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Compare the Efficacy of Eccentric Exercises Integrated with either Ultrasound-Guided Leukocyte-Rich PRP Injection (Including Dry Needling) or Ultrasound-Guided Dry Needling Alone: Case Series

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Abstract

➢ ***Background***

As already well known, patellar tendinopathy symptoms are recovered after the injections of platelet-rich plasma (PRP), still to date, rarely few studies have worked on comparison of PRP with dry needling (DN) for this condition.

➢ ***Purpose***

To compare the efficacy of eccentric exercises integrated with either ultrasound-guided leukocyte-rich PRP injection (including dry needling) or ultrasound-guided dry needling alone in the treatment of patellar tendinopathy.

➢ ***Study Design***

Retrospective, nonrandomized, open label, comparative case series included 50 patients of PT visited at Era's medical college, Lucknow, Uttarpradesh between October 2018 to October 2019.

➢ ***Methods***

As per exclusion and inclusion criteria, the patient was recruited in the study after diagnosed by clinical investigation and magnetic resonance imaging. Patients (n=50) divided into two groups and received ultrasound-guided DN alone (DN group; n = 23) or with the injection of leukocyte-rich PRP (PRP group; n = 27), along with standardized eccentric exercises. After treatment during further follow-up visits (at baseline, 12 and 26 weeks) enrolled patients were asked to complete patient-reported outcome questionnaires. Victorian Institute of Sports Assessment (VISA) scores, the visual analog scale (VAS) for pain. Tegner activity scale, Lysholm knee scale, and short form (SF-12) questionnaire were the outcome parameter that was estimated at baseline and follow up visits.

➢ ***Results***

There was a significant difference in the mean VISA score for DM group (M=4.2, SD=1.3) and PRP group at the baseline (*P*=<0.001) and after 12 weeks (*P*=0.001) and 26 weeks (*P*=<0.001) of treatment. Similarly, the mean Lysholm score was significantly more evident in DM group compared to the PRP group after 26 weeks (*P*=<0.001) of treatment. Controversy, the mean Lysholm score was significantly less evident in the DM group compared to the PRP group at baseline (*P*=<0.001) and after 12 weeks (*P*=0.001) of treatment. SF-12 score was significantly higher in DM group compared to the PRP group at baseline (*P*=0.015) and, in further follow-up, it was not significantly different.

➢ ***Conclusion***

Remedial of standardized eccentric exercise and ultrasound-guided leukocyte-rich PRP injection with DN group induces the improvement in symptoms of patellar tendinopathy compared to ultrasound-guided DN alone, but over time, the explicit advantage of PRP disappeared.

Keywords:- *Tendinopathy; Eccentric Exercise; Platelet-Rich Plasma; Ultrasound-Guided Dry Needling; Victorian Institute of Sports Assessment Score.*

ABBRIVATIONS

- PRP: Platelet-Rich Plasma
- DN: Dry Needling
- VISA: Victorian Institute of Sports Assessment score
- VAS: Visual Analogue Scales
- SF-12: Short Form–12

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I. INTRODUCTION

Patellar tendinopathy (PT) also termed as patellar tendonitis or tendinitis, is a degenerative disorder of the patellar tendon leading to anterior knee pain accompanying with focal and palpable tenderness at the inferior pole of the patella. Typical findings in magnetic resonance imaging show smaller tendon cross-sectional region, anomalies of the posterior border of the patellar tendon and infrapatellar fat pad. PT often labelled as "jumper's knee because it usually occurs in athletes who involved in the sports activity. PT is highly predicted in male compared to female. Factors that trigger the development of PT were mainly classified into two groups: intrinsic and extrinsic. Gender, ethnicity, genetics, bone structure and density, muscle length and strength, joint range of motion, diet, and body composition are the intrinsic factors defined as those included within a person, whereas, training volume (frequency, duration, and intensity), types of conditioning activities, specific sport activity, training surface, shoes, and environmental conditions are the extrinsic factors described as those remains outward of a person [1].

