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Percutaneous Intra-meniscal platelet-rich plasma injection for meniscal tears: A mid-term

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Percutaneous intra-meniscal platelet-rich plasma (PRP) is a promising tool for managing low-grade meniscal injuries in non-athletic patients. The study evaluates the clinical and radiological outcomes of PRP intra-meniscal injection in meniscal tears. Forty-eight patients were injected with 3 injections of PRP at an interval of one week with a standardised technique under sonographic guidance. All the patients had MRI evidence of meniscal injury with failed conservative management for at least 3 months. The IKDC score and VAS score were recorded initially and during follow-ups. MRI was performed on at least 12 months post-injection. Medial meniscus tear (n=33) was most commonly present. The mean follow-up of the patient was 14.4 months (Range: 12-16 months) except for 1 patient. Horizontal or oblique tears were the most common injury suffered by the patients (n=35). According to MRI classification, 6 patients had grade 1 lesions, 28 patients had grade 2 lesions, and 14 patients had grade 3 lesions. The mean IKDC and VAS scores improved significantly at the last follow-up. Pain at the site of the injection for 1-2 days was the most common adverse effect. Two patients were surgically intervened at 4 and 6 months respectively. Intra-meniscal PRP injection can be a promising modality to manage low-grade meniscal injuries. It is easy, and minimally invasive to manage meniscal tears. Although there was no radiological evidence of healing, clinical improvement was seen in all the patients. Further, long-term randomized studies are required to ascertain the benefits.

Keywords: Platelet-rich plasma, intra-meniscal injection, sonography, Stoller classification, clinical outcome, pain.

INTRODUCTION

Meniscus injuries are not uncommon lesions in the knee. Young individuals generally suffer meniscal injuries due to high-velocity trauma or sustaining repetitive injuries. Such injuries can not only restrict physical activities but in the long run can cause cartilage degeneration and early-onset osteoarthritis[1]. The severity grading of the meniscal injury on MRI helps guide the management protocol. In non-athletic patients with a low grade of injury, conservative treatment can also be tried[2,3]. Conservative management can be unsatisfactory in some patients and surgical intervention would be too aggressive for low-grade meniscal injuries[3,4].

Percutaneous injection of platelet-rich plasma (PRP) might be a promising tool to fulfil the need. Activated platelets release various growth factors, and play a critical role in the proliferation of cells, chemotaxis, cell differentiation, and angiogenesis[5]. Percutaneous PRP injection for meniscal injuries seems to be an encouraging tool as it has shown its beneficial effect on tendinopathy[6]. This study is performed to report the results of intra-meniscal administration of PRP for meniscal injuries.

MATERIALS AND METHODS

Patients

This was a retrospective study performed over 2 years. Forty-eight patients were included in the study considering the minimum follow-up of 12 months. The inclusion criteria include more than 18-year-old patients of either gender with isolated meniscal injury and absence of locking of the knee. The grading of meniscal injury was performed on MRI using Stoller grading into three grades[7]. All the patients were initially managed conservatively for meniscal injury for at least 3 months. The patients who were unsatisfied with conservative treatment were also included in the study. The patients not willing to move into surgery (even with complex tears) were also given an option for intra-meniscal PRP injection. The patients with associated injuries like cruciate, collaterals, or

osteochondral lesions were excluded from the study. The patients with a prior knee injury, inflammatory arthropathy, pregnancy, severe infection, bleeding disorder, prior knee injections, osteoarthritis grade 3 (Kellgren- Lawrence classification) and above, and on anticoagulant medications or antiplatelet medications for any reasons were not included in the study.

Grading of meniscal tear[9]:

Grade 1: one or several punctate signal intensities not contiguous with an articular surface (the capsular margin of the meniscus is not considered an articular surface).
Grade 2: linear intra-meniscal signal intensity without articular surface extension.
Grade 3: signal intensity extended to at least one articular surface.
Procedure

All the patients underwent PRP injection via the same technique of PRP preparation and percutaneous injection.

After skin decontamination, 20 ml of blood was collected in an ACD (Acid citrate dextrose) vial. The double spin technique (hard spin and soft spin) was employed to prepare 3-4 ml of pure PRP for every session. The collected blood samples and PRP samples were analyzed for platelet concentration, leucocyte, and red blood cell counts. A leucocyte-rich PRP was prepared with a platelet concentration of 10 times (baseline peripheral blood levels) and a platelet capture yield of 65%.

