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RESEARCH ARTICLE

EFFECTIVENESS OF ULTRASOUND GUIDED PLATELET RICH PLASMA INJECTION IN COMPARISON WITH EXTRACORPOREAL SHOCK WAVE THERAPY ON IMPROVING PAIN AND FUNCTION IN PATELLAR TENDINOPATHY: A RANDOMIZED CONTROLLED TRIAL

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Abstract

Background: Patellar Tendinopathy is an insertional tendinopathy of the extensor apparatus of the knee that affect athletes practicing several sports at every level of participation but is found mainly in elite athletes involved in jumping activities. The characteristic complaint is an anterior knee pain with insidious onset, localized in the involved area. Diagnosis is clinical and is typically based on medical history and clinical findings. Many methods to treat Patellar Tendinopathy have been evaluated, and there is no true consensus on the most efficacious treatment strategy.

Objectives: To determine the effectiveness of ultrasound guided platelet rich plasma injection in comparison with extracorporeal shock wave therapy on improving pain and function among athletes with Patellar Tendinopathy.

Study Design: Randomized controlled trial

Methods: Forty-four athletes with patellar tendinopathy meeting the inclusion and exclusion criteria were selected for this study and randomized into 2 treatment groups: autologous PRP injections under ultrasound guidance (PRP group; n = 22), and 3 sessions of focused extracorporeal shock wave therapy (ESWT group; n = 22). The outcome measures were Victorian Institute of Sports Assessment–Patella (VISA-P) questionnaire and pain visual analog scale (VAS). For descriptive statistics mean, standard deviation and frequency were used. Continuous variables were analysed by student's t-test. Categorical variables were analysed using Chi-square test. Within the group comparison (baseline and follow-up data of each group) was done by Repeated measures ANOVA. Between the groups comparison was analysed using student's t-test. A p-value <0.05 was taken as significant.

Results: The 2 groups were homogeneous in terms of their baseline characteristics like age, gender, duration of symptoms and side of affection. Within group comparison showed statistically significant improvement in VISA-P score and reduction in VAS from baseline at all follow ups (p=0.00) in the PRP group. While in the ESWT group, maximum improvement was seen from baseline to 1st follow up at 4 weeks (p = 0.01). However subsequent follow up showed reduction in

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VISA-P Scores and increased VAS but remained above the baseline values and it was statistically significant ($p < 0.05$) (Table III).
Conclusion: Ultrasound guided injection of platelet rich plasma lead to significant improvement in pain and function over the long term in comparison with focused ESWT in the treatment of patellar tendinopathy in athletes and thereby enabling faster return to sports.

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Introduction:-

Patellar tendinopathy is an insertional tendinopathy of the extensor apparatus of the knee that may affect athletes practicing several sports at every level of participation but is found mainly in elite athletes involved in jumping activities. This syndrome is characterized by pain at the insertion either of the quadriceps tendon at the upper pole of the patella (20%) or of the patellar tendon at the lower pole of the patella (70%) or at the tibial tuberosity (10%).[1] The characteristic complaint is an anterior knee pain with insidious onset, localized in the involved area, which is unleashed during or immediately after repetitive running or jumping activity. The pain usually disappears after a short period of rest but comes back after resumption of physical activity.[2]

Diagnosis is clinical and is typically based on medical history and clinical findings. The imaging techniques of choice for the study of patellar tendinopathy are ultrasonography and MRI. Ultrasonography can locate intratendinous lesions that appear as zones of lower echogenicity, typically in the posterior portion of the patellar tendon adjacent to the inferior pole of the patella. Other common sonographic findings include thickening of the patellar tendon, irregularity of the paratenon, intratendinous calcifications, and erosions in the inferior pole of the patella. The sensitivity and specificity of ultrasonography for patellar tendinopathy are 58% and 94%, respectively.[3]

Many methods to treat Patellar Tendinopathy have been evaluated, and there is no true consensus on the most efficacious treatment strategy. Physical therapy is a common intervention with treatment emphasizing eccentric quadriceps exercises. Other nonsurgical techniques that have been employed to address this condition include injections with sclerosing agents, low-intensity pulsed ultrasound, shockwave therapy, and corticosteroid injections.[4]

The utility of extracorporeal shock wave therapy (ESWT) for patellar tendinopathy is based on three theories. The first theory is that pain relief is achieved by hyperstimulation analgesia, in which overstimulation of the painful area leads to a diminished transmission of signals to the brain stem. A second theory presumes that the mechanical load developed by ESWT stimulates tissue regeneration. The third theory asserts that ESWT destroys calcifications in tendons in the same way that lithotripsy destroys kidney stones.[5]