The management of PT has been somewhat complicated due to the unavailability of efficient treatment options. Over the past two decades, eccentric quadriceps exercise has been the mainstay in the therapy of PT [2-9]. Jonsson et al [10] compared eccentric versus concentric exercises in PT and, from his study hypothesized that a statistically significant improvement in visual analogue scores (VAS) and Victorian Institute of Sports Assessment (VISA) scores with the eccentric group was observed yet, improvement was not noticed within the concentric group. Although, several clinical studies investigating eccentric exercises in PT were systematically reviewed and revealed no significant improvement in come back to activity [11]. As concluded, there is a paucity of evidence to endorse eccentric exercise in PT therapy regimens.

In almost treatment algorithm, eccentric exercises remains a backbone, yet several patients are unsuccessful in the improvement and require further treatment. Usually, inflammation is less or absent in case of PT, so ibuprofen and other nonsteroidal anti-inflammatory drugs are not useful [12]. Similarly, however, glucocorticoids may be efficient in the treatment of acute tendon inflammation by inhibiting collagen production and, thereby contributing to poor long-term outcomes in PT [13].

With the advent of time, newer therapeutics have emerged focusing on sclerotherapy (inhibition of neovascularization by intratendinous injection of substances), prolotherapy and platelet-rich plasma (stimulate tendon repair) and acupuncture, shock wave therapy (improve pain through other pathways). Recently published studies have postulated the use of aprotinin [14], corticosteroids [15], and sclerosing [16] injections in PT. In literature, there was the paucity of data to assist the efficacy of prolotherapy, sclerotherapy, matrix metalloproteinase inhibitors, acupuncture, or shock wave therapy in the treatment of PT [17]. One reported study was in favour of the treatment regime of ultrasound-guided dry needling (DN) with autologous blood injection in terms of VISA score [18].

In new research era, the studies on regenerative medicines are going on in the treatment of tendinopathy. As expected, they may capable to reverse the process of degeneration. Use of PRP is widely spread across the sports orthopaedic physicians for growth factor release. It is an autologous blood fraction loaded with platelets. One of the reasons to use PRP in PD is that platelets are initially reached at the area of tissue injury and thereby potentiate to liberate growth factors that play a crucial role in the healing process [19]. Since the 1970s, PRP is used and studied; recently interest is increasing in using PRP for injuries related to sport [20] and nowadays, usually practiced worldwide [21]. Since PRP is an autologous blood product, no higher risks such as immunological reactions and transmission of the disease are associated with it, but as with any injection procedure, a local anesthesia reaction, infection and bleeding may occur. The study was aimed to compare the efficacy of eccentric exercises integrated with either ultrasound-guided leukocyte-rich PRP injection (including dry needling) or ultrasound-guided dry needling alone in the treatment of PT that has failed to respond to at least 6 weeks of physical therapy.

II. MATERIALS AND METHODS

This retrospective, nonrandomized, open label, comparative case series was performed at Era's medical college, Lucknow, Uttarpradesh. The study was conducted in accordance with the Helsinki Declaration of 1975 and patient consent was taken prior to enrolment in the study.

In total, 50 patients who were diagnosed with PT during October 2018 to October 2019 were enrolled in the study. The diagnosis of PT was made by clinical examination and later on, confirmed by magnetic resonance imaging. Patients with age more than 18 years, diagnosed with PT, and continuation of symptoms later 6 weeks (12 sessions) of physical therapy with eccentric exercise were included in the study. The patients who had taken the injection in past or faced surgery in the affected knee, not capable to fill patient-reported outcome questionnaires and not giving the consent were completely excluded from the study.

Clinically, tenderness to palpation at the inferior pole of the patella with the knee entirely extended and, the quadriceps relaxed is the typical representation of PT. The magnetic resonance imaging features consistent with PT included enhanced signal intensity in the proximal patellar tendon, increased tendon size in the anteroposterior direction, and poor definition of the posterior tendon border. Nonsteroidal anti-inflammatory drugs should be avoided for 4 weeks before and after treatment.

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As per treatment protocol, patients (n=50) classified into two groups.

