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Original Research Article

Effectiveness of ultrasound guided platelet rich plasma injection in comparison with standard conservative treatment on improving pain and function among the athletes with partial anterior cruciate ligament injury of knee: a randomized controlled trial

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ABSTRACT

Background: Anterior cruciate ligament (ACL) injuries are one of the most common ligamentous injuries of knee. Treatment options for partial ACL tear range from conservative treatment up to partial reconstruction. PRP may have enhancing effect on ACL cell viability and promotion of cell proliferation in partial tear of ACL. Thus, the purpose of this study is to determine the role of PRP on partial ACL tear.
Methods: A RCT was done among athletes with partial ACL injury who visited department of Sports Medicine, RIMS, Imphal during June 2019-December 2020. Patients with MRI diagnosed grade 1 and 2 ACL injury (n=48) randomized into PRP injection plus rehabilitation, (n=24) and rehabilitation alone, (n=24) groups. The outcomes were compared using International Knee Documentation Committee (IKDC) score, Lysholm score and VAS at baseline, 1st month, 4th month, 8th month and 12th month respectively.
Results: Baseline characteristics were not statistically significant. At the end of 1st month, there were statistically significant improvement in both mean difference of IKDC score (.001), Lysholm score (0.001) and VAS (0.007). At the end of 4th month, there were statistically significant improvement in both mean difference of IKDC score (0.001), Lysholm score (0.026) and VAS (0.001). At the end of 8th and 12th month, improvement in mean difference of IKDC score, Lysholm score, VAS were observed however not statistically significant.
Conclusions: Ultrasound guided PRP injection along with conservative rehabilitation program might be a treatment choice for ACL partial tear.

Keywords: ACL, PRP, IKDC score, VAS, Lysholm score, USG guided

INTRODUCTION

Anterior cruciate ligament (ACL) injury is one of the most commonly seen injury in sports and has a devastating influence on patients' activity levels and quality of life.[1] ACL is an intra-articular and extra-synovial structure two separate bundles, anteromedial and posterolateral bundles with which maintain different tensions according to different degrees of knee flexion angle.[2] Partial tears of ACL account for 10% to 30% of all ACL tears.[3] In general, the incidence is higher in people who participate in high-risk sports, such as soccer, football, skiing, and basketball. Female athletes had a higher incidence compared with their male counterparts.[1] Injuries can be contact or non-contact types, most commonly occur through a non-contact mechanism where there is involvement of frequent sudden deceleration, landing and pivoting manoeuvres.[4]

Partial ACL ruptures are a challenging condition for orthopaedic surgeons.[5] There is still considerable

controversy regarding the diagnosis, natural history and treatment of this type of lesion. Diverse criteria are often used to define a partial ACL tear. Magnetic resonance imaging (MRI) features include the estimation of the percentage of torn fibers, specific affected bundle (anteromedial or posterolateral) and location of the tear (proximal, middle third or distal). A partial ACL tear combines a positive Lachman's test with a firm endpoint.[6] The physical examination is decisive in this type of lesion. Finally, arthroscopy remains the gold standard for the diagnosis of macroscopic integrity of the intact bundle.[3]

Therapeutic options for treatment of partial ACL tears historically range from conservative treatment up to partial reconstruction in terms of bundle augmentation/ complete ACL reconstruction according to injured bundles.[5] Conservative therapy of partial ACL tears is associated with a high failure rate and often consecutive complete ACL rupture, followed by ACL reconstruction. Initial ACL reconstruction is reported to be potentially associated with diminished proprioception, postoperative muscular weakness, no fully restoration of normal kinematics, donor site morbidity, and possible premature osteoarthritis. Thus, ACL preserving techniques have to be favoured.[5]

Due to the evolving understanding of tissue engineering and regenerative medicine, there has been a recent interest in the development of new biological treatment techniques to address partial injuries of intra-articular structures, such as the ACL.[6] Partial tear prefers conservative treatment, rehabilitation, exercise training, or platelet-rich plasma (PRP) injection.[2] Regarding the awareness on the role of biologic agents, such as growth factors and stem cells, in promoting tissue healing, further therapeutic options for partial ACL tears were developed.[8] Recently, PRP is used for augmentation of the healing of partial ACL tear, and the PRP can be precisely applied to the ACL torn region under ultrasound guidance.[2]

PRP is known to contain platelets and several growth factors, involving platelet-derived growth factor (PDGF) and transforming growth factor (TGF)-beta. Both PDGF and TGF-beta have been reported to be the most critical modulators in healing process by enhancing proliferation and collagen production. TGF-beta is key regulator during embryologic tendon development and plays an important role in the early modulation of scar tissue during healing.[2]

PRP products are already clinical practice for many orthopaedic disorders, in such as osteoarthritis, tendinopathies, or ligament injuries. Preclinical studies demonstrated the qualities of PRP in the regulation of the articular environment, exerting a positive metabolic modulation on all joint tissues and promoting tissue healing.

