

## Original Research Article

## Safety and Effectiveness of Platelet Rich Plasma versus Hyaluronic Acid Injection in Pain Management of Hip Osteoarthritis

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**Abstract: Background:** Platelet rich plasma therapy is a simple, low cost and minimally invasive method that provides a natural concentrate of autologous blood growth factors that can be used to enhance tissue regeneration (1). Recent evidences have shown that Platelet Rich Plasma Therapy can be helpful as an osteoarthritis (OA) therapeutic tool by intra-articular injection (2). Hyaluronic acid (HA) is widely used therapy for relief of OA pain and stiffness by intra-articular injection. In addition, there is a sufficient evidence for being significant disease modifying effects. **Objectives:** The aim of the study was to compare the clinical efficacy of Platelet Rich Plasma with that of hyaluronic acid viscous supplementation. **Methods:** This study included forty patients with hip osteoarthritis. These patients were selected from the Out Patient Department (OPD) of Dhaka Pain Management Center (DPMC) and Ava Pain & Intervention Center (APIC), Dhaka, Bangladesh during the period from January 2020 to December 2020. Patients were randomly divided into two groups. The first group consisted of 20 patients treated by using intra-articular injection of 2 ml autologous Platelet Rich Plasma Therapy. The second group consisted of 20 patients they were treated by using intra-articular injections of low molecular weight (hyaluronic acid [HA]) (32mg/2mL) of HA (HA group). All patients received 3 injections with one week interval (3) For Follow up: The subjective clinical outcome were measured at baseline, 1, 3, 6 and 12 months after the last treatment dose using the Visual Analog Scale (VAS) (5). **Results:** The Platelet rich plasma and Hyaluronic Acid groups showed an improvement, with significant difference between the two groups. However after 6 months follow up there was significant improvement in Platelet Rich Plasma Therapy group than HA group (P<0.005). The follow up after 12 months revealed subsided improvement than that was at 6 months. Nevertheless, this subsidence was less in Platelet Rich Plasma Therapy group. **Conclusions:** Autologous Platelet Rich Plasma therapy injections in Hip OA showed more and longer efficacy than HA injections in reducing pain and symptoms and recovering articular function. Further studies are needed to confirm these results and to investigate the persistence of the beneficial effects observed.

**Keywords:** Platelet rich plasma; Hyaluronic Acid Injection; Osteoarthritis.

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## INTRODUCTION

Hip osteoarthritis is a common disease associated with progressive deterioration of the cartilage and narrowing of the joint space [1]. It was reported that Hip Osteoarthritis in the USA was nearly 27 million, and the number of Hip Osteoarthritis is continually growing due to the aging population [2, 3]. Patients often advance through multiple treatments to block the progresses; however, there are no therapies

proven to alter the progression of Hip Osteoarthritis development [4]. Current treatments are mainly concentrated on the symptom's remission with the aim of pain relief and function recovery [5]. Nonsurgical therapies are met with both nonpharmacological and pharmacological approaches [6]. Diet and exercise are the two recommended nonpharmacological treatments but often with poor compliance [7]. Pharmacological treatments for Hip Osteoarthritis are focused on the