Group I: DN group (n=23), received ultrasound-guided dry needling alone, along with standardized eccentric exercises
Group II: PRP group (n=27), received ultrasound-guided dry needling with PRP, along with standardized eccentric exercises

➢ *Ultrasound-Guided Dry Needling and PRP*

For all patients, regardless of treatment group, 55 mL of peripheral blood was obtained through venipuncture by a certified nurse. Then, for PRP group patients, blood was processed with a GPS III (Biomet Inc, Warsaw, Indiana, USA) PRP kit as per instructions provided by manufacturer. In the DN group patients; the 55 mL of blood was discarded. For all patients, a, through ultrasound and patient's response, trained radiologist identified the region of tendinopathy and, then injected 3 mL of 0.25% bupivacaine with 1:100,000 epinephrine subcutaneously using sterile technique. Do not anaesthetize the tendon or tendon sheath by considering this proper care should be taken. The radiologist was 10 times penetrating the tendinopathy area. To resume weight-bearing as tolerated was advised to patients.

➢ *Eccentric Exercises*

Each patient was informed to attend a standardized 5-phase program of eccentric exercises that was provided directly to their physiotherapist. On the basis of current abilities, every patient was evaluated to decide appropriate starting phase. Treatment strategies centered on eccentric strengthening and improving flexibility, cardiovascular fitness, balance, core strength, and sport-specific skills. Patients recommended physical therapy twice a week and were directed to do standardize extra home-based exercises during the entire study period. Physiotherapists directly updated orthopedics for patients' overall progress.

➢ *Outcome*

Complete written questionnaires were taken from participants at baseline and further follow-up appointments at 12 weeks and 26 weeks. The most significant patient-reported findings were the VISA score at 12 weeks, as the VISA is a standardized questionnaire that, can be used for quantitative evaluation the severity of symptoms, especially, in patients with PT. [22]. The second most important patient-reported findings were Tegner activity scale (Tegner) [23], Lysholm knee scoring scale (Lysholm) [24], visual analogue scales for pain (VAS) [25] and Short Form–12 (SF-12) measurement of quality of life concerning health [26] at 12 weeks and 26 weeks.

➢ *Statistical Analysis*

The data analysis was done by SPSS 21 (IBM, Armonk, NY, USA), at the significance level of 0.05; quantitative and categorical data were expressed as mean±standard deviation and frequency (percentage), respectively. To compare continuous parametric variables, unpaired 2-tailed T-test was used, whereas, the categorical variable was compared using the Chi-square test. Unpaired 2-tailed t-tests were used, to compare the mean change at baseline, 12 weeks and 26 weeks between the two treatment groups (DN vs PRP).

III. RESULTS

Out of 50 patients, 23 patient enrolled in the DN group and the remaining 27 patients enrolled in the PRP (n = 10) groups. After 12 weeks, all patients had completed treatment in both groups were included in the preliminary analysis; their characteristics are compiled in **Table 1**. Patient's sex, Tegner and VAS score were similar between two groups. However, the mean age, height, weight, baseline VISA score, Lysholm and SF-12 were significantly different among DN group and PRP group with *P*-value <0.001**,** <0.001, 0.004, <0.001, <0.001 and 0.015, respectively. **Table 2** demonstrated mean VISA, Tegner, Lysholm, VAS, and SF-12 scores at baseline, 12 weeks and 26 weeks for the DN and PRP groups. Mean VISA score was significantly higher in DM group compared to the PRP group at the baseline (*P*=<0.001) and after 12 weeks (*P*=0.001) and 26 weeks (*P*=<0.001) of treatment. Similarly, the mean Lysholm score was significantly higher in DM group compared to the PRP group after 26 weeks (*P*=<0.001) of treatment. Controversy, the mean Lysholm score was significantly less in the DM group compared to the PRP group at baseline (*P*=<0.001) and after 12 weeks (*P*=0.001) of treatment. SF-12 score was significantly higher in DM group compared to the PRP group at baseline (*P*=0.015) and, in further follow-up, it was not significantly different.

