Effect of intra-articular Platelet Rich Plasma injection on knee Osteoarthritis patients

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Abstract

Background: Osteoarthritis (OA) is one of the most common problems that affects human body which may lead to disability. Among the joints of the human body knee joint is most commonly affected by osteoarthritis. Quality of life is greatly affected by OA as it may hamper daily life activities. Several treatment modalities have been adopted to combat the difficulties of knee osteoarthritis. Along with oral medication, lifestyle modification and surgical procedures are also used frequently to treat OA Knee. Sometimes it may be costly and burdensome for patients. Platelet-Rich Plasma (PRP) is a new modality of treatment that is derived from patients' blood containing growth factors that is effective for the healing process of the damaged articular cartilage and also for tissue regeneration. PRP preparations have been used to treat cartilage lesions to regenerate tissue homeostasis and retard the progression of knee osteoarthritis (OA). The purpose of this study is to determine the effectiveness of intra-articular PRP injections in patients with knee OA and to evaluate clinical outcomes.

Methodology: This quasi-experimental study was conducted at the Transfusion Medicine Department in Dhaka Medical College and Hospital. A total of 15 patients who were referred from different departments to Transfusion Medicine for platelet-rich plasma preparation and fulfilled the inclusion criteria were included in this study.

Result: Patients received 3 intra-articular PRP injections 21 days apart. Females were predominant 10 (66.66%). Platelet count of the patients was recorded before making PRP and after 1st, 2nd, and 3rd dose of PRP, which was significant by ANOVA test p -value < 0.001. Western Ontario and McMaster Universities Arthritis Index (WOMAC) score comparison among baseline, 21 days after 1st, 2nd, and 3rd dose of PRP showed significant results in ANOVA post-HOC test with a p - value < 0.001.

Conclusion: The use of intra-articular PRP may be considered as an effective method for treating osteoarthritis knee joint. The result of our study provides a significant clinical improvement. Therefore, our study result can be found to be helpful for further researches on this area.

Key words: Osteoarthritis, Platelet Rich Plasma, WOMAC score

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Introduction

Platelet Rich Plasma (PRP) is now being used in various fields of medical science, specially It is a biological product that contains aportion of autologous plasma with a raised platelet concentration above the baseline of an individual before centrifugation.[1] PRP contains a high level of platelet and also is enriched with growth factors, chemokine, cytokine and other plasma proteins. In other word, PRP is a simple, efficient and minimally invasive procedure to get autologous growth factors.[2] PRP is made by centrifugation of autologous blood and then separating the plasma and buffy coat of the centrifuged blood which yields high concentration of platelet. Patient's blood is collected through peripheral venesection, then centrifuged properly to separate the cellular and plasma portion rich in platelet. The PRP is then administered to that patient by an intra- articular injection.[3]The use of PRP got consideration because it acts as a reservoir of many growth factors.[4] Scientific background of using PRP is grading the advantage of many biologically active factors that can induce tissue healing process.[5] PRP can act on articular cartilage of joint which is avascular connective tissue made up of hyaline cartilage primarily contains type 2 collagen and chondroitin sulphate.[6] When the articular cartilage get

damaged, it results Osteoarthritis (OA).

OA is a type of degenerative disease that affects around 250 million people globally.[7] Knee OA is a common progressive joint disorder characterized by chronic pain and functional disability. [8] Osteoarthritis can be graded from 0-4 depending on radiological findings. Diminished joint space, loss of cartilage, presence of cyst, sclerosis and osteophyte are seen in radiographic investigation of an osteoarthritic patient.[7-9] Kellgren-Lawrence (KL) classification was used to classify OA knee in this study.

KL classification

Grade 0: no pathological features

Grade 1: doubtful narrowing of joint space and possible osteophytic lipping

Grade 2: definite osteophytes and possible narrowing of joint space

Grade 3: moderate multiple osteophytes, definite narrowing of joint space, some sclerosis, and possible deformity of bony ends

Grade 4: large osteophytes, marked narrowing of joint space, severe sclerosis, and definite deformity of bone ends.[10]

To measure the severity of pain, stiffness and functional limitation of affected joint that is perceived by a patient WOMAC score (Western Ontario and McMaster Universities Osteoarthritis Index) is used. Several modalities of treatment have been adopted like various medication, intraarticular injections and surgery to overcome the difficulties of osteoarthritis.[11,12] Among those, Platelet rich plasma is thought to be like a choice of treatment for osteoarthritis that can bring the desired effect. Study done by Syed Ahmed Raeissadat concluded that, PRP injections can be an alternative therapy for osteoarthritis knee joint patients.[12] They showed mean WOMAC score was 39.12±16.25 before treatment and reduced to 21.05±14.73 after PRP injections. Mean total WOMAC revealed a significant reduction after PRP injections.[12] In Bangladesh, Atiqul Islam SM. et al reported that PRP might be an effective treatment method for OA knee joint.[13] They showed that the baseline mean WOMAC score reduced significantly after treating osteoarthritis knee joints with PRP injections. So, this study was designed to determine PRP's effectiveness in knee osteoarthritis patients by assessing WOMAC scores in our hospital setup.

