

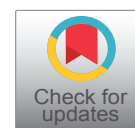


REVIEW ARTICLE

Effectiveness of Ultrasound Guided Platelet Rich Plasma Injection in Comparison with Corticosteroid Injection on Improving Pain and Function in the Treatment of Biceps Tendinopathy: A Randomized Controlled Trial

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Abstract

Title: Effectiveness of Ultrasound Guided Platelet Rich Plasma Injection in Comparison with Corticosteroid Injection on Improving Pain and Function in the Treatment of Biceps Tendinopathy: A Randomized Controlled Trial.

Background: Bicipital tendinosis is an inflammatory process of the long head of the biceps tendon and is a common cause of shoulder pain due to its position and function. Patients with biceps tendinitis often complain of a deep, throbbing pain in the anterior shoulder that is intensified when lifting and usually localized to the bicipital groove. The first line of treatment comprises nonoperative therapeutical means as rest, ice, restriction of overhead activities, nonsteroidal antiinflammatory drugs (NSAIDs), and physical therapy. Local anesthetic and corticosteroid injections have been advocated as additional treatment options but with known side effects. Platelet rich plasma (PRP) is believed to be a promising alternative safer and effective treatment option.

Objectives: To determine the effectiveness of ultrasound guided Platelet rich plasma injection in comparison with corticosteroid injection on improving pain and shoulder function in the treatment of biceps tendinopathy.

Study design: Randomized controlled trial.

Methods: Thirty two athletes with biceps tendinopathy meeting the inclusion and exclusion criteria were selected for this study and randomized into 2 treatment groups: platelet rich plasma injection under ultrasound guidance (PRP group; n = 16), and corticosteroid injection under ultrasound guidance (CS group; n = 16). The outcome

measures were visual analog scale (VAS) and Single Assessment Numerical Evaluation (SANE) for pain and Quick DASH for assessment of shoulder function. Both the groups underwent rehabilitation programs. 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 group 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 the group comparisons showed significant improvement in outcome measures in the PRP group at all follow ups. In the Corticosteroid group, improvement in outcome measures was found only at 4 weeks and 12 weeks follow up. Between the groups comparisons showed that the improvement in outcome measures was more in the corticosteroid group in the short term i.e. at 4 weeks and 12 weeks. However, over the long term, PRP was found to be superior to corticosteroids in improving outcome measures at 24 weeks.

Conclusion: Ultrasound guided injection of platelet rich plasma lead to significant improvement in pain and function over the long term in comparison with corticosteroid injection in athletes with Biceps tendinosis and thereby enabling faster return to sports.

Keywords

Biceps tendinosis, Platelet rich plasma, Corticosteroid, Ultrasound, Quick DASH, VAS, SANE

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Introduction

The long head of the biceps (LHB) brachii tendon originates at the supraglenoid tubercle and superior glenoid labrum. Its labral origin is mostly posterior in over half of cases. Inside the joint, the tendon is extrasynovial and passes obliquely, heading toward the bicipital groove. The LHB tendon distally joins the short head of the biceps (SHB) tendon as both transition into their respective muscle bellies in the central third of the upper arm, and after crossing the volar aspect of the elbow, inserts on the radial tuberosity and medial forearm fascia. The latter occurs via the bicipital aponeurosis [1].

The bicipital groove is an anatomic landmark that sits between the greater and lesser tuberosities and serves as a critical location of proximal biceps stability. The soft tissue components of the groove create a tendo-ligamentous sling to support the LHB tendon. They include portions of the rotator cuff muscles (subscapularis and supraspinatus), coracohumeral ligament (CHL), and the superior glenohumeral ligament (SGHL) [2].

Biceps tendonitis describes a clinical condition of inflammatory tenosynovitis, most commonly affecting the tendinous portion of the LHB as it travels within the bicipital groove in the proximal humerus. The continuum of clinical pathology ranges from acute inflammatory tendonitis to degenerative tendinopathy.

Primary bicipital tendonitis is much less common than cases where it is associated with concomitant primary shoulder pathologies (i.e., secondary cases). The etiologies for primary bicipital tendonitis are not well understood compared to the more common secondary presentations.

Secondary cases are much more common and have been described in the literature with increasing frequency dating back to at least the early 1980s. Associated shoulder pathologies include [2-4]:

- Rotator cuff tendonitis and tendinopathy
- Subscapularis injuries
- LHB tendon instability/dislocation
 - o Often seen in association with subscapularis injuries/tears
- Direct or indirect trauma
- Inflammatory conditions
- Internal impingement of the shoulder ("Thrower's" shoulder)
 - o Glenohumeral internal rotation deficit (GIRD)
 - o Superior labral lesions (the "peel-back" mechanism)
- External impingement/Subacromial impingement

syndrome (EI/SIS)

- Glenohumeral arthritis

The pathophysiology of LHB tendonitis/tendinopathy begins with the early stages of tenosynovitis and inflammation secondary to repetitive traction, friction, and shoulder rotation. Inflammation develops early on in the tendinous portion in the bicipital groove. The tendon increases in diameter secondary to swelling and/or associated hemorrhage, further compromising the tendon as it becomes mechanically irritated in its confined space.

The resultant increased pressure and specific sites of traction predispose the tendon to pathologic shear forces. In addition, the sheath of the biceps tendon is a direct extension of the synovial lining of the glenohumeral joint. Thus, concomitant or preexisting RC pathology can directly compromise the LHB tendon itself. In the early stages of the disease, the LHB tendon remains mobile in the bicipital groove.