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administration of oral glucosamine, chondroitin, acetaminophen, celecoxib, glucosamine, and chondroitin [8]. However, the use of NSAIDs and analgesics is often accompanied with side effects [9]. Intra-articular injection, as a minimally invasive therapy, is reported safe and effective for the treatment of Hip Osteoarthritis [10]. Injections of intra-articular hyaluronic acid (HA) and platelet-rich plasma are used as other non-surgical treatment options for the patients with Hip Osteoarthritis [11]. HA, a high-molecular weight glucosamine, is generated by chondrocytes, synoviocytes, and fibroblasts and responsible for the viscoelasticity and lubrication of the hip joint [12]. It is shown that HA concentrations in osteoarthritic hips have been reduced. Increasing evidences have demonstrated that HA is able to improve joint function, relieve pain, and reduce the dosage of analgesics [13]. Injection of intra-articular HA had been recommended in the management of patients with Hip Osteoarthritis by the American College of Rheumatology (ACR) in 2012 [14]. Platelet Rich Plasma is an autologous product derived from patients' own blood through the process of gradient density centrifugation. Platelet Rich Plasma contains various growth factors and other bioactive molecules, which may regulate the aberrant inflammatory processes, regenerate tissue structures and thus promote tissue healing [15]. Autologous Platelet Rich Plasma involves a minimum risk of immune reactions and transmission of infectious diseases, and it has been widely used for the recovery of rotator cuff tendinopathy [16]. Previously, a RCT conducted by Lin *et al.*, [17] revealed that intra-articular injections of leukocyte-poor Platelet Rich Plasma can provide clinically significant functional improvement for at least 1 year in patients with mild-to-moderate osteoarthritis of the hip. However, there is still no consensus about which treatment (i.e., Platelet Rich Plasma vs. HA) is the best possible treatment for hip OA [18]. A study about Platelet Rich Plasma versus HA for Hip Osteoarthritis, and results found that Platelet Rich Plasma intra-articular injection may be an effective alternative treatment for Hip Osteoarthritis, though some included studies suggested that the efficacy of

Platelet Rich Plasma was no better than HA. Nevertheless, some studies for to show Platelet Rich Plasma providing a superior clinical improvement with respect to HA [19, 20]. This study aimed to compare the efficacy and safety of intra-articular Platelet Rich Plasma and HA for Hip Osteoarthritis patients.

## METHODS

This study included forty patients with hip osteoarthritis. These patients were selected from the Out Patient Department (OPD) of Dhaka Pain Management Center (DPMC) and Ava Pain & Intervention Center (APIC), Dhaka, Bangladesh, during the period from January 2020 to December 2020. Patients were randomly divided into two groups. The first group consisted of 20 patients treated by using intra-articular injection of 2 ml autologous Platelet Rich Plasma Therapy. The second group consisted of 20 patients they were treated by using intra-articular injections of low molecular weight (hyaluronic acid [HA]) (32mg/2mL) of HA (HA group). All patients received 3 injections with one week interval (3) For Follow up: The subjective clinical outcome were measured at baseline, 1, 3, 6 and 12 months after the last treatment dose using the Visual Analog Scale (VAS) (5). The centralized laboratory testing system was introduced to reduce laboratory-specific variability in the measurements. For statistical analysis, the SPSS version 21 was used as a statistical tool.

## RESULTS

The Platelet Rich Plasma (PRP) therapy and Hyaluronic Acid groups showed an improvement, with significant difference between the two groups. However after 6 months follow up there was significant improvement in Platelet Rich Plasma therapy group than HA group (P<0.005). The follow up after 12 months reveled subsided improvement than that was at 6 months. Nevertheless, this subsidence was less in Platelet Rich Plasma therapy group.

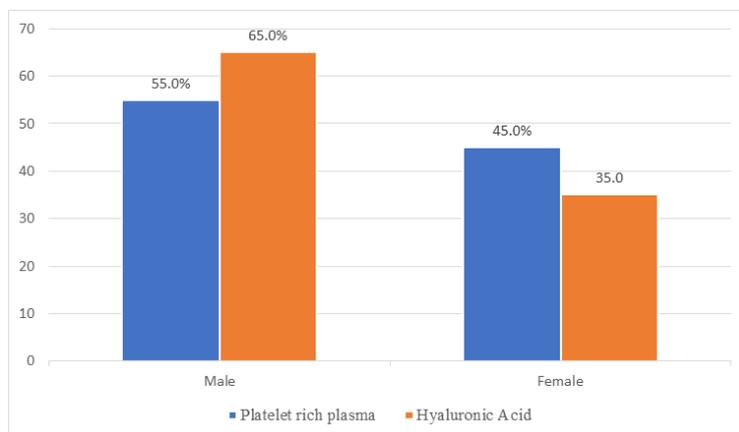


Figure I: Distribution of the study according to sex

**Table I: Characteristics of Patients Included in the two treatment groups**

Characteristics of Patients	Platelet rich plasma (n=20)	Hyaluronic Acid (n=20)	p-value
Age, y, Mean±SD	50.2±13.2	55.5±11.7	0.0001 <sup>s</sup>
BMI Mean±SD	27.2±7.6	26.3±4.2	
Previous treatments			
	n(%)	n(%)	
No treatment	4(20.0)	3(15.0)	
Non-operative treatment	6(30.0)	8(40.0)	
Surgical Treatment	10(50.0)	9(45.0)	