For the DM group, the mean VISA score of 47.52±1.27 at baseline rapidly increased to mean VISA score of 56.23±7.57 after 12 weeks of treatment and then further increased to mean VISA score of 81.78± 4.41 after 26 weeks of treatment. A similar observation was visible for the PRP group in graphical representation **(Fig. 1 and 2)**. In detail, the trend of change in VISA, Tegner, Lysholm, VAS and SF-12 score at Baseline, 12 weeks and 26 weeks of treatment for both DN group and PRP group were graphically illustrated in **Fig. 1 and 2**. SF-12 score was significantly higher in DM group compared to the PRP group at baseline with *P*-value 0.015.

IV. DISCUSSION

Verdicts obtained from the current study points out that a therapeutic regimen of DM group, as well as the PRP group, were accelerated the recovery from PT, but ultimately the advantages of PRP disappeared over time.

Based on the (VISA) function and stability (Lysholm) of PT symptoms, the statistical comparison among the two groups at 12 weeks revealed that the PRP group improved more significantly than the DN group. Nonetheless, these advantages of PRP had disappeared at 26 weeks. Later on, the DN group also displayed statistically and clinically significant improvements on the Lysholm knee questionnaire at 26 weeks, whereas, the PRP group not obtained statistically significant achievements in any

scoring system. In summary, overall, the DM group had improved more compared to the PRP group.

Victorian Institute of Sport Assessment (VISA) questionnaire was created to evaluate symptoms among patients diagnosed with PT comprising brief questionnaire related to symptoms, simple tests of function and athletic performance. On a visual analogue scale from 0-10, six of the eight questions are scored and, 10 scores are representing optimal health. The maximal VISA score is 100 points for healthy individuals and, 0 points indicates the theoretical minimum value [22]. VISA score is the central outcome scale, in our study. Based on this measure, we inferred that PRP seems to accelerate recovery from PT relative to dry needling but, does not influence the patient's outcome at a minimum of 6 months.

The VAS pain is a unidimensional pain intensity meas ure that has been widely accepted in different rheumatic dis eases [25]. Nowadays, the Tegner activity score has become a famous patient-administered activity rating system for patients with various knee disorders. Based on work and sports, Tegner activity scale graded activities on a scale of 0 to 10. Zero signifies disability due to knee problems and, 10 represents national or international level soccer [26]. In the present study, the improvement in VAS pain score and Tegner activity scale was observed is in favors of finding reported by Kon et al [27] Filardo et al [28] and Dragoo et al [29].

The 12-item short-form survey (SF-12) is a public health survey, in 1995; it was first published, as part of the medical outcomes study. This information will aid the doctors to know how you feel and how well you can do your normal activities. In our study, this score is improved in both the DM group and the PRP group [26].

Our study reflects the advantageous effects of PRP relative to alternative treatments like dry needling were most prominent in the first few weeks and, later on, by 26 weeks, this advantage was diminished, at which time dry needling gave the comparable improvement in PT symptoms. In contrast to our results, the study by Vetrano et al [30] showed a growing effect of PRP over time.

From these conclusions, it is obvious to raise a question in our mind: Why does PRP seem more efficient than DN initially, yet no contrasts over long-time follow-up?

Over time, the effect of a single PRP injection may fade; perhaps this is the problem reason to justify this issue. Many other reported studies used 2 or more PRP injections and, their findings are controversial from our findings [27, 30]. In the current study, we used a single PRP injection or dry needling treatment. The second possible reason behind this is that high leukocyte content of the PRP used in our study [31] provoked extremely strong inflammatory response in the initial weeks after treatment; quicken the recovery of the PRP group related to the DN group within the first 12 weeks after treatment. Perhaps over time, the advantage of this early inflammatory response has diminished. This matter is evident by histological studies was performed in animals by Dragoo et al [31].

Here, we graphically represented the trend of change in the previously mentioned score at baseline, 12 weeks and 26 weeks of treatment for both the DM group and the PRP group. This will help to understand the pattern of the shifts in their ratings over time.