As the pathophysiology escalates, there is an ensuing LHB sheath thickening, fibrosis, and vascular compromise. The LHB tendon undergoes degenerative changes, and associated scarring, fibrosis, and adhesions eventually compromise LHB tendon mobility. In effect, the tendon becomes pathologically "anchored" in the groove, further exacerbating the potential points of traction and overall increasing shear forces experienced by the LHB tendon along its course [2].

Numerous methods can be used for diagnosing biceps tendonitis. Patients with biceps tendonitis often complain of a deep, throbbing pain in the anterior shoulder that is intensified when lifting. The pain is usually localized to the bicipital groove and might radiate toward the insertion of the deltoid muscle [5]. A history of occupational or sports overuse trauma could be the cause of biceps tendonitis in patients. Pain from biceps tendonitis usually worsens at night, especially if the patient sleeps on the affected shoulder. Repetitive overhead arm motion, pulling, or lifting may also initiate or exacerbate the pain [6]. The pain is most noticeable in the follow-through of a throwing motion [7]. Instability of the tendon may present as a palpable or audible snap when range of motion of the arm is tested. In addition to obtaining the physical history of the patient, a physical examination in clinics can help us to differentiate biceps tendonitis from other possible causes of shoulder pain. The most common finding of biceps tendon injury is bicipital groove point tenderness [8]. During physical examination, the patient stands or sits with the arm at his or her side in 10 degrees of internal rotation. When the arm is in this position, the humeral head with the bicipital groove faces forward. External rotation of the arm and humeral head places the tender bicipital groove in a posterolateral position. This movement is one of the most specific findings of biceps tendon injury.

Other provocative tests are often used in evaluations, such as Speed's and Yergason's tests. The first evaluates the resistance force of the patient forearm by using a posture of shoulder flexion, elbow extension, and forearm supination; the second evaluates the forearm supination resistance by using elbow flexion. Both tests are defined as positive when the pain is provocative on the bicipital groove when using resistance force [2].

Although clinical physical examinations are easily performed in clinics and can be helpful for biceps diagnosis, their sensitivity and specificity are insufficient for a precise diagnosis. According to Chen, et al., Yergason's tests had a sensitivity of 32% and specificity of 78%, whereas Speed's tests had a sensitivity of 63% and specificity of 58% [9]. By contrast, ultrasound (US) examinations are more accurate. An US examination is also noninvasive and less expensive than magnetic resonance imaging (MRI) for evaluating soft tissue injuries but still offers the accuracy of a musculoskeletal US examination, which is comparable with MRI, and has a high accuracy [10,11].

The first line of treatment comprises nonoperative therapeutical means as rest, ice, restriction of overhead activities, nonsteroidal antiinflammatory drugs (NSAIDs), and physical therapy. Local anesthetic and corticosteroid injections have been advocated as additional treatment options, which may also help to differentiate the origin of shoulder pain [12]. Subacromial injections have been used for concomitant impingement symptoms, while intra-articular injections to the glenohumeral joint (GHJ) may also be beneficial to decrease the intra-articular biceps irritation. Injections directly to the bicipital groove are common for primary LHB tendinosis. Injections of corticosteroids provide symptomatic pain relief but there is no concrete evidence that triamcinolone/methylprednisolone can promote healing. The procedure is effective but only produces short term relief. Moreover, it is also accompanied by complications, such as local infections, in some cases even biceps tendon rupture in case of multiple injections [13].

Recent studies of platelet rich plasma (PRP) suggest it to be a promising alternative treatment option of shoulder tendinopathies and various other musculoskeletal conditions. Series of both in vitro and clinical studies have demonstrated the safety and efficacy of PRP in the treatment of various tendinopathies, most notably in lateral epicondylitis. PRP has been found to have several essential protein growth factors that initiate wound healing, including platelet-derived growth factors, vascular endothelial growth factor, and epithelial growth factor. Although the exact mechanism of action has not been detailed in the literature, there is mounting evidence that these growth factors play a primary role in tendon repair [14].

Therapeutic injections have been traditionally performed in a blind fashion, using the anatomical landmarks. However, imaging-guided injections have gradually gained popularity. In general, imaging guidance during shoulder injections has been reported to improve accuracy. Considering the literature is limited for injections for the treatment of bicipital tendinosis, this study was performed to compare the efficacy of PRP injection in comparison with the conventional corticosteroid injection with the help of ultrasound in the treatment of bicipital tendinosis.

Review of Literature

Moon YL, et al. [15] conducted a randomized comparative study to study Platelet-Rich Plasma therapy (PRP) and prolotherapy for shoulder pain and dysfunction related to symptomatic biceps tendinopathy, and to judge effective results. 100 cases that had significant inflammatory effusion of the biceps tendon (that was shown on MRI), and was refractory to conservative treatment. The cases were followed up for more than one year and were divided into 2 groups. The 1st group received PRP therapy; the 2nd group received prolotherapy under sonographic guidance. The study found that there was no significant difference between the 2 groups in the first month after the procedure. However, in the third, sixth and twelfth months after the procedure, the 1st group showed significant improved results for VAS, KSS, UCLA, and CSS scores compared to the 2nd group ($p < 0.05$).

