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The role of platelet-rich plasma in osteoarthritis of knee-joint

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Abstract
Background: *Platelet-rich plasma (PRP) has received a lot of attention as an intra-articular treatment for osteoarthritis symptoms. Platelets that have been activated release a slew of soluble mediators such as growth factors and cytokines, inducing complex interactions that vary across tissues within the joint.*
Aim of the study: *The current study was carried out to assess the outcome of intra-articular platelet-rich plasma (PRP) injection in our patients with knee osteoarthritis.*
Methods: *This study was conducted in 250 Bedded General Hospital, Pabna, Bangladesh, from January 2021 to January 2022. The study included all patients between the ages of 35 and 60 who had been diagnosed with grade I or II arthritis. Three PRP injections were given in the knees four weeks apart. Patients were followed up on in the outpatient department (OPD) and were assessed for pain and physical activity related to arthritis using the Western Ontario and McMaster University Arthritis Index (WOMAC) score at the time of study initiation and at 6 months intervals. All collected data was entered into a Microsoft Excel Work Sheet and analyzed in SPSS 11.5 using descriptive statistics.*
Results: *There were 145 (67.44%) females and 70 (32.56%) males. The mean WOMAC score before the start of treatment was 81.05 (±4.1) and after 6 months it was reduced to 34.83 (±5.3), which was statistically significant (p = 0.000). WOMAC score was improved more in the subgroup with patients having symptoms less than 2 years (p = 0.005). There was no significant difference in the WOMAC score at 6 months among males or females (p = 0.069) and subgroups with Kellgren–Lawrence grade 1 or 2 (p = 0.110).*
Conclusion: *In our study, the sequential use of PRP injections for the treatment of early osteoarthritis proved to be effective.*
Keywords: *Platelet-rich plasma (PRP), Osteoarthritis, Knee-joint, Articular.*

I. INTRODUCTION

Osteoarthritis is the most common articular disease caused by articular cartilage defects. It has a significant impact on one's quality of life and is one of the leading causes of musculoskeletal disability [1]. Osteoarthritis can affect any joint, but it is most commonly observed in the knees, hips, hands, facet joints, and feet [2]. The prevalence of symptomatic knee osteoarthritis increases with age, with the annual incidence being highest in people aged 55 to 64 in the US population [3]. Osteoarthritis is more than just cartilage wear and tear. It is, rather, a complex disease characterized by the secretion of inflammatory mediators such as inflammatory cytokines, which are thought to play a key role in the pathophysiology of this debilitating disease [4]. In a normal joint, chondrocytes are inactive, and the cartilage matrix rotates very slowly. In osteoarthritis, stimulation of extracellular matrix receptors on chondrocytes causes them to become activated. They proliferate and form clusters, as well as produce matrix degrading proteinases and inflammatory cytokines [5]. Osteoarthritis is distinguished by synovial inflammation, subchondral sclerosis, ligament laxity, and osteophyte formation, in addition to cartilage destruction [6]. The progression of these pathological changes in all joint tissues led to the classification of osteoarthritis as an organ disease [5]. There have been a number of supportive treatments for osteoarthritis, such as analgesics, viscosupplements, and corticosteroids, which are used to relieve arthritis symptoms [7]. Intra-articular hyaluronic acid is another treatment option that has been used for a long time in this regard [8]. The use of platelet-rich plasma (PRP) for the treatment of osteoarthritis has recently increased. PRP,

which is derived from autologous blood and contains growth factors, is said to activate the healing process in damaged cartilage and aid in tissue regeneration [9, 10]. When hyaluronic and PRP injections are compared, some studies show that PRP is superior in terms of symptom relief [11, 12]. The goal of this study was to see how our patients with knee osteoarthritis responded to intra-articular PRP injections.

II. METHODOLOGY

This study was conducted in 250 Bedded General Hospital, Pabna, Bangladesh, from January 2021 to January 2022. The study included all patients between the ages of 35 and 60 with grade I and II osteoarthritis, symptoms lasting more than 6 months, hemoglobin levels above 12 g dL^{-1}, platelets levels above 150,000 mL^{-1}, and failure of pharmacological and physiotherapy to provide significant long-term relief. Patients with autoimmune/platelet disorders, anticoagulant or immunosuppressive therapy, diabetes mellitus, infection, recent trauma, or malignancy were excluded. According to the inclusion criteria, all patients presenting in outpatient clinics were briefed in detail about the procedure, potential benefits, and complications, and were included after providing written and informed consent. A questionnaire was created, and data on demographics, occupation, BMI, blood group, duration of symptoms, and grade of arthritis were collected. Three PRP injections were given in the knees four weeks apart. Patients were followed up on in the outpatient department (OPD) and were assessed for pain and physical activity related to arthritis using the Western Ontario and McMaster University Arthritis Index (WOMAC) score at the time of study initiation and at 6 months intervals. All collected data was entered into a Microsoft Excel Work Sheet and analyzed in SPSS 11.5 using descriptive statistics.