Percutaneous intra-meniscal injection

All the injections were given under the guidance of sonography. 0.5-1 ml of PRP was injected at the site of the tear using a 21 Gauge needle (Figure 1), 1-2 ml in the peri-meniscal space, and the rest of 1-1.5 ml was injected into the meniscus along the path of the needle while withdrawing through the infrapatellar approach. In case, the tear was not appreciable well on sonography, 2 ml was injected in the peri-meniscal space and 2 ml in the meniscus along the

Fig. 1 — Illustrating the ultrasound-guided PRP injection.

path of the needle. Three sequential injections were given to all the patients at one-week intervals.

Rehabilitation

The patient was kept under observation for 1-2 hours after the injection. The patients were allowed partial weight-bearing till the last injection either using a cane or walker. Afterwards, full weight-bearing was allowed as per the comfort of the patient. Ice packs with analgesics were given to reduce post-injection pain in all the patients. Non-steroidal anti-inflammatory drugs were not allowed for the next 6 days. Physiotherapy was initiated 1 week post the last injection in all the patients. Knee bending and quadriceps strengthening exercises were started from day 1 of the first injection and continued thereafter for the next 3 months.

Data Collection

In all the patients, meniscus injury was assessed on MRI according to Stoller classification[7].

All patients with isolated meniscal tears not requiring any surgical procedure, and patients not willing to move on to the surgery with grade 3 meniscus injury or complex tears were also included in the study. Patients suffering from locking of the knee joint were excluded as per the study inclusion criteria. The IKDC score and VAS score (scale 1-10) were recorded in all the patients.

MRI was performed in follow-up at least 12 months after the last injection. The MRI was assessed by the radiologist for further deterioration of the grade of the tear or a change in the signal intensity at the meniscal tear site. Sonography (Siemens Acuson S2000, California, USA) was performed using a linear array probe (5-14 MHz).

All the patients underwent a 1.5 T MRI (Siemens Magnetom Skyra, Muenchen, Germany) using the same protocol and 3mm section thickness.

Statistical analysis

The data was analysed using SPSS version 22 and Microsoft MS Excel software. The mean
and standard deviation of the quantitative data were calculated. The correlation between
variables was analyzed. The significance was set at $P<0.05$.

RESULTS

Demography

A total of 48 patients were included in the study. There were 28 male and 20 female patients in the study with an average age of 40.7+5.2 years (Range: 32-47 years). Thirty-two patients had meniscus injury on the right side whereas 16 had on the left side. The medial meniscus tear was found in 33 patients, 7 patients had lateral meniscus tears whereas 8 patients had both medial and lateral meniscal tears. The mean duration of injury was 4.8 + 1.6 months (Range: 3-6.5 months). The mean follow-up of the patients was 14.4 + 2.3 months (Range: 12-16 months) except for 1 patient. Two patients (patients number 4 and 22) required surgery at 4 and 6 months respectively.

The meniscus status

Horizontal or oblique tears were the most common injury suffered by the patients (n=30), with radial tears in 5 patients whereas complex tears were present in 13 patients. According to Stoller classification on MRI, 6 patients had grade 1 lesions, 28 patients had grade 2 lesions whereas 14 patients had grade 3 lesions. There was no significant relationship between age and type of meniscus tear ($p>0.05$).

Grade 2 osteoarthritis (Kellgren Lawrence classification) was seen in 15 patients and grade 1 in 11 patients.

Scores

The mean initial IKDC was 47.43% + 9.8% and the mean IKDC score, at the last, follow-up was 74.2% + 11.6%. there was a significant improvement in the IKDC score with $p <0.05$. the mean initial VAS score was 5.9 + 0.9 and the mean VAS score, at last, follow-up was 2.12 + 0.8. there was a significant improvement in the VAS score with $p<0.05$. There was a linear correlation between the IKDC and VAS score at the follow-up ($r=1$).

MRI was performed in all the patients at least 12 months post-injection. No significant radiological evidence of meniscal healing was found in any of the patients. Two patients had a progression of tears in the follow-up. One patient (Patient number 4) initially had a Stoller grade 3 oblique tear of the body and posterior horn of the medial meniscus. Due to clinical deterioration, an MRI at 4 months showed a complete bucket handle tear. Another patient (Patient number 22) initially had Stoller grade 2 horizontal tear of the body and posterior horn of medial meniscus with grade 2 osteoarthritis. The MRI at 6 months illustrated a complex tear of the posterior horn of the medial meniscus.