Yisnnapopoulos CK, et al. [16] conducted a randomized controlled study to compare accuracy, patient discomfort, and clinical outcome of ultrasound-guided versus palpation-guided corticosteroid injections to the bicipital groove in patients with long head of biceps (LHB) tendinosis. Forty-four patients with primary LHB tendinosis were randomized into two groups (group A, $n = 22$; group B, $n = 22$). All patients underwent treatment with a single corticosteroid injection to the bicipital groove. Injections in group A were performed under ultrasound-guidance, while in group B using a palpation-guided technique. The duration of each procedure was recorded. To assess accuracy, ultrasound examination was performed in both groups after injection. Patient discomfort was evaluated with visual analogue scale (VAS) for pain. The clinical outcome was assessed comparing the VAS, the Single Assessment Numeric Evaluation (SANE) score and the Quick DASH score before treatment and after 4 weeks and 6 months. Injection accuracy in group A was 100% and in group B 68.18%. Discomfort was lower in group A, as compared to group B (22.10 vs. 35.50; $p < 0.001$). Symptoms, as measured by VAS, SANE and Quick DASH scores, improved in both groups at 4 weeks and 6 months ($p < 0.05$). Superior clinical improvement was recorded in group A in both time points ($p < 0.05$).

Barker SL, et al. [17] conducted a study to find the effectiveness of ultrasound-guided platelet-rich plasma injection for distal biceps tendinopathy. Six patients with clinical and radiological evidence of distal biceps tendinopathy underwent ultrasound-guided platelet-rich plasma (PRP) injection. Clinical examination findings, visual analogue score (VAS) for pain and Mayo Elbow Performance scores were recorded. The Mayo Elbow Performance Score improved from 68.3 (range 65 to 85) (fair function) to 95 (range 85 to 100) (excellent function). The VAS at rest improved from a mean of 2.25 (range 2 to 5) pre-injection to 0. The VAS with movement improved from a mean of 7.25 (range 5 to 8) pre-injection to 1.3 (range 0 to 2). No complications were noted.

Serrania LC, et al. [18] conducted a non-randomized clinical trial to compare the efficacy of a single injection of PRP versus single peritendinous injection of methylprednisolone acetate in the treatment of chronic tendinopathy of the long portion of biceps. 26 patients with chronic tendinopathy of the long portion of brachial biceps refractory to pharmacological treatment and physical therapy were divided into two groups. One group received Single peritendinous PRP injection while the other group received single peritendinous injection of methylprednisolone acetate. Both groups received home physical therapy program. Visual analog pain scale (VAS), disability questionnaire (DASH), functional scale (Constant) were the main output measurement tools. The study found that in the PRP group a final mean VAS of 1 (initial VAS of 8) was obtained while the final EVA for corticosteroid group was 8 (initial EVA 9) at week 6 with a difference between groups of 6 ($p < 0.0001$ U of Mann-Whitney). DASH with an initial median of 57.5% and final 9.3% for the PRP group; initial median 58.3% and final 67.5% for the control group with a difference between groups of 57.4% ($p < 0.0001$ with MannWhitney U test). The study concluded that the peritendinous injection of PRP showed superiority in the decrease of pain and disability, as well as increase in the functionality of the affected shoulder.

Dadgostar H, et al. [19] conducted a randomized clinical trial study for evaluating the role of both corticosteroids and platelet-rich plasma (PRP) in the treatment of rotator cuff (RC) tendinopathies have been contradicting. 58 patients entered the study. Comparison of pain, range of motion (ROM), Western Ontario RC (WORC), Disability of Arm-Hand-Shoulder (DASH) scores, and supraspinatus thickness showed significant improvement during follow-ups in both groups ($p < 0.05$). During 3 months of follow-up, pain improvement was significantly better within the PRP group during (from 6.66 ± 2.26 to 3.08 ± 2.14 and 5.53 ± 1.80 to 3.88 ± 1.99 , respectively; $p = 0.023$). Regarding ROM, the PRP group had significant improvement in adduction ($20.50^\circ \pm 8.23^\circ$ to $28^\circ \pm 3.61^\circ$ and $23.21^\circ \pm$

7.09° to $28.46^\circ \pm 4.18^\circ$ for the PRP and corticosteroid groups, respectively; $p = 0.011$) and external rotation ($59.66^\circ \pm 23.81^\circ$ to $76.66^\circ \pm 18.30^\circ$ and $57.14^\circ \pm 24.69^\circ$ to $65.57^\circ \pm 26.39^\circ$, for the PRP and corticosteroid groups, respectively; $p = 0.036$) compared to the corticosteroid group. We found that PRP renders similar results to that of corticosteroids in most clinical aspects among patients with RC tendinopathies; however, pain and ROM may show more significant improvement with the use of PRP. Considering that the use of corticosteroids may be contraindicated in some patients and may be associated with the risk of tendon rupture, we suggest the use of PRP in place of corticosteroid-based injections among patients with RC tendinopathy.

Sanli I, et al. [20] conducted a prospective multicenter cohort study to assess the effectiveness of ultrasound (US)-guided injection of PRP in relieving pain and functional impairment in the treatment of refractory distal biceps tendonitis. Twelve patients from two large tertiary referral hospitals were recruited over a period of 20 months. Clinical diagnosis of distal biceps tendonitis was confirmed using magnetic resonance imaging. All patients had a single US-guided injection of PRP carried out by the two senior authors. Patients were objectively assessed for clinical and functional improvement using visual analogue (VAS) rest and activity pain scores, subjective satisfaction scale, elbow functional assessment (EFA) and isometric muscular (biceps) strength. Symptom severity and subsequent functional outcome were measured pre-injection and at final follow-up. At a median follow-up of 47 months (36-52 months), all patients showed significant improvement in pain ($p < 0.002$) and functional outcome ($p < 0.004$). Median resting VAS score improved from 6 (3-8) to 0.5 (0-2) and the activity VAS score improved from 8 (6-9) to 2.5 (0-4). EFA improved from 63 to 90. In the English cases, isometric muscular strength also showed significant improvement. All patients were satisfied with the clinical and functional outcomes at final follow-up.