III. RESULT

A total of 230 patients were registered for this clinical trial based on the inclusion criteria. At the end of the trial, 215 patients completed the study period, while 15 patients did not complete the study period and lost to follow up. The mean age of the patients was 65.20 (±7.53) years. Females outnumbered males in presenting with knee osteoarthritis. Table 1 shows that there were 145 (67.44%) females and 70 (32.56%) males. One hundred fifty-five (72.09%) patients were classified as having Kellgren–Lawrence grade 1 osteoarthritis, while 60 (27.91%) were grade 2. Most of the patients (n = 190; 88.37%) had clinical symptoms for less than 2 years and 25 (11.63%) for more than 2 years. The mean WOMAC score before the start of treatment was 81.05 (±4.1) and after 6 months it was reduced to 34.83 (±5.3), which was statistically significant (p = 0.000; Table 2). WOMAC score was improved more in the subgroup with patients having symptoms less than 2 years (p = 0.005). There was no significant difference in the WOMAC score at 6 months among males or females (p = 0.069) and subgroups with Kellgren–Lawrence grade 1 or 2 (p = 0.110; Table 3). Three patients developed minor hyperemia which was managed conservatively with activity limitation and ice application, but none of the patient developed gross infection. Table 4 shows that the platelet growth factors present in platelet-rich plasma (PRP), with their main effects or role in the joint.

Table-1: Sex of the victims

Sex	Frequency	Percent
Female	145	67.44
Male	70	32.56
Total	215	100

Table -2: Difference between WOMAC score at the start of treatment and at 6 months follow-up

Characteristics	WOMAC(Mean ± SD)	p value
At the start of treatment	81.05 (4.1)	0.000
At 6 months follow-up	34.83 (5.3)	

Table-3: Comparison of WOMAC score after 6 months between subgroups

Characteristics	WOMAC(Mean ± SD)	p value
Gender		
Females	37.3 (5.2)	0.069
Males	35.8 (5.5)	
Kellgren–Lawrence		
Grade 1	37.4 (5.4)	0.110
Grade 2	39.8 (5.0)	
Duration of symptoms		
<2 years	38.4 (5.5)	0.005
>2 years	41.7 (4.4)	

Table-4: Platelet growth factors present in platelet-rich plasma (PRP), with their main effects

Growth factors	Role in the joint
Transforming growth factor beta (TGF)	Regulates collagen production and proteoglycan synthesis Promotes chondrocyte proliferation and differentiation Stimulates angiogenesis Regulates the release of other growth factors
Hepatocyte growth factor (HGF)	Inhibits the pro-inflammatory NF-B pathway Stimulates angiogenesis
Vascular endothelial growth factor (VEGF)	Increases angiogenesis and blood vessel permeability
Platelet-derived growth factor (PDGF)	Promotes endothelial cell proliferation Increases angiogenesis Promotes fibroblast and osteoblast proliferation and differentiation Regulates collagen production and proteoglycan synthesis
Insulin-like growth factor (IGF)	Inhibits the pro-inflammatory NF-kB pathway Stimulates osteoblast and chondrocyte proliferation and differentiation Stimulates the production of extracellular matrix
Fibroblast Growth Factor-2 (FGF)	Promotes chondrocyte and mesenchymatous stem cell differentiation Stimulates chondrocyte proliferation Stimulates hyaluronic acid production by synovial cells
Connective tissue growth factor (CTGF)	Increases angiogenesis Stimulates angiogenesis Promotes chondrocyte differentiation Promotes platelet adhesion