Furthermore, PRP was associated with beneficial effects in stimulating fibroblasts proliferation, collagen fibers deposition, and reducing catabolic distress, when applied to ACL-derived tenocytes.[5] The use of plasma rich in growth factors has proven useful in improving ligament maturation and specifically ACL *in vitro*, in animals and in humans.[7] PRP can be precisely applied to the ACL torn region under ultrasound guidance. With the assistance of sonography, the architecture, quality, insertion, and origin of the soft tissue can be evaluated. Moreover, we gain more confidence of identifying ACL torn region.[2]

The aim of the study was to determine the effectiveness of ultrasound guided platelet rich plasma injection on improving pain and function among the athletes with partial ACL injury of knee which will be compared with standard conservative treatment for partial ACL tear.

METHODS

A randomized controlled trial was done among athletes with partial ACL injury who visited department of Sports Medicine, RIMS, Imphal during June 2019-December 2020. Patients with knee pain following injury were clinically examined and sent for MRI. Patients with MRI diagnosed grade 1 and 2 ACL injury (n=48) randomized into PRP injection plus rehabilitation, (n=24) and rehabilitation alone, (n=24) groups.

Inclusion criteria

Patient of age between 18 to 40 years, with history of knee injury within 3 months duration and MRI diagnosed grade 1 and 2 ACL tear, platelet count more than 1.8 lakh/microliter were included in the study.

Exclusion criteria

MRI proven associated PCL injury, grade 3 meniscal tear and grade 3 collateral ligament tear, patients who received corticosteroid injection within last 12 weeks, history of platelet dysfunction syndromes, malignancy, systemic illnesses, haemoglobin level less than 10 mg% were excluded from the study.

A sample size of 48 was calculated using formula

$$N = \frac{(Z\alpha + Z\beta)^2 ({S_1}^2 + {S_2}^2)}{(m_1 + m_2)^2}$$

According to a study conducted by Kumar et al considering 90% power, and 5% level of significance and 10% for drop outs to counter attrition bias.[9]

Ethical approval

The study was approved by institutional ethics committee.

Outcome measures

Perception of knee symptoms, function and ability to participate in sports measured by IKDC score, Lysholm score and VAS for pain.

Patient who met inclusion and exclusion criteria and gave consent for participation in the study were randomized (n=48) into PRP injection plus rehabilitation, (n=24) and rehabilitation alone, (n=24) groups by block randomization technique. After taking informed consent, all subjects were evaluated for IKDC score, Lysholm score and VAS at baseline before starting any intervention. And after starting the interventions, at the end of 1st month, 4th month, 8th month and 12th month, patients were evaluated with IKDC score, Lysholm score and VAS.

PRP injection plus rehabilitation group

PRP is prepared using double spin method. The 25 ml whole blood was drawn under proper aseptic and antiseptic precautions, and put in 3 vials containing acid citrate dextrose anticoagulant. The three vials were centrifuged at 2400 revolutions per minute for 10 minutes. The clear supernatant fluid was taken out using a 20-gauge spinal needle and put in plain vials and centrifuged again at 3600 rpm for 15 minutes. The lower 1/3rd is PRP and upper 2/3rdis platelet-poor plasma (PPP). 4 ml of PRP is procured by removing the PPP (Figure 1).

Figure 1: Steps of PRP preparation.

Figure 2: Ultrasound guided PRP injection.

The patient lied in the supine position with knee flexion at 90°. The 10 MHz linear transducer was placed parallel to patellar tendon with the proximal end of transducer pivoting to the lateral side of the knee joint to clarify the insertion of both anteromedial and posterolateral bundles over tibial plateau. The needle tip reached tear region of ACL under out-of-plane approach.[2] 4 ml of PRP is given within the ligament under USG guidance (Figure 2). All patients has followed a functional rehabilitation program which has four phases.

Rehabilitation group

Patient in the rehabilitation group will follow the same functional rehabilitation program which has four phases.[10]

Goal of phase 1 includes elimination of swelling, partial weight bearing to full weight bearing, 0-100-degree ROM, 4±5 quadriceps strength, 5/5 hamstring strength with exercise program including gentle flexion ROM, extension ROM to 0-degree, quadriceps VMO setting, supported B/L calf raises, hip abduction and extension, hamstring pulleys/rubbers, gait drills.