Ibrahim DH, et al. [21] conducted a randomized comparative study to compare the efficacy of ultrasound-guided platelet rich plasma (PRP) versus corticosteroid injection for treatment of Rotator Cuff Tendinopathy (RCT). Thirty patients with RCT of the shoulder were randomly divided into 2 equal groups (15 each) treated by subacromial subdeltoid ultrasound-guided injection of PRP (group I) or corticosteroid (group II). Patients were evaluated using Visual Analogue Scale (VAS) for pain, functionally assessed using the Shoulder Disability Questionnaire (SDQ) and range of motion (ROM) determined before and 8 weeks after injection. Ultrasonographic findings of the patients were also reported. Patients mean age was comparable between both groups (group I: 46.8 ± 10.6 and group II: 41.5 ± 12.5 years). The VAS at baseline in group I (8.3 ± 1.1) and II (8.1 ± 1.2) significantly improved

after injection (2.3 ± 1.4 and 2.3 ± 1.3 ; $p = 0.0008$ and $p = 0.0009$ respectively). The SDQ significantly improved in group I (90.3 ± 9.5 to 24.3 ± 5 ; $p = 0.0009$) and group II (89.3 ± 7.3 to 23.3 ± 6.2 ; $p = 0.0007$) after injection. There was a significant improvement in both groups after injection regarding the ROM (flexion, abduction, extension, internal and external rotation). There was a significant improvement in the frequency of tendinitis/bursitis in group II (66.6%) vs. group I (50%) ($p = 0.0008$) while the improvement in the tear and effusion was higher in group I (66% and 60%) compared to group II (28.5% and 50%; $p = 0.0005$ and $p = 0.001$ respectively).

Niazi GE, et al. [22] conducted a single-arm interventional study to assess the effect of ultrasound-guided injection of platelet-rich plasma on patient symptoms and supraspinatus tendon thickness in cases of rotator cuff tendinopathy. 30 patients with age ranging between 27 and 54-years-old entered the study. Following US-guided injection of PRP, patients were evaluated clinically using the Shoulder Pain and Disability Index (SPADI) scoring system and radiologically using ultrasonographic supraspinatus tendon thickness measurements at 4, 8, 12, and 24 weeks. Our study showed remarkably noticeable changes when comparing the pre-injection and post-injection SPADI scoring system. There is highly statistically significant pain and disability score and percentage improvement, yet on the other hand, the radiological improvement shows no statistically significant difference found between baseline tendon thickness and its follow-up at 4, 8, and 12 weeks while only there was a statistically significant decrease in tendon thickness found at 24 weeks with P value = 0.043.

Castro BKC, et al. [23] conducted systemic review of a randomized controlled trial to investigate efficacy of conservative therapy on pain and function in people with tendinopathy-related shoulder pain. Searches were conducted on six databases. All randomized controlled trials investigating efficacy of any conservative therapy on pain and function in people with tendinopathy-related shoulder pain were included. Estimates for each specific conservative therapy were presented as weighted mean differences (WMDs) or mean differences (MDs), with 95% confidence intervals (CIs). Quality of the evidence was assessed using GRADE. Five randomized controlled trials were included. Extracorporeal shock-wave therapy (ESWT) was effective on pain at short-term (i.e., ≤ 3 months) when compared with control (WMD = -1.7 out of 101 points, -3.1 to -0.3; $n = 158$). Individual trials also suggested effects of non-steroidal anti-inflammatory drugs (NSAIDs) (-13.7 to -2.3; $n = 365$) and extracorporeal radial pressure pulse therapy (rESWT) (-40.0 to -27.0; $n = 79$). Laser therapy and ESWT were not effective on pain and function at short-term, respectively. No trials investigated medium- or long-term effects, and quality of the evidence ranged from low to very low quality.

Ibrahim VM, et al. [14] conducted a novel pilot study designed to explore the efficacy of PRP injections in the wheelchair population with biceps tendon pathology. Validated study outcomes included the Ultrasound Shoulder Pathology Rating Scale (USPRS), the Physical Examination of the Shoulder Scale (PESS), and the Visual Analogue Scale (VAS). Spinal cord injured athletes with chronic shoulder pain were recruited for this study. Members of the tetraplegic rugby and the wheelchair basketball teams at the National Rehabilitation Hospital were specifically targeted for recruitment because of the high prevalence (50%) of bicipital tendinopathy in this population. Participants in the study demonstrated ASIA Impairment Scale (AIS) scores of A-D for at least 1 year, shoulder pain for at least 6 months, and required the use of a manual wheelchair for the preceding year. Each participant enrolled underwent baseline analysis including USPRS, PESS, VAS, and functional scores. Participants then underwent a unilateral biceps tendon sheath injection of PRP and were followed every 2 weeks to monitor VAS scores and adverse events. The study was concluded at 8 weeks, when participants returned for repeat assessment of baseline parameters. The study analysis at this point includes 8 participants who have completed the full course of treatment and analysis. Despite this admittedly small sample size, there is remarkably convincing data on the effects of this intervention. Comparison of baseline and 8-week data using a non-parametric Wilcoxon signed ranks test demonstrated significant change in the non-injected shoulder on USPRS score ($Z = 2.207$, $P = 0.027$), in PESS score ($Z = 2.120$, $P = 0.034$), and in the VAS pain score ($Z = 2.041$, $P = 0.041$). An interesting link between level of education and injected arm USPRS score assessed at baseline was noted. Repeated measure general linear model analysis revealed statistical trends in the change of pain score measured via VAS at 5 time points (0, 2, 4, 6, and 8 weeks) for injected arm ($F = 6.68$, $P = 0.061$) but not for the untreated arm. No adverse reactions were reported during the study period.