Complications

Pain at the site of the injection was the most common adverse effect. The pain persists for 24-48 hours and

requires an ice pack and analgesics for management. The pain was experienced at all three sittings of the injection by the 27 patients ranging from 2 to 6 on the VAS scale (scale 1-10).

Patient no 4 initially had a Stoller grade 3 oblique tear of the body and posterior horn of the medial meniscus. The patient was given three sequential PRP injections as per the protocol.

Later at 4 months, the patient developed moderate to severe pain and frequent locking of the knee joint. MRI at 4 months showed a complete bucket handle tear not amenable to repair andunderwent arthroscopic partial meniscectomy.

Patient no 22 initially had Stoller grade 2 horizontal tear of the body and posterior horn of medial meniscus (Figure 2) with grade 2 osteoarthritis. The patient was given three sequential PRP injections as per the protocol. Although there was a slight improvement in the IKDC (52.8% to 59.7%) and VAS score (6 to 5) but the patient was not satisfied. The MRI at 6 months depicted a complex tear of the posterior horn of the medial meniscus (Figure 3) and the patient underwent arthroscopic partial meniscectomy. None of the patients had any joint infection or neurovascular deficit.

Fig. 2 — Illustrating T2 MRI sagittal section illustrating the posterior horn tear of the medial meniscus.

DISCUSSION

The study was conducted to assess the preliminary results of intra-meniscal PRP injection as a treatment modality in low-grade meniscal injuries. The management of meniscal lesions generally requires conservative treatment initially[8]. Surgical interventions were required for patients with high-grade meniscal injury, associated cruciate ligament injury, or failed conservative management. The most common symptoms of such patients include locking of knees and moderate-severe pain impeding the activities of daily living. Thus, there is a lacuna in the treatment options for patients with low-grade meniscal injuries not requiring surgical management but not managed with conservative treatment. This gap was filled by intraarticular injections providing mid-term functional outcomes. Intra-articular hyaluronic acid or steroid injections were practised in such patients without any medical evidence for the same[9].

Recently the use of PRP has increased many folds. PRP has shown some functional benefits not only in osteoarthritis knee[10] but in various tendinopathies as well as enthesopathies[11]. The activated PRP has various growth factors promoting the proliferation of mesenchymal cells, chondrocytes, and fibrous tissue and also helps in angiogenesis[12]. Various such

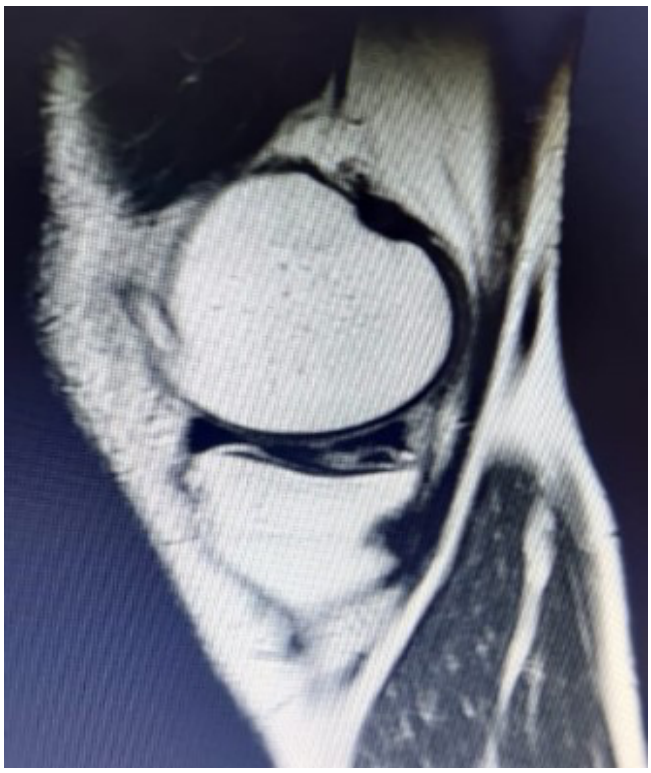

Fig. 3 — Illustrating T2 MRI sagittal post-PRP injection showing the increased extent of the posterior horn of medial meniscus tear.

pathways not only augment healing but also decrease pain in the damaged tissue. Cerza et al.[13] demonstrated better clinical outcomes with PRP than with hyaluronic acid in moderate knee arthritis (grade <3).