One of the major drawbacks of this study is that after treatment anatomic tendon changes by ultrasound or magnetic resonance imaging was not documented. Also, more youthful patients in the PRP group may become a matter of debate. The higher concentration of growth factors is present in the PRP generated from youthful patients, responsible for a more beneficial effect in younger patients compared to the older one. Likewise, ageing tendon fibroblasts may be less responsive to PRP or other treatment modalities. Tegner activity level is inversely associated with age, was postulated in many studies, while, in the present study, Tegner scores were not different between two groups, despite the age difference. As obvious, the study is retrospective in nature can be biased, in future randomized controlled trials with greater sample size is recommended.

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FIGURE AND TABLE

Characteristics	Group I:DN (n=23)	Group II:PRP(n=27)	*P*-value
Age, (mean± SD) (range), years	37.83±2.19(34-41)	28.26±2.80(23-35)	<0.001***
Male, n(%)	15(65.22)	19(70.37)	0.700
Height, in.	62.62±1.35(60-66)	64.84±2.19(62-69)	<0.001***
Weight,(mean± SD) (range), kg	76.04±4.05 (69-84)	79.93± 4.87(69-86)	0.004*
Baseline scores,(mean± SD) (range) VISA Tegner Lysholm VAS SF-12	 47.52±1.27(45-49) 3.60±0.50(3-4) 47.00±1.28(45-49) 3.43± 0.51(3-4) 48.87± 1.69(45-51)	 42.52±1.99(40-47) 3.59±0.50(3-4) 56.04±2.14(52-59) 3.44± 0.51(3-4) 47.26± 2.63(44-51)	 <0.001*** 0.944 <0.001*** 0.945 0.015*

Table 1:- Characteristics of Participants Included in the Study

† SD, Standard Deviation. SF-12, Short Form–12.VAS, Visual Analog Scale. VISA, Victorian Institute of Sports Assessment. **P*- value <0.05 considered being significant. *** *P*- value <0.001 considered being significant.

	Baseline			12 weeks			26 weeks		
	Group I: DN (n=23)	**Group II: PRP (n=27)**	***P***	**Group I: DN (n=23)**	**Group II:PRP (n=27)**	***P***	**Group I:DN (n=23)**	**Group II: PRP (n=27)**	***P***
VISA	47.52±1.27 (45-49)	42.52±1.99 (40-47)	<0.001***	56.23±7.57 (40-66)	65.33±10.36 (53-79)	0.001***	81.78± 4.41 (75-89)	68.52±9.22 (52-84)	<0.001***
Tegner	3.60±0.50 (3-4)	3.59±0.50 (3-4)	0.944	3.73± 0.45 (3-4)	3.74± 0.45 (3-4)	0.938	5.83±0.78 (5-7)	6.11± 0.89 (5-7)	0.247
Lysholm	47.00±1.28 (45-49)	56.04±2.14 (52-59)	<0.001***	74.87± 9.03 (62-87)	84.30± 9.96 (65-96)	0.001***	88.23± 5.19 (80-100)	67.15± 10.06 (50-86)	<0.001***
VAS	3.43±0.51 (3-4)	3.44± 0.51 (3-4)	0.944	2.78± 0.67 (2-4)	2.48± 0.75 (2-4)	0.146	0.91± 0.73 (0-2)	0.78±0.70 (0-2)	0.524
SF-12	48.87±1.69 (45-51)	47.26±2.63 (44-51)	0.015*	50.22± 2.71 (46-58)	50.74± 3.99 (44-58)	0.599	49.78± 1.73 (45-53)	51.04± 2.90 (44-56)	0.074

Table 2:- Scores for the Dry Needling (DN) and Platelet-Rich Plasma (PRP) Groups[#]

† SD, Standard Deviation. SF-12, Short Form-12.VAS, Visual Analog Scale. VISA, Victorian Institute of Sports Assessment.

#Values are reported as mean ± standard deviation (range). *P-value <0.05 considered being significant. *** P-value <0.001 considered being significant.