Objectives

To determine the effectiveness of ultrasound guided Platelet rich plasma injection in comparison with corticosteroid injection on improving pain and shoulder function in the treatment of biceps tendinopathy.

Materials and Methods

Study design

Randomized Controlled Trial.

Study setting

Department of Sports Medicine, Regional Institute of Medical Sciences, Imphal. In a year, around 5500 patients are seen in the outpatient department Sports Medicine, out of which 8 to 10 percent present with shoulder pain.

Duration of study

1 year starting from June 2023.

Study population

Patients with shoulder 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 bicipital tendinosis
2. Age between 18 to 60 years of age
3. Failure of conservative treatment > 3 months
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 rotator cuff tear, GHJ deformity or rupture of LHB tendon on MRI
4. Uncontrolled systemic disease
5. Thrombocytopenia (< 1.5 lakhs/cumm)
6. Bleeding disorder
7. Pregnancy

Sample size

The total sample is 16 in each group.

The sample size is calculated using the formula:

$$N = \frac{(\sigma_1^2 + \sigma_2^2) \times [Z_{1-\beta} + Z_{1-\alpha/2}]^2}{(m_1 - m_2)^2}$$

$$N = \frac{(8^2 + 8.1^2) \times [0.84 + 1.96]^2}{(23.7 - 15.4)^2}$$

$$N = \frac{(129.61) \times [7.84]}{(8.3)^2}$$

N = 15

Where,

N = sample size

m_1 = mean Quick DASH in study group

m_2 = mean Quick DASH in the control group

σ_1 = standard deviation of Quick DASH in study group

σ_2 = standard deviation of Quick DASH in control group

$Z_{1-\alpha/2}$ = function of the confidence level = 1.96 at $\alpha =$

0.05, 95% confidence level

$Z_{1-\beta}$ = function of the power of the test = 0.84 at 80% power

Considering 10% drop out rate, sample size = 16

Total Sample size = 32

The sample size is calculated from a previous study conducted by Yiannakopoulos CK, et al. [16]

Working definition

Bicipital tendinosis is diagnosed:

1. Clinically, when there is pain and localized tenderness at the bicipital groove region, Speed test and Yergason test are found to be positive
2. On ultrasound examination, at least one of the following: (1) Tendon sheath swelling (transverse view: For women \geq 4.6, for men \geq 5.5 mm; longitudinal view: for women \geq 2.5, for men \geq 2.8 mm and (2) Tendon sheath fluid accumulation (abnormal hypoechoic or anechoic accumulation relative to the subdermal fat as adopted from Bruyn, et al. [24]

Recruitment and sampling

Patients presenting with shoulder pain meeting the inclusion and exclusion criteria, attending the Sports Medicine OPD on all working days were recruited. Convenience sampling was done for recruiting the patients until a sample size of 32 is reached.

Randomization

The patients were allocated after getting their informed consent into two groups namely, A = Intervention group and B = Control group by block randomization technique. Randomization was done by one staff nurse. A block size of four was used. Possible treatment allocations within each block are: (i) AABB; (ii) BBAA; (iii) ABAB; (iv) BABA; (v) ABBA; (vi) BAAB. Using computer generated table, a list of 8 blocks was prepared to reach a sample size of 32. Darting was done to select a block by using pen after closing the eyes. For each selected block, there was a sequence of treatment options. The sequence of treatment option in each block was put in an envelope and sealed. Corresponding envelope was labeled 1, 2, 3, 4... up to 8 according to appearance of treatment allocation in each selected block. The sealed envelope with label 1 was opened only when we have the first eligible patient and the treatment was allocated. A single blinding was done in which the assessor was blinded. The assessor was a senior resident of the department. The patients in group A were treated by ultrasound guided platelet rich plasma injection whereas patients in group B were treated by corticosteroid injection.

Study variables

Independent variables:

1. Age
2. Gender
3. Duration of symptoms
4. Sports discipline
5. Side of affection
6. Interventions: Platelet Rich Plasma
7. Corticosteroid injection

Dependent variables:

1. Pain measured by VAS and SANE
2. Shoulder function assessed using Quick DASH score

Study tools

1. Pretested structured proforma will be used. It consists of 5 parts

PART A: Personal data of the patient

PART B: Clinical history

PART C: Clinical examination

PART D: Laboratory investigations

PART E: Outcome measures

1. USG machine: SONOACE X6 version of ultrasound machine, Made in Korea (SNB21510300046) with 5-12 MHZ linear probe
2. REMI Bench Top PRP Machine Model- R8C-BL, Made in India
3. Visual Analogue Scale: The visual analogue scale (VAS) is a psychometric response scale designed to document the characteristics of disease related symptom severity in individual patients and helps to achieve a rapid classification of the same. The most common VAS consists of a 10 cm horizontal or vertical line with the two end points labeled as "NO PAIN" and "WORST PAIN EVER". Patients are required to place a mark on the 10 cm line at the point that corresponds to the level of pain intensity they presently feel. The distance in centimetres from the low end of the VAS to the patient's mark is used as a numerical index of the severity of pain.
4. Single Assessment Numeric Evaluation (SANE): The SANE is a single-question outcome measure that asks patients to rate their function, as it pertains to the area being treated, on a scale of 0 to 100.
5. The Quick DASH is an abbreviated version of the original DASH outcome measure. In comparison to the original 30 item DASH outcome measure, the Quick DASH only contains 11 items. It is a

questionnaire that measures an individual's ability to complete tasks, absorb forces, and severity of symptoms. The Quick DASH tool uses a 5-point Likert scale from which the patient can select an appropriate number corresponding to his/her severity/function level.

Intervention

Patient's baseline complete haemogram, blood sugar profile, PT-INR, HBsAg, HCVAb and R-Ab was done. The baseline pain measurements for all the patients were taken with the help of the visual analogue scale (VAS). Functional assessment of the shoulder was done with the help of the Single Assessment Numeric Evaluation (SANE) score and the Shortened Disabilities of the Arm, Shoulder and Hand Score (Quick DASH).

The patients were then consequently divided into 2 groups:

GROUP A (Intervention Group): Ultrasound guided platelet rich plasma injection.

GROUP B (Control Group): Ultrasound guided Corticosteroid injection.

Group A:

PRP was prepared using the double spin method. Whole blood was drawn in a 20 ml syringe by venipuncture which is 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 was then collected in a separate plain vial and centrifuged again using a hard spin of 3600 rpm for 15 minutes to obtain a platelet concentrate. The lower 1/3rd is platelet rich plasma (PRP) and upper 2/3rd is platelet poor plasma (PPP). 2 ml of PRP was then procured by removing the PPP. The patient was made to lie comfortably in supine position with the affected arm in neutral rotation. The skin of the anterior shoulder was prepped and draped in a sterile fashion. The transducer of the ultrasound was placed longitudinally over the bicipital groove and a 22 gauge spinal needle was introduced at a 30 degree angle in a distal to proximal direction, with the long axis of the transducer being parallel to the axis of the needle producing an in plane ultrasonographic view of the needle. 2 ml of the freshly prepared PRP was then be administered with the distension of the bicipital sheath by the injectate being visible under ultrasound. Needle was then removed and local homeostasis will be achieved by applying pressure over the injection site.

Group B:

Corticosteroid injection solution was prepared by a combination of 1 ml of triamcinolone acetate (40 mg/ml) and 1 ml of 0.5% bupivacaine. The patient was made to lie comfortably in supine position with the affected arm in neutral rotation. The skin of the anterior shoulder

will be prepped and draped in a sterile fashion. The transducer of the ultrasound was placed longitudinally over the bicipital groove and a 22 gauge spinal needle was introduced at a 30 degree angle in a distal to proximal direction, with the long axis of the transducer being parallel to the axis of the needle producing an in plane ultrasonographic view of the needle. 2 ml of the corticosteroid solution was then administered with the distension of the bicipital sheath by the injectate being visible under ultrasound. Needle was removed and local homeostasis achieved by applying pressure over the injection site.

Post-procedure protocol

After the procedure, the participants were allowed to apply ice and advised local rest. They were instructed to avoid lifting heavy objects with the injected shoulder. Patients were allowed to take paracetamol as rescue analgesia for 2-3 days only to reduce the pain caused by the injection. NSAIDS are to be avoided by the participants.

Follow up assessment

Outcome variables were measured at baseline before intervention and the participants for both the groups were assessed at the end of 1 week, 4 weeks, 12 weeks and 24 weeks post-intervention. VAS was used for assessing decrease in pain; SANE and QuickDASH score was used to assess the functional improvement. The patients were assessed for any intervention related adverse effects.

Data collection

Baseline information of the participants was collected in a pre-designed proforma. Outcome variables were measured at baseline before intervention and follow up assessment was done at 1, 4, 12 and 24 weeks post-intervention. Patients were asked to stop analgesics and anti-inflammatory medications if any, 48 hours prior to the follow up assessment. Collected data will be checked for completeness and consistency.

Statistical analysis

Data was entered and analysis done using IBM-Statistical Package for the Social Sciences (IBM-SPSS) version 21 Armonk, NY: IBM Corporation. Descriptive statistics mean, frequency, percentage and standard deviation was used. For comparing mean change in VAS, SANE and QuickDASH score between the two groups, student t-test was used. Chi-square test was used for comparing categorical variables (age, gender, side of affection, interventions) and student t-test for comparing continuous variables between the two groups (intervention and control groups). For within group comparison (baseline and follow up), repeated measures ANOVA was used. A p-value < 0.05 was considered as statistically significant.

Ethical issues

The ethical approval was obtained from Research Ethics Board, Regional Institute of Medical Sciences, Imphal for this clinical study. All the participants were informed about the nature of study, risk of infection and treatment options available in case of recurrence of pain. The willing participants were asked to sign the informed written consent form. Privacy and confidentiality of participants was maintained by identifying the patients using unique identification number/MRD number and the collected data was made accessible to me and my guide only. CTIR registration for this study was also done following REB approval.

