities Arthritis Index (WOMAC). The follow up was done prior to the administration of PRP, at 1 month, 3 month and 6 months after administration. Data was analyzed using SPSS program. Ethical approval was gained from the hospital as well as from patients.

Results: The mean age of the patients was 48.5 ± 8.3 years. The study included 200 participants, among them, 60 were females and 140 were males. There was improvements in all parameters of WOMAC at 3 and 4 weeks following administration of PRP. The effect of PRP continued until 6 months of follow up with no differences between the two groups. Group A baseline WOMAC parameters (pain, stiffness, physical function and total score) mean score were 15.8, 6.24, 43.01 and 65.22 respectively. At the follow up, the mean scores were 4.73, 1.78, 13.88 and 19.56 respectively. This shows significant improvement. On the other hand, group B baseline mean scores were 16.31, 6.81, 40.89 and 64.77 respectively. At the final follow up of group B, the parameters mean scores were 4.40, 1.11, 13.64 and 20.27 respectively. Both groups were compared to each other and no benefit for the double dose over the single dose (P value, 0.66).

Conclusion: Previous results suggests improvement in functionality in both groups of the trial. There was pain and stiffness relief among all patients. It is concluded that double dose has no additional effect to the single dose regimen.

Keywords: Platelet rich plasma; osteoarthritis; knee; elderly.

1. INTRODUCTION

Degenerative bone diseases are a major cause of disability. Osteoarthritis (OA) is one of the most common disorders that affects the activity of an individual [1]. It is a chronic inflammation in the synovial joints. It mainly affects large joints and most frequently knee joint. Osteoarthritis leads to progressive destruction and softening of the articular cartilage [2]. It is not a constant process rather than a dynamic phenomenon. It sometimes shows features of destruction and repair at the same time. It is considered the fourth leading cause of “years lived with disability” (YLD). This means that OA affects about 3% of total YLD's in the world [3]. WHO expects that by the year 2030, there will be an increase in the demand of total knee arthroplasty [4].

The pathophysiology and the direct cause why osteoarthritis occurs are still not fully understood. However, it is a heterogeneous clinical disease [5]. The current explanation of the disease process is that it results from imbalance between the pro-inflammatory cytokines (including interleukins and tumor necrosis factor-1) and anti-inflammatory cytokines [6-7]. This imbalance leads to the activation of proteolytic enzymes which begins the process of cartilage destruction. The proposed autologous platelet rich plasma (PRP) constitutes of a group of growth factors which provide a media for these growth factors to enable the bone to regenerate [8-11]. There are some growth factors found to be more concentrated in the PRP. Those growth factors

are PDGF, VEGF, EGF and TGF-beta 1. They are more concentrated when compared to their concentration in the whole blood. When PRP are used in knee osteoarthritis, it provides a natural delivery of growth factors along with their cytokines which are responsible for anabolic as well as catabolic effect. The difference is that they are in ultra-physiological concentration [12-17]. This will optimize the healing environment and provide more opportunity for regenerating the injured positions. It is important to keep the environment in a hemostatic situation by repetitive injection of PRP which theoretically provides an abundance of growth factors for healing [18-20].

2. METHODS

2.1 Study Design

This is a prospective randomized clinical trial conducted on 200 patients with knee osteoarthritis.

2.2 Study Setting

The study was conducted at the main orthopedic department at the Al Qassimi Hospital Sharjah, United Arab Emirates. The participants were selected over a year during the period from July 2019 to July 2020.

2.3 Participants

Participants in this study were patients admitted to the orthopedic department suffering from

knee joint osteoarthritis. All study participants (patients) were adults above 18 years of age. Patients who were younger were excluded from the study.

2.4 Sample and Sampling

Since the study was a prospective, clinical trial, convenient non-probability sample was selected according to the criteria in the section of participants. Thus, the study included only adult patients admitted to the orthopedic department at the hospital during the study period.

2.5 Procedure and PRP Preparation

The first step of the procedure was to withdraw 50 ml of patient's venous blood by trained nurse. Blood then was transferred to 4.5 ml tube containing CPD-A1 as an anticoagulant. The second step was centrifugation of blood samples for 15 minutes at 1500 rpm with force of 200g. Then the blood was separated into PRP and residual RBCs. After that, the PRP was extracted into a test tube. Finally, PRP was supplied for injection in 10 ml syringe.

After this preparation, the patient was prepared at the operation room in supine position as shown in the figure. Injection of PRP was performed in the lateral para-patellar approach. The procedure was performed under aseptic technique. The injection was 5 ml into the knee joint. Patients were followed up for an hour after the procedure and in cases of discomfort, tramadol was prescribed (dosage, 50 mg bds). The PRP was activated and the second dose was given after two weeks.

2.6 Statistical Analysis

Data were entered and analyzed using SPSS program version 23 computer software. Independent T test and one-way Anova are used to show statistical significance among participants characteristics. Chi square test is used to show relationship between categorical variables.