The main concern is the delivery of PRP at the meniscal tear site to maximize its efficacy. Some surgeons have standardised techniques under fluoroscopy[14] but sonography seems to be a better dynamic tool to assess the PRP injection at the meniscal tear site. A cadaveric study performed by Baria et al.[15] included 20 latex injections at the meniscus site intended (body or posterior horn), seventeen injections were accurate under sonographic guidance. Two of three inaccurate injections infiltrated in the posterior horn of the medial meniscus rather than the body of the meniscus. One inaccurate injection was infiltered in the lateral meniscus. Baria et al.[15] proposed the technique for infiltrating the injection under sonographic guidance at various meniscus sites. A similar technique was used in the present study. The study by Popescu et al.[16] evaluated 30 adolescent patients with isolated meniscal injury, managed with intra-articular PRP injection. The study depicted that 76.7% of the patients had excellent and good outcomes concluding the effectiveness of PRP injection for adolescent meniscal injury patients in whom conservative treatment failed. Similarly, the study by Guenoun et al.[17] depicted the results of intra-meniscal PRP injection in 10 patients with degenerative meniscal lesions. There was an improvement in the KOOS score, VAS score, and return to sports activities. Although there was no improvement in the Stoller grade of the meniscal lesion but there was a functional improvement. Initially, various studies evaluated the efficacy of PRP injection in tissue healing and regeneration. Ishida et al.[18] depicted enhanced meniscal cell proliferation in animal models and glycosaminoglycan synthesis in vitro with PRP. The fibroblast growth factor-2 found in activated PRP enhances the healing of horizontal meniscal tears. All the cell proliferation, angiogenesis, and growth factors augmented the healing of avascular meniscal lesions. There is currently a lack of evidence to support the use of PRP in meniscal repair[19,20].

Blanke et al.[14] in their study considered intra-meniscal PRP injection as the treatment option to achieve pain relief and halt the progression of the tear. In this study, athletes demanding high functional activities with predictable results were excluded as PRP alone might not suffice for patients with meniscus injuries. Moreover, such active sportspersons suffer a high-grade meniscal injury along with other soft tissue injuries. The ultrasound-guided injection required skill and was performed by a radiologist. Even after that, it was sometimes difficult to identify the tear and inject it accurately. The procedure was accompanied by pain persisting for 1-2 hours post-injection of 4ml PRP. Although the VAS score in between the injections was not recorded but most of the patients reported a decrease in pain and improvement in functional activities. The various pathways or mechanisms by which PRP functions lead to a decrease in pain rather than actual meniscal healing[21]. This would have helped to increase the functional scores in the post-injection phase. Shin et al.[22] investigated the effect of leukocyte-rich PRP on the healing potential of horizontal medial meniscal tears in a rabbit model. There were no histological changes with leukocyte-rich PRP in healing at 2, 4, and 6 weeks after the surgery. Similarly, the study by Guenoun et al.[19] depicted no MRI changes in the follow-up of intra-meniscal PRP injection in degenerative meniscal lesions.

They proposed the anti-inflammatory effect of PRP was liable to decrease the pain leading to improved functional activities. The duration of the study was short to assess the healing of the meniscus, and lastly, the changes in scar tissue healing in the meniscus might be different to be assessed on MRI.

There were a few limitations to this study. Firstly, the small sample size of the patient population. It was difficult to find patients with isolated meniscus injuries without any osteoarthritis or soft tissue injury. Secondly, the sonographic technique might need improvement for better precision of intra-meniscal injections. Thirdly, there was no control group to compare the results of PRP injections. Fourthly, long-term follow-up might be required to assess the healing of meniscal tears. The MRI signal changes might be different and should be studied more precisely. Further long-term randomized control studies are required to ascertain the beneficial role of intra-meniscal PRP injection in meniscal tears.

CONCLUSION

Intra-meniscal PRP injection is a promising modality of treatment for low-grade meniscal injury. Although there was no radiological evidence of healing of the meniscus but functional improvement was seen all in the patients. Intra-meniscal PRP injection is a safe, easy, and effective tool to manage functional meniscal injuries. PRP thus seems to act as an intermediate modality of treatment adding some benefits to the patients not managed conservatively or not willing for surgery. Further, randomised control studies are required to demonstrate long-term results.

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