Methods

This quasi-experimental study was conducted in the department of Transfusion Medicine Department in Dhaka Medical College Hospital from April 2022 to March 2023. A total of 15 patients suffering from grade 1 and 2 osteoarthritis knee joints were enrolled in this study. For preparing PRP blood sample was collected in an anticoagulated test tube from each patient then was centrifuged by HETTICH EBA 20 centrifuge machine. Each of the patients took 3 sessions of PRP injection at 21 days intervals and they were evaluated by WOMAC scoring. WOMAC is a self-administered questionnaire consisting of 24 items divided into 3 subscales.

The questions are scored on a scale of 0-4, corresponding to 0 = none, 1 = mild, 2 = moderate,

3 = severe and 4 = extreme. Summation of all scores gives a total WOMAC score.[14] Finally collected data were entered into SPSS 26, analyzed and presented in tabulated form.

Result

This study included 15 patients suffering from osteoarthritis knee joint who completed all three sessions of PRP injections. Among them, 5 were of grade 1 and 10 of grade 2 Kellgren Lawrence classification of knee joint osteoarthritis. The mean age of the study participants was 51.4±2.88 years in K-L grade 1 and 55.7±5.23 years in K-L grade 2 with females predominant (80% female in grade 1and 60% female in grade 2). It was observed that 80% of KL grade 1 and 40% of KL grade 2 were of the 50-60 age group.

Each PRP unit's platelet count was checked by a complete blood count before injection into the intra-articular space to see the increment. We observed that the mean platelet count of venous blood or primary platelet count was 268600.0±64118.0 which raised to 945733.3±334156.2 in 1st dose of PRP, to 946720.0±331263.7 in 2nd dose and to 1123866.7±326141.5 in 3rd dose of PRP. Each PRP unit contained a significantly increased number of platelets in comparison among baseline, 1st dose, 2nd dose and 3rd dose of PRP in ANOVA with post-HOC test with a p-value<0.001.

A comparison of baseline WOMAC score, and WOMAC score after 21 days of 1st dose, 2nd dose and 3rd dose of PRP showed the score was lower than the baseline after 21 days of each PRP injection. It was statistically significant by ANOVA with post-HOC test with a p-value<0.001. Eighty percent (80%) of the total 15 participants experienced pain within 48 hours of PRP injection. Among them, 90% were of participants from osteoarthritis knee K-L grade 2 classification. 20% of participants experienced no adverse reaction.

Table-I: Gender distribution of participants and association with K-L classification (n=15)

Gender	Kellgren-Lawrence classification		p-value
	Grade 1 (n=5)	Grade 2 (n=10)	
Male	1(20.0%)	4(40.0%)	0.439
Female	4(80.0%)	6(60.0%)	
Total	5(100%)	10(100%)	

Table- II: Age distribution of the study subjects association with K-L classification (n=15)

Age group (years)	Kellgren-Lawrence classification		p-value
	Grade 1 (n=5)	Grade 2 (n=10)	
40-50	1(20.0%)	2(20.0%)	
51-60	4(80.0%)	4(40.0%)	
>60	0(0.0%)	4(40.0%)	
Total	5(100%)	10(100%)	
Mean ±SD	51.4±2.88	55.7±5.23	0.114

Table-III: Comparison of Platelet count among baseline and PRP units (n=15)

Platelet count			
Baseline	1st dose PRP (n=15)	2nd dose PRP (n=15)	3rd dose PRP (n=15)
	Mean ±SD	Mean ±SD	Mean ±SD
268600.0±64118.0	945733.3±334156.2	946720.0±331263.7	1123866.7±326141.5
			p-value
ANOVA test			<0.001
Post hoc (Bonferroni) test			
Baseline vs 1st dose			<0.001
Baseline vs 2nd dose			<0.001
Baseline vs 3rd dose			<0.001
1st dose vs 2nd dose			0.993
1st dose vs 3rd dose			0.013