3. RESULTS AND DISCUSSION

The pain parameter decreased from the baseline at week 4 and 3 months of follow up after the procedure of injecting PRP into knee joint in both groups. However, the pain parameter increased slightly at the follow up at 6 months. Nevertheless, this increase was not significant. It is important to mention that the mean value of

pain at 6 months follow up was less than the baseline mean value in both groups. The improvement in patients' condition was noticed and maintained during all the period of follow up. There was slight decrease in patients' overall condition at 6 months. There was no statistically significant difference between the two groups.

It was found that the same pattern of pain was found for the other parameters of WOMAC (stiffness, physical function and total WOMAC score). Table 1 shows the WOMAC parameters for both groups.

The degeneration of cartilage associated with osteoarthritis is difficult to treat and a clinical challenge for practicing orthopedics. The function and structure of cartilage are difficult to replace in cases of degeneration such as in osteoarthritis. Many research is undergoing to reduce the degenerative effect of osteoarthritis and many methods are proposed to solve this issue. The current medication use delay the pain and reduce the stiffness, but only for short time and no proven therapy is found to the moment [21-23].

In this randomized trial, patients were allocated into two groups, one group for single dose PRP administration and the second group for double dose. WOMAC scores were assessed at a baseline before the administration of PRP and at 1, 3 and 6 months after that. The concentration of platelet was 5 times more than the physiologic state which mean it was 5.5×10^{10} per 50 ml. In a study conducted to use PRP for the same purpose, patients were found to benefit from PRP at first and third month of follow up which is similar to our study [24]. Another study concluded that the effect of PRP fades after 8-10 months of administration [25].

In the present study, all patients shows decrease in all WOMAC parameters' scores. This decrease and improvement in the overall health conditions continued up to the 6 months of the follow up. This could be explained by the fact that the administered PRP may have a role at different levels of repairing the cartilaginous lesions. Thus, PRP has an anabolic effect or it slows the catabolic process in the chondral site of knee joint [25-27].

It was mentioned in the results that there was no statistically significant difference between two groups. However, not all patients had equal outcomes of the PRP administration. There were some patients who benefited a lot from the PRP

Table 1. WOMAC parameters mean value for trial groups

| WOMAC parameter | Pain | Stiffness | Physical activity | Total WOMAC | |
|-----------------|----------|-------------|-------------------|--------------|--------------|
| Group A | Baseline | 15.8 ± 3.8 | 6.24 ± 0.3 | 43.01 ± 5.3 | 65.22 ± 5.7 |
| | 1 month | 7.81 ± 2.1 | 2.36 ± 0.1 | 21.67 ± 3.4 | 32.66 ± 4.1 |
| | 3 months | 4.73 ± 0.8 | 1.78 ± 0.07 | 13.88 ± 2.1 | 19.56 ± 6.3 |
| | 6 months | 4.88 ± 0.6 | 1.97 ± 0.04 | 14.12 ± 3.2 | 20.25 ± 3.02 |
| Group B | Baseline | 16.31 ± 2.5 | 6.81 ± 1.4 | 40.89 ± 4.8 | 64.77 ± 4.1 |
| | 1 month | 5.67 ± 1.1 | 3.21 ± 0.5 | 18.36 ± 6.04 | 27.84 ± 5.2 |
| | 3 months | 4.40 ± 1.3 | 1.11 ± 0.02 | 13.64 ± 2.4 | 20.27 ± 2.8 |
| | 6 months | 4.51 ± 1.06 | 1.62 ± 0.4 | 13.78 ± 3.7 | 20.88 ± 4.07 |

Presented as means and standard deviation

injection and some others had fair good results in both groups. The effectiveness of PRP injections varied among participants. Obese patients with other morbidities had lower results from other patients. This is consistent with the results of [28] where authors concluded that the presence of other comorbidities besides osteoarthritis lowers the effect of PRP injections. Moreover, there is a need for further research and investigations to determine how long would the follow up be in such studies.

In our study, there some patients who reported pain immediately after the infiltration of PRP. However, there were no systematic or long-term complications. In the study of [29], authors reported that they documented some systemic side effects of PRP injections. On the other hand, in [30] authors mentioned some local side effects at 30 minutes interval after the procedure.

There were some limitations of this study as age, body mass index were not considered in the selection criteria of patients. There was no predefined classification system for the study participants. The study maximum follow up period was 6 months and it should be longer.

It is recommended for further research to consider the previous variables and to follow the patients for longer periods.

4. CONCLUSION

From study results, we can conclude that PRP autologous infiltration in cases of early knee osteoarthritis has a beneficial effect on pain, stiffness and physical activity of patients for at least 6 months period. The most important thing of PRP is that is free of side effects. It is highly recommended to use PRP to manage patients with knee osteoarthritis. However, patients need to rest in the period after administration of PRP as labor and heavy work may reduce the benefits of PRP. There is no difference between single

and double dose regimens when used. Double dose doesn't give additional advantage.

CONSENT AND ETHICAL APPROVAL

An approved permission was gained from ethical committee of our hospital to enroll patients in to the trial. After explanation of trial objectives and risk of adverse events, patients were asked to volunteer to participate at our trial. In addition, written informed consent was gained from patients before doing the procedure.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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