IV. DISCUSSION

Among the arthritis patients in this study who had PRP injections, there was a notable clinical improvement. There was a substantial difference in WOMAC score after six months. The WOMAC score improved more in those who had symptoms for under two years. More improvement in the WOMAC score was seen in patients with symptoms that had been present for less than two years. Osteoarthritis is a crippling condition that impairs people's mobility and quality of life. Physicians have prescribed nonsurgical treatments like PRP, corticosteroids, and hyaluronic acid with positive short-term outcomes. PRP is one of the biological and regenerative techniques that is gaining popularity [16, 17]. It should be emphasized, nevertheless, that any invasive surgery might result in some placebo effects. It is always advised to include a comparator group in any experiment to better understand the impact of each treatment modality. Unfortunately, we did not have a comparison group with another type of treatment in our study. However, there are several comparison studies and meta-analyses that support the use of these modalities and show positive results in the literature. In a recent comprehensive review and meta-analysis, Sadabad et al. found that PRP was more effective than hyaluronic acid at reducing clinical symptoms over a two-year period. They did, however, urge further research into PRP's effects over the long run [12]. Multiple successive PRP injections provide superior symptomatic alleviation than hyaluronic acid or regular saline solution, according to Khoshbin et al.'s additional systematic review [18]. In our study, individuals who had PRP injections at 6-month intervals showed a significant improvement in their WOMAC scores. PRP therapy, a straightforward and minimally invasive alternative, is used to speed up tissue regeneration and recovery. It has the capacity to raise quality of life, reduce discomfort, and improve knee joint performance [19]. The effects of PRP injection in the treatment of chronic knee degeneration were investigated by Kon et al. At follow-up intervals of 6 and 12 months, they examined the effects in 115 patients. At 6 and 12 months, there was a considerable overall improvement; nonetheless, they saw that the results were steady for the first six months; nonetheless, the results deteriorated over the next seven to twelve months, reaching a level that was lower than the initial six months. Additionally, the outcomes were better in those with early-stage arthritic disease [20]. Although our study's overall study duration was shorter (i.e., a follow-up of only 6 months), we saw positive benefits at 6 months. In addition, we had picked out patients with early-stage arthritis (Kellgren grades 1 and 2). The results of Jang's 65 patients who received PRP injections were presented by him and his colleagues.

Scores on the Visual Analogue Scale (VAS) and the International Knee Documentation Committee (IKDC) improved, although PRP's clinical benefits were less pronounced due to the joint's deteriorating condition. In younger age groups with early osteoarthritis, the results were better [21]. The study group in our study was somewhat younger (mean age, 65.20 years) and had early arthritis, however at the 6-month follow-up, they had significantly improved. After comparing the effects of PRP in three subgroups, Patel et al. came to the conclusion that patients who received either one (group A) or two (group B) PRP injections significantly improved. The third group (group C), which got ordinary saline rather than PRP, displayed worsening symptoms. Some patients experienced mild problems including nausea and dizziness, however they only lasted a short time [22]. Sadly, there was no comparison group in our study, but PRP injection demonstrated a considerable clinical improvement. Three patients had mild hyperemia, which was handled conservatively. In numerous investigations, the benefits of PRP and hyaluronic acid had been compared. In comparison to hyaluronic acid, Kon et al.9 showed greater results with PRP in younger patients with early arthritis. After comparing the outcomes in 192 patients, Filardo et al. came to the conclusion that neither modality of treatment differed significantly from the other [23]. In 111 individuals, Cole et al. compared the two injection techniques. The key end measure, the WOMAC score, did not significantly differ between the two groups; however, PRP produced greater outcomes on other outcome measures [24]. Contrary to these individual research' conflicting findings, several systematic evaluations favour PRP's advantages over. In numerous investigations, the benefits of PRP and hyaluronic acid had been compared. In comparison to hyaluronic acid, Kon et al.9 showed greater results with PRP in younger patients with early arthritis. After comparing the outcomes in 192 patients, Filardo et al. came to the conclusion that neither modality of treatment differed significantly from the other [23]. In 111 individuals, Cole et al. compared the two injection techniques. The key end measure, the WOMAC score, did not significantly differ between the two groups; however, PRP produced greater outcomes on other outcome measures [24]. Contrary to these individual research' conflicting findings, several systematic evaluations favor PRP's advantages over injecting hyaluronic acid [12, 18].

Limitation of the study:

This study had a single focal point and small sample sizes. Additionally, the study was completed in a very condensed amount of time. Therefore, it's possible that the study's findings don't accurately capture the overall situation.

V. CONCLUSION & RECOMMENDATION

According to the study, the sequential use of PRP injection for the treatment of early osteoarthritis proved to be effective. However, larger studies are required to observe the long-term effects in patients.

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