With the assumption that tendinopathy is a degenerative condition with failed healing response of the tendon, the rationale for the use of PRP is promotion of tendon healing through high content of growth factors and cells in hyperphysiologic doses, which should enhance tissue repair mechanisms. Numerous studies have examined the effects of PRP in vitro and in vivo, demonstrating benefits that include improved cellular remodeling and decreased healing time.[2]

There has been advances in understanding the histopathology, imaging and surgical outcomes in patellar tendinopathy in the past few decades. Nevertheless successful management of the jumping athlete with patellar tendinopathy remains a major challenge for the physician and the athlete. The purpose of this randomized controlled clinical study was to compare the effectiveness and safety of ESWT and PRP injections in athletes with jumper's knee and thereby enable faster return to training and sport.

Objective:-

To determine the effectiveness of ultrasound guided platelet rich plasma injection in comparison with extracorporeal shock wave therapy on improving pain and function among athletes with patellar tendinopathy

Material And Methods:-

Study Design:

A Randomized Controlled Trial

Study Setting:
Department of Sports Medicine, Regional Institute of Medical Sciences, Imphal.

Duration of Study:
1 and half year starting from April 2022

Study Population:
Patients with anterior knee pain not responding to conservative treatment presenting to the out-patient department (OPD) of Sports Medicine, Regional Institute of Medical Sciences, Imphal during the study period

Inclusion Criteria:
1. Clinical and Ultrasound diagnosed cases of patellar tendinopathy
2. Age between 18 to 40 years of age
3. Failure of conservative treatment > 3months
4. Willingness to comply with treatment and follow up assessment

Exclusion Criteria:
1. Local injection within 6 weeks
2. Local infection at the site of injection
3. Evidence of other associated knee pathology
4. Uncontrolled systemic disease
5. Thrombocytopenia (<1.5 lakhs /cumm)
6. Bleeding disorder
7. Pregnancy

Sample size was calculated using the formula N = N = $(Z_{1-\alpha/2} + Z_{1-\beta})^2 (S_1^2 + S_2^2)/(m_1 - m_2)^2$. Taking into consideration the study conducted by Vetrano et al[2] in 2014 a sample size of 20 was calculated and considering a dropout rate of 10%, 22 patients were taken in each group giving a total sample size of 44 patients. Patients who met inclusion and exclusion criteria were recruited based on availability and willingness to take part in the study until sample size of 44 was reached. Randomization was done using block of four technique and patients were allocated into two groups namely A=intervention group and B=control group. A list of 11 blocks was prepared to reached a sample size of 44. For each selected blocks, there was sequence of treatment options. The sequence of treatment option in each block was put in an envelope and sealed. Corresponding envelope was labelled 1, 2, 3, 4.... upto 11 according to the appearance of treatment allocation in each selected block. The sealed envelope with label 1 was opened only when we had the first eligible patient and the treatment was allocated.

In the control group a focused electromagnetic shock wave device was used. Each participant received 3 sessions at 48 to 72 hour intervals. In each session, 2400 impulses were administered with a frequency of 6 Hz, depending on patient's pain tolerance. The treatment area was prepared with a coupling ultrasound gel to minimize the loss of shock wave energy at the interface between applicator tip and skin whereas in Intervention group received a single ultrasound guided PRP injection. PRP was prepared using the double spin method. Whole blood was drawn in a 20ml syringe by venipuncture which was then transferred to Acid Citrate Dextrose tubes. These tubes were then centrifuged using a soft spin at 2400 rpm for ten minutes. The supernatant plasma containing platelets is then collected in a separate plain vial and then centrifuged again using a hard spin of 3600 rpm for 15 minutes to obtain a platelet concentrate. The lower $1/3^{rd}$ is platelet rich plasma (PRP) and upper $2/3^{rd}$ is platelet poor plasma (PPP). 2ml of PRP is procured by removing the PPP. The patient was then made to lie comfortably in supine position with the affected knee flexed and relaxed. The skin of the affected knee was then prepared aseptically and draped by a sterile green sheet. The transducer of the ultrasound was placed longitudinally (long axis) over the site of the patellar tendon. The designated injection location was recorded before the injection (hypoechogenicity of the tendon). The injection technique involved a single skin portal using a 22G needle and then multiple small aliquots into the tendinous lesion, with color Doppler guidance. Approximately 2 to 3 ml of PRP was injected, and no local anesthesia was applied. Needle was removed and local homeostasis will be achieved by applying pressure over the injection site. After the injection, the patient rested in a supine position without moving the leg for 10 minutes, and ice application was done for 10 minutes every 2 hourly. Patients were allowed full loading of the limb after 3 days and could perform normal activities of daily living. If necessary, patients were allowed to use acetaminophen, but the use of non steroidal anti inflammatory medication was prohibited.