Goal of phase 2 includes full knee hyper extension, knee flexion to 130-degree, full squat, good balance and control, unrestricted walking with exercise program including ROM drills, VMO setting, mini squats and lunges, leg press double to single, steps-ups, bridges double to single, hip abduction and extension with TheraBand, single leg calf raises, gait re-education drills, balance and proprioceptive drills.

Goal of phase 3 includes full ROM, full strength and power, return to jogging, running and agility, return to restricted sports specific drills with same exercise program as above with increase difficulty, repetitions and weight, jump and land drills, agility drills. Goal of phase 4 is progressive return to sports with high level sports specific strengthening as required.

Statistical analysis

Data were entered and analyzed by using SPSS version 21. The baseline characteristics between the PRP plus rehabilitation group and rehabilitation group were studied by chi-square test for categorical variables, and independent t test was used for continuous variables. For descriptive statistics, mean and standard deviation were used. For outcome measures, the mean changes from baseline to 1st month, 4th month, 8th month and 12th month follow-up for each group were compared by repeated measure ANOVA test followed by post hoc analysis (Bonferroni). For comparison between the groups, independent t test was used. $P<0.05$ taken as significant.

RESULTS

The baseline characteristics of the patients in control and intervention group were not statistically significant (Table 1). ACL injury was more commonly seen in female athletes in both the groups (56.3%; n=27), 41.7% (n=20) of them play soccer, 60.4% (n=29) were due to non-contact types of injury. Outcome measures at baseline were not statistically significant (Table 2). At the end of 1st month, there was statistically significant improvement in both mean difference of IKDC score (p=0.001),

Lysholm score (p=0.001) and VAS (p=0.007). At the end of 4th month, there was statistically significant improvement in both mean difference of IKDC score (p=0.001), Lysholm score (p=0.026) and VAS (p=0.001). At the end of 8th, there was improvement in mean difference of IKDC score (p=0.108), Lysholm score (p=0.444), VAS (p=0.800), were observed however not statistically significant. At the end of 12th month, there is improvement in mean difference of IKDC score (p=0.348), Lysholm score (p=0.833), VAS (p=0.679), was observed however not statistically significant (Table 3).

Table 1: Comparison of baseline characteristics between the groups, (n=48).

Variables, n (%)	PRP + rehabilitation, (n=24) (%)	Rehabilitation, (n=24) (%)	P value
Age (Years)			
18-25	13 (54.2)	12 (50)	0.773
26-40	11 (45.8)	12 (50)	
Gender			
Male	10 (41.7)	11 (45.8)	0.771
Female	14 (58.3)	13 (54.2)	
BMI (kg/m^2)			
18.5-20.5	8 (33.3)	10 (41.7)	0.776
20.5-22.5	8 (33.3)	8 (33.3)	
22.5-24.5	8 (33.3)	6 (25)	
Type of sports			
Soccer	10 (41.7)	10 (41.7)	1.00
Basketball	5 (20.8)	6 (25)	
Taekwondo	3 (12.5)	2 (8.3)	
Wushu	2 (8.3)	2 (8.3)	
Badminton	2 (8.3)	2 (8.3)	
Judo	1 (4.2)	1 (4.2)	
Kickboxer	1 (4.2)	1 (4.2)	
Side of affection			
Right	14 (58.3)	13 (54.2)	0.771
Left	10 (41.7)	11 (45.8)	
Type of injury			
Contact injury	10 (41.7)	9 (37.5)	0.768
Non-contact injury	14 (58.3)	15 (62.5)	
Duration (Months)			
1-2	13 (54.2)	14 (58.3)	0.771
2-3	11 (45.8)	10 (41.7)	
MRI grading			
Grade 1	11 (45.8)	13 (54.2)	0.564
Grade 2	13 (54.2)	11 (45.8)	

Table 2: Comparison of baseline outcome measures.

Intervention (Mean±SD)	PRP + rehabilitation, (n=24)	Rehabilitation, (n=24)	P value
IKDC	34.58±2.358	35.58±3.189	0.223
VAS	8.513±0.7291	8.650±0.6692	0.500
Lysholm	32.63±3.932	32.33±4.931	0.822

Table 3: Comparison of mean changes of IKDC score, VAS scores and Lysholm score between the two groups from baseline to 1st month, 4th month, 8th month and 12th month follow up, (n=48).

Variables	Mean changes from base line, (Mean±SD)		P value
	PRP + rehabilitation, (n=24)	Rehabilitation, (n=24)	
Mean differences IKDC score (Months)			
1st	19.5417±4.04302	13.6250±6.19826	0.001
4th	30.8333±5.76094	21.9583±6.93748	0.001
8th	40.9167±4.25202	38.9167±4.19022	0.108
12th	50.4583±2.91889	49.5417±3.72978	0.348
Mean differences VAS score (months)			

Continued.