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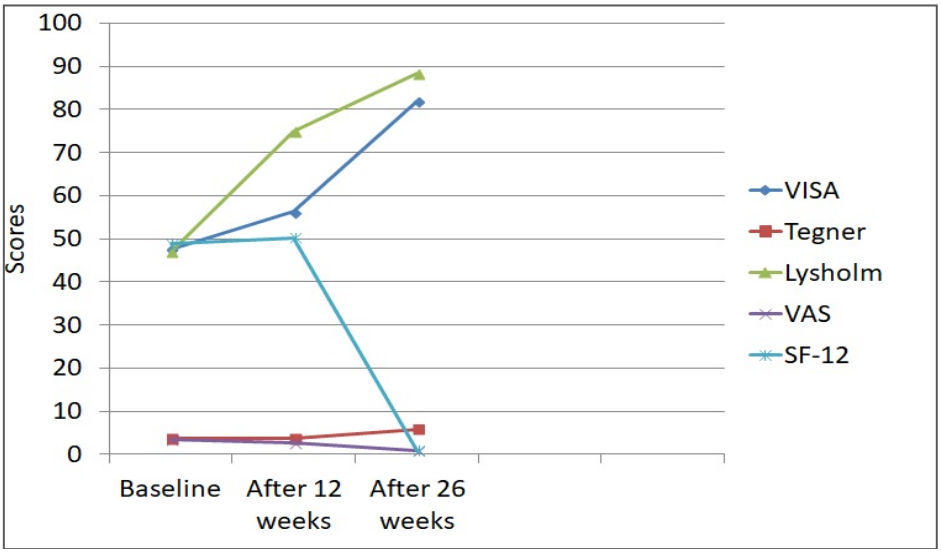

Fig 1:- Trend of change in VISA, Tegner, Lysholm, VAS and SF-12 score at Baseline and after12 weeks and 26 weeks of treatment, for DN group.

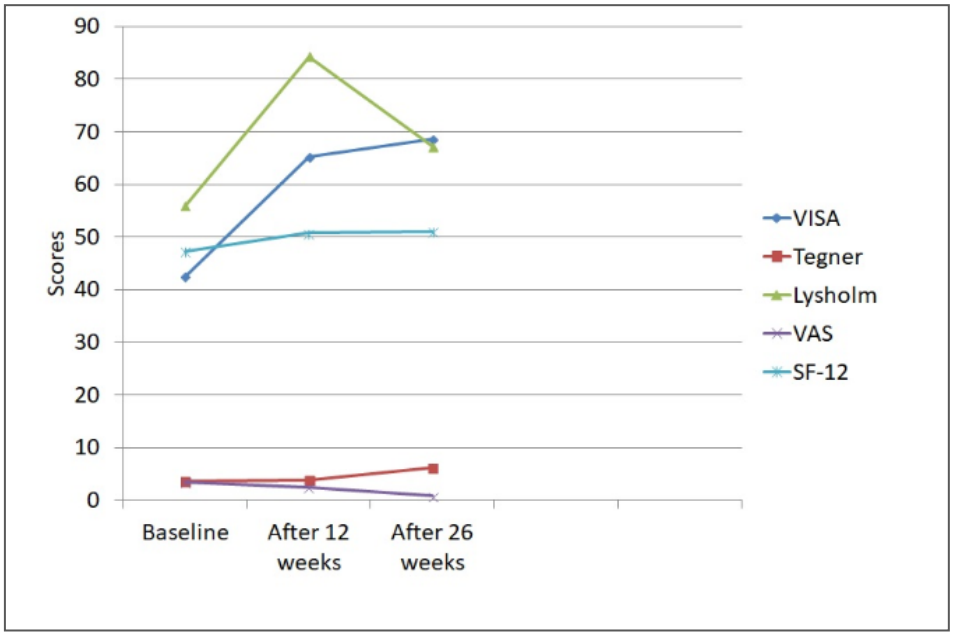

Fig 2:- Trend of change in VISA, Tegner, Lysholm, VAS and SF-12 score at Baseline and after12 weeks and 26 weeks of treatment, for PRP group.