Single blinding was done where assessors were blinded. One week after the last treatment session, patients of both PRP injection group and ESWT group were given a standardized stretching and muscle strengthening protocol to be followed. After 4 weeks patients were allowed to gradually return to previous training activity if there was minimal or no pain. Complete return to sports activities took place in accordance with the patient's pain tolerance and absence of clinical signs.

Study variables were

Independent variables:

1. Age
2. Gender
3. Duration of symptoms
4. Side of affection
5. Interventions

A. USG guided Platelet rich plasma injection

B. Extracorporeal shock wave therapy

Dependent variables:

1. Pain measured by using Visual Analogue Scale (VAS)
   The visual analogue scale is a validated scale for subjective measure of pain. It consists of a 10 cm horizontal or vertical line with the endpoints defining extreme limits such as 'no pain at all' and 'pain as bad as it could be'. Patients were asked to mark their pain level that they feel on the line between the two endpoints which represents the perception of their current state. The distance along the line in cm from the 'no pain at all' end of the VAS to the patient's mark represents the numerical index of the severity of pain.
2. Victorian Institute of Sport Assessment - P
   The Victorian Institute of Sports Assessment–Patella (VISA-P) questionnaire designed specifically for patients suffering from patellar tendinopathy to assess severity of symptoms, function, and ability to participate in sport. VISA-P is the only published clinical scale validated for patellar tendinopathy. The questionnaire contains 8 questions that cover the 3 domains of pain (questions 1-3), function (questions 4-6), and sport activity (questions 7 and 8). Questions 1 through 7 are scored out of 10, while question 8 carries a maximum of 30. Scores are summed to give a total out of 100. For question 8, participants must answer only part A, B, or C. The maximum score possible, which corresponds to an asymptomatic athlete, is 100 points. The theoretical minimum is 0 points.

Follow-up was done at end of 4, 12 and 20 weeks. Collected data were checked for completeness and consistency. Statistical analysis was done usingIBM-Statistical Package for the Social Sciences (IBM-SPSS) Version 21. For descriptive statistics mean, standard deviation and frequency were used. Continuous variables (age, duration of symptoms, VAS, VISA-P) were analysed by student's t-test. Categorical variables (gender, side of affection) were analysed using Chi-square test. Within the group comparison (baseline and follow-up data of each group) was done by Repeated measures ANOVA test. Between the groups comparison (intervention group and control group) was analysed using student's t-test. A p-value <0.05 was taken as significant.

Ethical approval of the Research Ethics Board, RIMS, Imphal was taken for this clinical study.

Results:-

VISA-P Score

In the PRP group, within group comparison showed statistically significant improvement in VISA-P score from baseline at all follow ups ($p = 0.00$). While in the ESWT group, maximum improvement was seen from baseline to 1st follow up at 4 weeks ($p = 0.01$). However subsequent follow up showed reduction in VISA-P Scores but remained above the baseline value and it was statistically significant ($p = 0.01$). (Table III).

Between the group comparison showed statistically significant improvement in VISA-P scores in both the groups but was found to be better in the PRP group and this was statistically significant ($p <0.05$) (Table IV).

Visual Analog Scale (VAS)

In the PRP group, within group comparison showed significant reduction in VAS scores at all follow up (p = 0.00) (Table III). In the ESWT group, within group comparison showed reduction in VAS score was seen at 4 weeks, however the VAS score gradually increased again but remained below baseline level (p = 0.02) (Table III).

Between the groups comparison shows statistically significant reduction in VAS scores in both the groups. However, the reduction was more in the PRP group at 6 months (Table IV).

Table I:- Comparisons of background characteristics between the between PRP group (study) and ESWT group (Control) at baseline.

Characteristics	Group		p-value
	Intervention Group	Control group	
Mean Age (years)	24.77 ± 6.156	26.82 ± 4.182	**0.204***
Mean duration of symptoms (months)	6.09 ± 2.18	7.22 ± 2.40	**0.108***
Gender			
Male	12	14	**0.760****
Female	10	8	
Side of Affection			
Right	16	13	
Left	6	9	**0.526****

*Independent t test, **Chi-square test, p value <0.05 taken as significant

Table II:- Comparisons of baseline dependent variables between the between PRP group (study) and ESWT group (Control).