Variables	Mean changes from base line, (Mean±SD)		P value
	PRP + rehabilitation, (n=24)	Rehabilitation, (n=24)	
1st	-1.9625±0.83083	-1.1875±1.04645	0.007
4th	-3.6875±1.53434	-2.2167±1.23840	0.001
8th	-4.6792±1.05624	-4.6083±0.86372	0.800
12th	-6.2625±1.29676	-6.1083±1.26419	0.679
Mean differences Lysholm score (months)			
1st	21.8750±7.82033	14.0000±7.34255	0.001
4th	28.9167±8.38174	23.2917±8.56423	0.026
8th	35.1250±7.00504	33.4167±8.27209	0.444
12th	54.2500±5.39928	53.9167±5.46862	0.833

DISCUSSION

In our study, we gave injection PRP inside the torn ligament under ultrasound guidance which is followed by functional rehabilitation program and in the control group; we gave the same rehabilitation program without PRP injection. There was significant improvement in pain, symptoms perception, function and ability to participate in sports in the subsequent follow up in both the groups. And, there was significant improvement in the PRP plus rehabilitation group in 1st and 4th month follow up in comparing with rehabilitation group. At 8th and 12th months follow up, there was improvement in PRP plus rehabilitation group in comparing with rehabilitation group, however not statistically significant.

Healing process starts with platelet aggregation and clot formation and forms a scaffold, which acts as a temporary matrix for cell growth and differentiation. Platelets actively secrete pre-synthesized growth factors (GF) and synthesize more GFs for several days during their life span.[11]

PRP injection reduces the pain intensity in short term therefore rehabilitation program can be accelerated to its later stages in a shorter time with sooner returning to sport activities, which is a major issue in athletes. Functional rehabilitation groups provide the same result but in a longer duration. Our study showed that PRP injection causes a significant improvement of perception of symptoms, knee function in the 1st and 4th month follow ups which allows faster progression of rehabilitation, and sooner return to sport activities, though control group have that same level of improvement in pain, perception of symptoms and function later, in the 8th and 12th month follow up.

Zicaro et al found that all the patients returned to sports at a mean of 3.8 months in PRP plus rehabilitation group and 4.2 months in rehabilitation alone group.[8] Steadman et al developed the healing response technique to promote ACL tissue healing. Based on their purpose to preserve healthy ACL tissue and regarding the increasing knowledge about stimulation of endogenous regenerative potential by the use of biologic agents, such as growths factors and stem cells.[12] Centeno et al concluded that a minimally invasive, percutaneous injection of bone marrow concentrate and platelet products into the ACL under fluoroscopic guidance may be a viable alternative to surgical ACL reconstruction for the treatment of grade 1, 2 and non-retracted grade 3 tears of the ACL.[13] Li et al found that thermosensitive hydrogel-PRP was shown to be effective in enhancing the healing of ACL partial tear in the rat model, and potentially this complex can be used as a treatment for patients with ACL partial tear.[14]

Patients who underwent nonsurgical ACL treatment produced limb symmetry index, with the side-to-side torque difference expressed as a percentage, and values at or above 90% for all 4 single-leg hop tests and strength tests similar to ACL-r patients.[4] Partial ACL tears must be treated early enough to prevent a large number of secondary instability-derived events, particularly meniscal damage, accelerated cartilage degenerative changes and functional disability. Preserving native ACL remnant fibers, when partially torn, may provide several theoretical advantages over reconstruction, including preservation of the natural anatomy, physiology, proprioception, and intrinsic cell populations, as well as some of the complex biomechanical properties of the knee.[6] These alternatives to the current surgical reconstruction techniques have the potential to preserve the native insertion site of the remaining fibers and therefore its proprioceptive function, which may in turn lead to biomechanics that are more natural.[6]

Limitations

The study could have been more reproducible if done with bigger sample size and longer follow ups.

CONCLUSION

Partial ACL tears which are often managed conservatively may be more satisfactorily treated with the addition of PRP to stimulate repairs. Enhanced healing effect and short-term pain reduction effect of PRP is definitely beneficial for the elite athletes who needs faster recovery and sooner return to the play through faster progression of rehabilitation so it can be recommended to use PRP injection in athletes with partial ACL tear. Moreover, we can avoid the deleterious effect of surgical reconstruction of ACL tear. Under ultrasound guidance, PRP can be precisely injected to the torn region of ACL. Therefore,

PRP injection under ultrasound guidance along with conservative rehabilitation program might be a treatment choice for partial tears of ACL. Further studies are warranted with bigger sample size and longer follow to define the role of these approaches in the treatment of the partial tears of ACL and to assess the long-term outcomes.

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