**Table II: Visual Analog Scale (VAS) Different Follow-up times in both treatment groups.**

Variables		Baseline	1 Month	3 Months	6 Months	12 months
	Range	8-10	1-3	1-3	1-3	1-2
Platelet rich plasma	Mean±SD	8.76±0.50	5.26±0.67	4.03±0.72	3.50±0.56	1.09±0.29
Hyaluronic Acid	Mean±SD	8.1±0.47	6±0.59	5±0.68	4±0.35	2±0.42
	P-value	0.0001 <sup>s</sup>				

Table II shows VAS in different follow-up period. It was observed that Platelet rich plasma baseline mean VAS was found 8.76±0.50, 1 month mean VAS was found 5.26±0.67, 3 month mean VAS was 4.03±0.72, 6 month mean VAS was 3.50±0.56 and 12 month mean VAS was 1.09±0.29. The mean VAS was statistically significant (p value is 0.001) compare with different follow up period. It was also observed that Hyaluronic Acid (HA) baseline mean VAS was found 8.1±0.47, 1 month mean VAS was found 6±0.59, 3 month mean VAS was 5±0.68, 6 month mean VAS was 4±0.35 and 12 month mean VAS was 2±0.42. The mean VAS was statistically significant (p value is 0.001) compare with different follow up period.

## DISCUSSION

The main finding of the present study is that there is no significant difference, in either clinical outcome or effect duration, between leukocyte-rich PRP and HA in the treatment of hip OA at long-term evaluation. Among all scores and evaluations used, the only significant difference found was in favor of PRP in the reintervention rate at 12 months, with a tendency for lower reintervention rate at the final evaluation. This is the first double-blind RCT available on a large cohort of patients, reporting long-term data on clinical outcome, retreatment rate, and duration of symptomatic relief, after either PRP or HA injective treatment at more than 5 years of follow-up; the presented 2- and 5-year findings are the mid and long term follow-up points for patients whose short-term results were previously published [11]. This Study the Platelet Rich Plasma therapy and and Hyaluronic Acid groups showed an improvement, with significant difference between the two groups. However after 6 months follow up there was significant improvement in Platelet Rich Plasma Therapy group than HA group (P<0.005). The follow up after 12 months reveled subsided improvement than that was at 6 months. Nevertheless, this subsidence was less in Platelet Rich Plasma therapy group. Despite the high interest in biological agents, the past decade has seen a lack of high quality clinical

research, which should have preceded the indiscriminate clinical use of these blood-derived products.10 Most of the available RCTs have major flaws, such as being underpowered [16, 26, 27, 29] or treating unblinded patients with the inherent risk of a placebo effect, the contribution of which may be particularly relevant in this field [7, 30, 37]. Of the double-blind RCTs comparing PRP versus HA, the few available studies present contradictory outcomes [8, 11, 17, 23, 33]. The overall positive, but not conclusive, results of these short-term studies leave open the question of possible differences in outcomes of these treatments over time, especially considering the different rationales for the two injective procedures. In theory, the biological approach should have a more comprehensive effect on the intra-articular tissues and should therefore lead to better results at longer follow-up times [14]. Beyond the mere trend of clinical scores, which have been shown to increase in the short- to mid-term evaluation in all published trials, the stability of the results is equally relevant to both physicians and patients. If different treatment approaches yield similar outcomes at 6 to 12 months of evaluation, this does not mean that these treatments are absolutely equivalent. A long-term observation is required to understand whether one treatment provides more stable results over time, thus leading to a lower reintervention rate, with inherently lower risks for patients. Injective treatments are very common and can be repeated over time, but they carry the risk of infective sequelae that could be devastating therefore, products that provide long-lasting results should be prioritized by clinicians. Among these failures, only a small percentage of patients required a prosthetic intervention, attributable to both the exclusion of the highest degrees of degeneration via the study criteria and the willingness of these patients to postpone such invasive procedure by undergoing further injective procedures. This difference (detected at a later follow-up than the most common early evaluations of the injective studies at 6 to 12 months) confirms that like surgical treatments, injective treatments require long-term data on their potential effectiveness. The