Characteristics	Group		p-value*
	Intervention Group (Mean ± SD)	Control group (Mean ± SD)	
VAS	6.73 ± 0.985	6.68 ± 1.086	**0.885**
VISA-P	46.45 ± 8.92	50.64 ± 7.92	**0.10**

*Independent t test, p value <0.05 taken as significant.

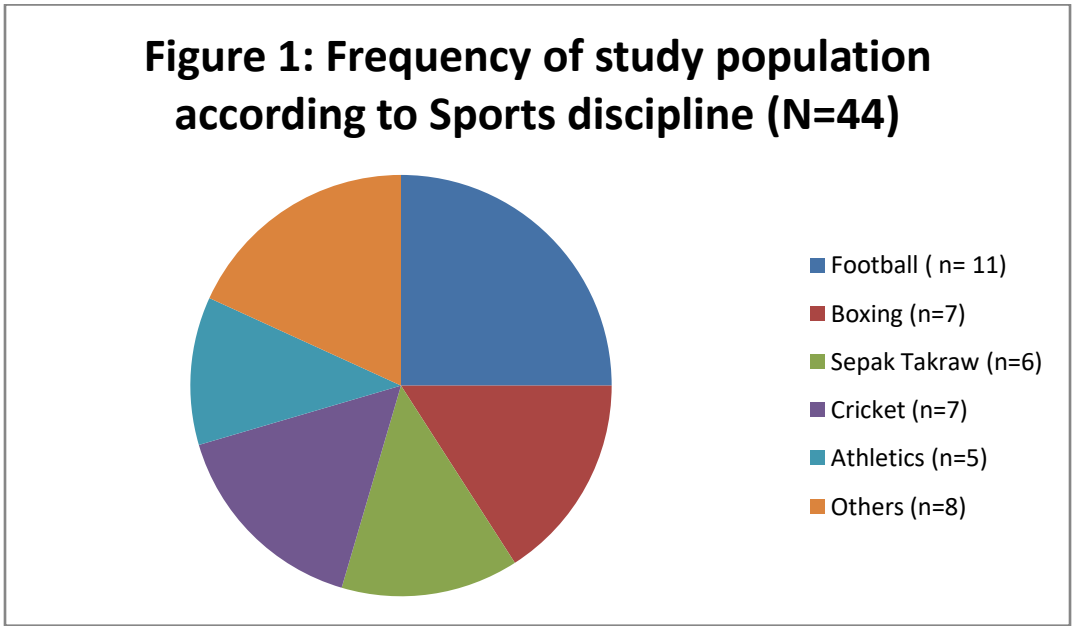

Table III:- Within the group comparison of outcome measures in both groups.

Outcome measures	Study groups	Baseline	4 weeks	12 weeks	24 weeks
VAS	**Intervention (PRP)**	6.73 ± 0.985	5.22 ± 0.752	3.41 ± 0.959	1.55 ± 0.858
	p value*		0.00		
	Control (ESWT)	6.68 ± 1.086	2.59 ± 0.666	3.27 ± 0.827	5.82 ± 0.958
	p value*		0.02		
VISA-P	**Intervention (PRP)**	46.45 ± 8.92	51.81± 7.27	66.36 ± 4.43	84.18 ± 4.27
	p value*		0.00		
	Control (ESWT)	50.64 ± 7.92	64.63 ± 5.63	58.90 ± 7.60	52.54 ± 7.61
	p value*		0.01		

*Repeated measures ANOVA, p-value < 0.05 is taken as significant

Table IV:- Comparisons of mean difference changes from baseline in outcome measures between PRP group (study) and ESWT group (Control).

OUTCOME MEASURE	FOLLOW UP	Intervention Group (Mean ± SD)	Control group (Mean ± SD)	p- value*
VAS Score	4 weeks	1.50 ± 0.91	4.09 ± 1.34	0.00
	12 weeks	3.31 ± 1.32	3.40 ± 1.53	0.03
	24 weeks	5.18 ± 1.29	0.86 ± 1.08	0.03
VISA-P	4 weeks	-5.36 ± 3.28	-14.00 ± 6.41	0.02
	12 weeks	-19.90 ± 7.39	-8.27 ± 7.76	0.00
	24 weeks	-37.72 ± 9.32	-1.90 ± 3.72	0.00

*Independent t test, p value <0.05 taken as significant

Discussion:-

Patellar tendinopathy is a common painful overuse disorder. Although many different treatment modalities have been described, there is no consensus on the optimal treatment for this condition. This single blinded randomized controlled trial aimed to investigate the possible beneficial effects of ultrasound guided PRP injection in comparison with extracorporeal shock wave therapy on improving pain and function in individuals with patellar tendinopathy. We compared the effects on pain by measuring the VAS while functional assessment was done with the help of the VISA-P score.