Results

The 2 groups were homogeneous in terms of baseline characteristics like age, sex, side of affection, mean duration of symptoms, VAS, SANE and Quick DASH scores. No patients were lost to follow-up or had undergone a surgical intervention during the follow-up period. The mean age of the participants was 28.69 ± 4.32 in years. The mean duration of symptoms was 4.94 ± 1.58 in months. Males were affected more than females and the right shoulder was more affected than the left (Table 1 and Table 2).

Table 1: Comparisons of background and baseline characteristics between the between PRP group (study) and ESWT group (Control).

Characteristics	Group		p-value
	Intervention Group	Control group	
Mean Age (years)	29.13 \pm 4.080	28.25 \pm 4.655	0.576*
Mean duration of symptoms (months)	4.88 \pm 1.544	5.00 \pm 1.673	0.828*
Gender			
Male	12	10	0.704**
Female	4	6	
Side of Affection			
Right	10	11	1.00**
Left	6	5	

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

Table 2: Comparisons of baseline dependent variables between the between PRP group (Study) and Corticosteroid group (Control).

Characteristics	Group		p-value*
	Intervention Group (Mean ± SD)	Control group (Mean ± SD)	
VAS	7.31 ± 0.793	7.38 ± 0.719	0.817
SANE	35.31 ± 6.945	33.13 ± 6.021	0.349
Quick DASH	73.75 ± 7.188	69.38 ± 8.921	0.137

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

Table 3: Within the group comparison of outcome measures in both groups.

Outcome measures	Study groups	Baseline	4 weeks	12 weeks	24 weeks
VAS	Intervention (PRP)	7.31 ± 0.79	4.94 ± 0.772	3.00 ± 0.730	0.88 ± 0.719
	p value*		0.00		
	Control (Corticosteroid)	7.38 ± 0.71	1.75 ± 0.775	1.69 ± 0.479	4.25 ± 1.125
	p value*		0.00		
SANE	Intervention (PRP)	35.31 ± 6.94	48.44 ± 7.89	63.44 ± 6.51	90.12 ± 6.05
	p value*		0.00		
	Control (Corticosteroid)	33.13 ± 6.02	75.63 ± 8.13	79.69 ± 6.70	61.63 ± 6.29
	p value*		0.00		
Quick DASH	Intervention (PRP)	73.75 ± 7.18	51.88 ± 8.34	30.63 ± 7.27	7.50 ± 5.77
	p value*		0.02		
	Control (Corticosteroid)	69.38 ± 8.92	23.13 ± 6.29	20.18 ± 6.32	24.14 ± 10.14
	p value*		0.03		

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

Table 4: Comparisons of mean difference changes from baseline in outcome measures between PRP group (study) and Corticosteroid group (Control).

		Intervention Group (Mean ± SD)	Control group (Mean ± SD)	p-value*
VAS Score	4 weeks	2.62 ± 0.88	5.81 ± 0.91	0.00
	12 weeks	4.56 ± 1.26	5.87 ± 0.61	0.01
	24 weeks	6.68 ± 0.87	3.31 ± 1.35	0.00
SANE	4 weeks	-13.12 ± 9.28	-42.50 ± 8.16	0.02
	12 weeks	-28.12 ± 8.13	-46.56 ± 9.25	0.01
	24 weeks	-54.68 ± 9.21	-27.50 ± 8.16	0.00
Quick DASH	4 weeks	21.87 ± 5.73	46.25 ± 8.46	0.00
	12 weeks	43.12 ± 7.93	49.37 ± 10.62	0.04
	24 weeks	66.25 ± 9.91	43.25 ± 10.56	0.00

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

Visual Analog Scale (VAS)

Within the group comparison showed statistically significant reduction in the VAS score from baseline at all follow ups (p < 0.05) in PRP group. In the Corticosteroid group, there was reduction in the VAS score at 4 week and 12 weeks follow up. However the VAS score increased at 24 weeks follow up but remained lower than baseline VAS score and this was statistically significant (Table 3). Between the groups comparison showed reduction in VAS scores in both the groups at all follow ups in

comparison to baseline which was significantly more in the corticosteroid group at 4 weeks and 12 weeks follow up but superior reduction was seen in the PRP group at 24 weeks follow up (Table 4).

Single Assessment Numerical Evaluation (SANE)

Within the group comparison showed statistically significant improvement in the SANE score from baseline at all follow ups (p < 0.05) in PRP group. In the Corticosteroid group, there was significant improvement in the SANE score at 4 week and 12 weeks follow up

but the SANE score reduced at 24 weeks follow up which however remained above baseline and this was statistically significant (Table 3). Between the groups comparison showed improvement in SANE scores in both the groups at all follow ups in comparison to baseline but it was significantly more in the PRP group at long term follow up of 24 weeks (Table 4).

Quick DASH

Within the group comparison showed statistically significant reduction in the Quick DASH score from baseline at all follow ups ($p < 0.05$) in PRP group. In the Corticosteroid group, there was significant reduction in the Quick DASH score at 4 week and 12 weeks follow up. However it increased at 24 weeks follow up but remained below baseline and this was statistically significant (Table 3). Between the groups comparison showed reduction in Quick DASH scores in both the groups at all follow ups in comparison to baseline but it was significantly more in the PRP group at long term follow up of 24 weeks (Table 4).