Table-IV: Comparison of WOMAC score 1st dose vs other doses (n=15)

WOMAC Score			
Baseline	**After 21 days of**	**After 21 days of**	**After 21 days of**
(n=15)	1st dose	2nd dose	3rd dose
Mean ±SD	(n=15)	(n=15)	(n=15)
	Mean ±SD	Mean ±SD	Mean ±SD
59.5±8.3	56.8±5.9	52.1±6.9	46.1±7.7
			p-value
ANOVA test			<0.001
Post hoc (Bonferroni) test			
Before injection 1st dose vs after 21 days of 1st dose			0.230
Before injection 1st dose vs after 21 days of 2nd dose			0.009
Before injection 1st dose vs after 21 days of 3rd PRP injections			<0.001

Table-V: Distribution of the study participants by adverse effects after PRP injection association with K-L classification (n=15)

Adverse reaction after PRP injection	Kellgren-Lawrence classification		p-value
	Grade 1 (n=5)	Grade 2 (n=10)	
Transient pain	3(60.0%)	9(90.0%)	0.171
No adverse effect	2(40.0%)	1(10.0%)	
Total	5(100.0%)	10(100.0%)	

Discussion

In this study total 15 participants were included. Among them 10 (66.66%) were of K-L grade 2 and 5(33.33%) were of K-L grade 1 knee joint osteoarthritis. 8 (53.3%) participants of both K-L grade 1 and K-L grade 2 were of age group 51-60 years. Mean age of K-L grade 1 and K-L grade 2 was 51.4±2.88 and 55.7±5.23 years respectively. Number of female participants 10 (66.7%) was over male. 5 (33.3%) In subgroup K-L grade 1 and K-L grade 2 female participants were 6(60%) and 4(80%) respectively. A study was done with 31 patients in North America where author showed similar type of results.[16] In their study mean age was 56.4 years with female predominance 55%. Another study conducted in India, reported mean age was 51.7 years and 64% were female.[17] In Bangladesh a study was conducted with 37 patients where they reported that (57%) were female patients. Highest patients of their study belonged to 41-50 years of age group.[14] In our study mean platelet count before preparing PRP was 268600.0±64118.0/cc. Platelet count increased 3.5fold in 1ST and 2ND PRP injection and 4.2fold in 3rd PRP injection compared to mean baseline platelet count. Similar to us a study conducted in Egypt on 28 patients with grade 1 and grade 2 OA knee where patients received 2 PRP injections 3 weeks apart. They also showed that platelet count 1001.25×10^9/l in PRP can show excellent result.[18] In this study all patients received 3 intra articular PRP injections at 21 days interval. And WOMAC score was assessed before injecting 1st dose of PRP, after 21 days of injecting 1st dose PRP, after 21 days 2nd dose of PRP and after 21 days of injecting 3rd dose of PRP. Mean WOMAC score was found 59.5±8.3 before 1st dose PRP injection. Mean WOMAC score gradually decreased on subsequent 21 days interval after 1st, 2nd, 3rd injection of PRP by 56.8±5.9, 52.1±6.9 and 46.1±7.7 accordingly with a p-value <0.001 by ANOVA testing. An study held in Iran reported that 2 PRP injections were given with a 4 weeks interval to 60 patients. After 6 months mean total WOMAC score revealed significant change (p-value 0.001) which is similar to our study.[13] A prospective observational study conducted in Bangladesh found similar results to us where all patients received 3 injections at 4 weeks apart. The mean WOMAC score reduced significantly after PRP therapy than the baseline WOMAC score indicating that intra-articular PRP injections are effective for osteoarthritis knee joints.[13]In our study, 90% patients of grade 2 and 60% patients of grade 1experienced a mild transient pain in the injecting site after receiving PRP injections for a maximum period of 48 hours which subsided spontaneously. Forty percent (40%) of grade 1 and 10% of grade 2 had no adverse reaction. Similar results were shown in other studies.[13] So it is apparent that, PRP injections are effective for treating osteoarthritis knee joint patient.

Conclusion

Intra-articular Platelet rich plasma injection with a raised platelet count of at least 3 times than the baseline platelet count reduced WOMAC score when administered 21 Days apart. It has a significant effect on total WOMAC score irrespective of some adverse effects like mild transient pain. Importance should be given on PRP quality to ensure the raise of platelet count at least fold from the baseline platelet count. Multicenter study should be held to determine the outcome and effectiveness of PRP in osteoarthritis knee joint patients to generalize the result. However, studies should be carried out to see the long-term effect of PRP in such patients.

Conflict of interest: Nothing to declare.

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