Several treatment options have been described in the literature, such as rest, anti-inflammatory drugs, eccentric exercises, injections, and surgical treatments. Extracorporeal shock wave therapy and PRP injections seem to be a safe and promising part of the rehabilitation program for patellar tendinopathy, although, given current knowledge, it is impossible to recommend a specific treatment protocol. Both treatments share the same disputes: lack of hard evidence through randomized clinical and no standardized treatment protocols. In 2009, van Leeuwen et al[6] published a review about ESWT for treating patellar tendinopathy. Only 7 studies were included in the review, and all of them concluded that ESWT seems to be an effective treatment for patellar tendinopathy with an estimate of approximately 74.7% of patients resulting in improvement of pain and knee function.

But the findings should be interpreted with caution since only 2 of 7 studies boasted a high methodological quality. In a randomized clinical trial in 2011 by Zwerver et al,[7] the effectiveness of ESWT on patellar tendinopathy was evaluated in 62 actively competing jumping athletes during the competitive season, and the investigators reported no benefit over placebo treatment over the 22-week study period.

With several studies suggesting tendinopathy to be a degenerative condition, PRP is an emerging regenerative, minimally invasive treatment modality for the treatment of various tendinopathy. The 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 and synthesize more growth factors for

several days during their lifespan. PRP injection to the affected site provides it with healing growth factors that in turn promote tendon proliferation, collagen synthesis and vascularisation invitro and invivo.[8,9]

In a randomized controlled trial conducted by Vetrano et al,[2] improvement in both PRP and ESWT groups was found in the short term (4-8 weeks) and mid term (6, 12 weeks follow up), however the PRP was more superior to ESWT in all clinical outcomes at midterm follow up. A prospective cohort study[10] evaluated the outcome of 36 patients with patellar tendinopathy treated with PRP injections, examining the differences between a group of patients receiving previous treatment that failed (injection of steroids, injection of polidocanol, and/or surgical treatment) and another group that received no prior therapy. The PRP treatment resulted in statistically significant improvement mainly in the group of patients who were not treated before, showing largest healing potential.

Our study found that within group comparison showed significant improvement in VAS and VISA-P at all follow ups in the PRP group while significant improvement in the ESWT group was found only at 4 weeks and thereafter in subsequent follow up at 12 and 24 weeks, there was increase in VAS score and reduction in VISA-P scores but these remained better than those at baseline. In an analysis, comparing the mean difference changes in outcome measures scores from baseline to all follow up, significant and maximum improvement in VAS and VISA-P scores was found at 24 weeks in the PRP group while maximum improvement was seen at 4 weeks follow up in the ESWT group.

The PRP injections may have a multifaceted mechanism of action involving platelet action as well as injection-related effects. Several studies have shown that needling of tendino pathic tissue has a positive effect itself on tendon healing.[11,12] Injections change the pressure- volume relationship in a given anatomic space, and these local mechanical effects are hypothesized to destroy pathological vascular and neural growth. All these factors inherent in the route of administration of PRP may enhance the biological mechanisms and increase the tendon healing response. All these reasons, as well as the relatively low age and the high motivation of the patients in our study, could possibly justify the better action of PRP than ESWT.

In conclusion, from this study we can infer that even though both PRP injections and ESWT are safe and effective in the treatment of athletes with patellar tendinopathy. PRP injection under ultrasound guidance was significantly more effective on improving pain and function than ESWT in the midterm (6 months).

Limitations:
This study has the following principal limitations: (1) small number of patients enrolled, (2) lack of a placebo control group, and (3) although the assessment was blinded, there was no way to blind the patients to the treatment. Therefore, it is possible that their awareness of the treatment modality may have had some effect on their perception of their response to the treatment.

Ethical Issues:
Ethical clearance was obtained from the Institute's Ethical committee

Financial Support & Sponsorship:
No financial support or sponsorship.

Conflicts Of Interest:
None.

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