Discussion

Bicipital tendinosis is an inflammatory process of the long head of the biceps tendon and is a common cause of shoulder pain due to its position and function [5]. The inflammation can be caused by the normal ageing process as well by a degenerative process which usually occurs in athletes with repetitive overhead movements. It is important to understand, that this inflammation has many different causes and maybe accompanied by other shoulder pathologies such as: SLAP-lesions, rotator-cuff tears or instability. The first line of treatment comprises nonoperative therapeutical means as rest, ice, restriction of overhead activities, nonsteroidal antiinflammatory drugs (NSAIDs), and physical therapy [12]. In persistent cases, corticosteroid injections maybe given especially in the acute inflammatory phase. However, corticosteroid injections are associated with an increased risk of rupture of the tendon especially if the technique of injection is incorrect. In some instances there has been increased risk of infections.

Early return to sports is the goal of both amateur and professional athletes. Multiple emerging therapies and modalities are being continuously explored to hasten the healing process. These include regenerative medicine modalities such as prolotherapy, platelet-rich plasma injection, stem cells injections, gene therapy, and growth factors among others. PRP is a biological agent which has gained popularity as an adjuvant treatment for musculoskeletal injuries as a safe and cheap natural physiological method. Therapeutic injections have been traditionally performed in a blind fashion, using the anatomical landmarks. However, imaging-guided injections have gradually gained popularity [9]. In general, imaging guidance during shoulder injections has been reported to improve accuracy. The need

and indication using ultrasound guided injections in musculoskeletal injuries have increased in the last years as physicians and patients pursue confirmation of needle position, so ultrasound-guided interventions developed as the favoured way for many doctors and patients.

This prospective randomized controlled study was conducted with the aim to find out the effectiveness of ultrasound guided platelet rich plasma injection, an emerging regenerative medicine modality in comparison with the traditional use of corticosteroid injection in the treatment of bicipital tendinosis which is a very common problem among athletes across various disciplines.

In a randomized controlled trial conducted by Dadgostar H, et al. [19] evaluating the role of both corticosteroids and platelet-rich plasma (PRP) in the treatment of rotator cuff (RC) tendinopathies, it was found that PRP renders similar results to that of corticosteroids in most clinical aspects among patients with RC tendinopathies; however, pain and ROM showed more significant improvement with the use of PRP. Ibrahim DH, et al. [21] conducted a study to compare the efficacy of ultrasound-guided platelet rich plasma (PRP) versus corticosteroid injection for treatment of Rotator Cuff Tendinopathy (RCT). Patients were evaluated using visual analogue scale (VAS) for pain, functionally assessed using the Shoulder Disability Questionnaire (SDQ) and range of motion (ROM) determined before and 8 weeks after injection. The study found that PRP injection lead to significant improvement in the outcome measures in comparison with the corticosteroid injection. The study concluded that both PRP and corticosteroid injections were effective in the treatment of RCT and PRP is a safe and good alternative to corticosteroid injection that promotes healing and decreases inflammation. Ultrasound-guided injection may increase the efficacy.

In another study conducted by Moon YL, et al. [15] to evaluate the effectiveness of Platelet-Rich Plasma therapy (PRP) and prolotherapy for shoulder pain and dysfunction related to symptomatic biceps tendinopathy, the study found that there was no significant difference between the 2 groups in the first month after the procedure. However, in the third, sixth and twelfth months after the procedure, the PRP group showed significant improved results for VAS, KSS, UCLA, and CSS scores compared to the prolotherapy group ($p < 0.05$). The study concluded that PRP was not only safe and effective but also had a long lasting symptomatic and functional improvement in bicipital tendinosis.

Yisnnakopoulos CK, et al. [16] conducted a randomized controlled study to compare accuracy, patient discomfort, and clinical outcome of ultrasound-guided versus palpation-guided corticosteroid injections to the bicipital groove in patients with long head of biceps (LHB) tendinosis. The study concluded that under ultrasound guidance, injections to the bicipital groove are faster and produce lower discomfort. Superior

accuracy and clinical outcomes can be achieved using the ultrasound-guided technique.

Serrania LC, et al. [18] conducted a non-randomized clinical trial to compare the efficacy of a single injection of PRP versus single peritendinous injection of methylprednisolone acetate in the treatment of chronic tendinopathy of the long portion of biceps. The study found that peritendinous injection of PRP showed superiority in the decrease of pain (VAS) and disability, as well as increase in the functionality (DASH) of the affected shoulder.

Our study used outcome measures VAS and SANE for pain and QuickDASH for functional assessment of athletes with bicipital tendinosis. We found that ultrasound guided platelet rich plasma injection led to significant improvement in all the outcome measures at all follow ups (4, 12 and 24 wks). In the corticosteroids group, there was a better improvement in all the outcome measures at 4 weeks and 12 weeks follow up in comparison with the PRP group. However this improvement was not seen at 24 weeks follow up visit and this was statistically significant.

To our knowledge, this is one of the few studies in the country directly comparing the effectiveness of ultrasound guided platelet rich plasma injection in comparison with the traditional corticosteroid injection in the treatment of bicipital tendinosis. This study further enhances our belief that PRP is a safe, effective and a superior long term alternative to corticosteroid injection in athletes with bicipital tendinosis.

Conclusion

Although corticosteroids injection is an effective treatment in the symptomatic management, platelet rich plasma injection is a safer, effective and superior long term alternative to steroids injection in the management of bicipital tendinosis.

Ethical Issues

Ethical clearance was obtained from the Institute's Ethical committee

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Conflicts of Interest

None.

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