findings reported in the present study do not have the strength to consider PRP clearly superior to HA, given that no significant intergroup difference was found in the overall effect duration and in the scores applied. No other differences were found in clinical scores between PRP and HA up to the evaluation at more than 60 months. However, these findings might not be representative of the potential benefit provided by other PRP treatments. PRP treatments entail several variables that could change the secreted molecules and influence the overall effect on the joint treated and the clinical benefits [15]. In this study, Table II shows VAS in different follow-up period. It was observed that Platelet rich plasma baseline mean VAS was found  $8.76 \pm 0.50$ , 1 month mean VAS was found  $5.26 \pm 0.67$ , 3 month mean VAS was  $4.03 \pm 0.72$ , 6 month mean VAS was  $3.50 \pm 0.56$  and 12 month mean VAS was  $1.09 \pm 0.29$ . The mean VAS was statistically significant (p value is 0.001) compare with different follow up period. It was also observed that Hyaluronic Acid baseline mean VAS was found  $8.1 \pm 0.47$ , 1 month mean VAS was found  $6 \pm 0.59$ , 3 month mean VAS was  $5 \pm 0.68$ , 6 month mean VAS was  $4 \pm 0.35$  and 12 month mean VAS was  $2 \pm 0.42$ . The mean VAS was statistically significant (p value is 0.001) compare with different follow up period. In particular, the role of leukocytes is currently the most debated aspect; authors of in vitro experiments have claimed that leukocytes stimulate the release of catabolic and pro inflammatory molecules [4, 36] that could be detrimental to the intra-articular environment. Nonetheless, a recent in vivo study showed that 1 week after the injection of leukocyte rich PRP, no increase occurred in the concentration of inflammatory molecules in the synovial fluid [25]. Even though different PRP formulations could exert different effects, as established by in vitro experiments on chondrocytes and synoviocytes [1, 5, 28], in vivo effects might be less predictable than suggested by in vitro tests, and the role of cellular components must still be investigated and clarified in regard to clinical outcome. The only available comparative trial revealed similar results when using leukocyte rich and leukocyte-poor formulations [13], leaving the question of the in vivo role of leukocytes unanswered. Beyond the aspects related to each PRP formulation and its mode of application, the selection of the patient treated may also play a role in the observed results. In this trial, patients with different grades of cartilage degeneration (Kellgren grades 0 to 3) were included. This may have affected the results since patients with more advanced OA tend to have less benefit from PRP application, with an inherent effect on the duration of symptomatic relief [8, 22]. Another limitation is the unblinding of the treatment after 1 year, which could have affected the results observed at subsequent follow-up points. Moreover, the PRP and HA groups differed in terms of age, a factor that could influence patient response to treatment. Despite these limitations, the results of this trial are relevant, being the first report in the literature of the long-term outcomes of PRP versus HA. The

long-term comparison revealed that other than a lower reintervention rate at 24 months, PRP had no clear overall superiority versus HA for the blood derivative used in this trial. Further research is needed to demonstrate whether other PRP formulations can yield more durable results than traditional treatments. In addition to providing double blinding and proper sample sizing, future studies should consider a longer follow-up period (at least 24 months) to assess fundamental aspects such as survival rate, effect duration, and need for reintervention, which could be key elements for the selection of the injective strategy to treat OA patients.

## CONCLUSION

Under the condition of present study it can be concluded that Platelet Rich Plasma (PRP) provides better pain management of hip Osteoarthritis than Hyaluronic Acid (HA) though both treatments were effective recovering articular function.

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