

Are Platelet Rich Plasma Injections More Effective in Tendinopathy or Enthesopathy?

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Abstract

Introduction: Chronic overuse insertional tendinopathy (entesopathy) is highly prevalent, but is an extremely difficult condition that generates a high medical expense. Alternative and co-adjuvant therapies to improve the quality of life and physical function of affected patients are currently being sought.

Materials and Methods: A total of 31 patients affected by entesopathy at different anatomical sites (elbow tendinopathy, greater trochanter pain syndrome and plantar fasciopathy) were treated with three peritendinous injections of autologous platelet rich plasma (PRP) and included in the present investigation. VAS scale and segmental scores for the affected site before the first injection of PRP and at 6 months after the last injection were used. One hundred and seven patients that underwent the same injection protocol in the same time lapse were used as a control group, and were represented by patients with non-insertional tendinopathy (shoulder and at Achilles tendon).

Results: Significantly lower values between pre-treatment and follow-up pain scores at all-time points were found in the patients affected by entesopathy compared to tendinopathy ($p < 0.001$). As a confirmative finding, the segmental scores at the shoulder and ankle did not improve overtime, differently from what occurred in patients with entesopathy.

Conclusion: At 6 months following peritendinous injections of PRP in patients with entesopathy there was a significant reduction of pain, associated to a significant improvement in recorded segmental scores. Conversely, the treatment was not effective in patients with pure tendinopathy at the shoulder and ankle level. These favorable findings point to consider PRP as a promising therapy for patients affected by entesopathy.

Keywords: Platelet rich plasma; Tendinopathy; Blood; Trochanteric pain syndrome

Introduction

Tendinopathies are very common in athletes. Traditionally, the first management is conservative, including analgesics, anti-inflammatory drugs [1], and physical therapy [2]. In the last decade, Platelet-rich-plasma (PRP) products have been increasingly used [3,4], but their effectiveness is still controversial. PRP is a plasma gel with high concentration of platelets, higher than that present in the blood, as clinical benefits have been shown when this concentration is at least 1,000,000/ μ l in 5ml of plasma [5]. There is evidence that PRP provide good excellent outcomes in patients with tendon disorders [6-10], but few studies have reported on the use of PRP in patients with insertional tendinopathies of the elbow [11,12] and patellar tendon (jumper's knee) [13,14]. The primary endpoint of this retrospective study is to assess clinical and functional outcomes of patients with

tendinopathies of the main body of the tendon and insertional tendinopathies who had undergone local injections of PRP.

Materials and Method

This study was carried out at the Department of Orthopaedic and Trauma Surgery and the Immuno-hematology Transfusion Medicine Unit of Campus Bio-Medico University Hospital. The Local Ethics Committee approved the study, and informed consent was obtained from all individual participants included in the study.

Subject's selection process

Four hundred patients underwent PRP injections for management of tendon disorders at Campus Bio-Medico University from January 2011 to July 2012. We enrolled patients with tendinopathy or insertional tendinopathy at clinical examination and US, older than 18 years, hemodynamically stable, with Hb values greater than 10g/dl, count of platelets greater than 150/ μ l, unresponsive to traditional

treatments including FANS therapy and steroid injections, with no history of rheumatic disorders neither previous surgery to the affected tendons. Patients with platelet dysfunction syndrome, hypofibrinogenemia, systemic or local infection at the site of injection, cancer history, neurological or psychiatric disorders were excluded. Patients who had assumed local or systemic non-steroidal anti-inflammatory drugs (NSAIDs) or steroids 2 weeks before the procedure were also excluded. 156 patients were considered eligible for the study. Medical records and score schedules were all examined before treatment and at an average follow up of 1 year. We included only patients who had undergone at least 3 injections of PRP for management of tendinopathy or insertional tendinopathy of all the tendons. At the end, 139 patients were enrolled in the study.

PRP preparation

Eight milliliters of whole blood of the patient were collected in a RegenLab THT tube® containing a special gel. Once the tube had been centrifuged for 9 minutes at 3100 rpm, the red blood cells were separated from the Platelet Rich Plasma. Then, the PRP is aspirated with an 18-gauge needle and injected. Adverse effects were recorded. Patients were advised not to undergo surgical procedures in the follow-up period (12 months); painkillers were allowed if necessary.

Patient's recruitment and intervention modalities

Patients were divided into two groups: The Group A (31 patients) included patients with insertional tendinopathy and the Group B (108 patients) included patients with tendinopathy of the body of the tendon. Injections were undertaken in a standard manner in patients with Achilles and elbow tendinopathy, with plantar fasciopathy and greater trochanteric pain syndrome. Specifically, once the site of pain had been identified at ultrasound (US), the skin was scrubbed and a needle was introduced perpendicularly to the axis of the probe, parallel to the tendon, along its side, within the paratenon. Taking care not to enter the body of the tendon, PRP was injected [15]. Injections to rotator cuff tendons were performed through the sub acromial space with the forearm in internal rotation, and the needle perpendicular to rotator cuff tendons [15]. All patients were been assessed for pain with VAS at baseline (before the treatment), 6 months, 1 year and 3 years after treatment. Specific scores were also administered. Specifically, University of California Los Angeles (UCLA) score was used for patients with rotator cuff disorders, the Harris Hip score for patients with greater trochanteric pain syndrome, the Quick Disability of Arm Shoulder and Hand (Quick DASH) for patients with elbow tendinopathy, the VISA-A score for patients with Achilles tendinopathy, and the American Foot and Ankle Score (AOFAS) for patients with plantar fasciopathy. Data about comorbidities and concomitant therapies were also recorded. After injection, patients were instructed to apply ice over the site of injection and avoiding stresses and heavy loads.

Statistical analysis

Blinded statistical analysis was performed. A paired t-test was used for intra-group comparison of VAS and specific scores at different follow-ups; unpaired T-test was used to compare inter group VAS values. The difference was significant when p was lower than 0.05. Mean, range, and 95% confidence intervals (C.I.) were also calculated. The version 16.0.1 of the SPSS software (SPSS Inc., Chicago, Illinois) was used.

Results

Medical records of 156 patients who had undergone PRP injections for different tendinopathies were screened. Of 139 patients enrolled in the study (76 males and 63 females), treated at an average age of 54 years (range 27-65), 31 patients were allocated in the Group A, 108 were included in the Group B. In the Group A, 11 patients were managed for elbow tendinopathy, 10 for greater trochanteric pain syndrome, and 10 for plantar fasciopathy. In the Group B, 93 underwent PRP injections for management of rotator cuff disease and 15 for mid-portion tendinopathy of the Achilles tendon. Flow diagram of patient's selection process is reported in Figure 1.

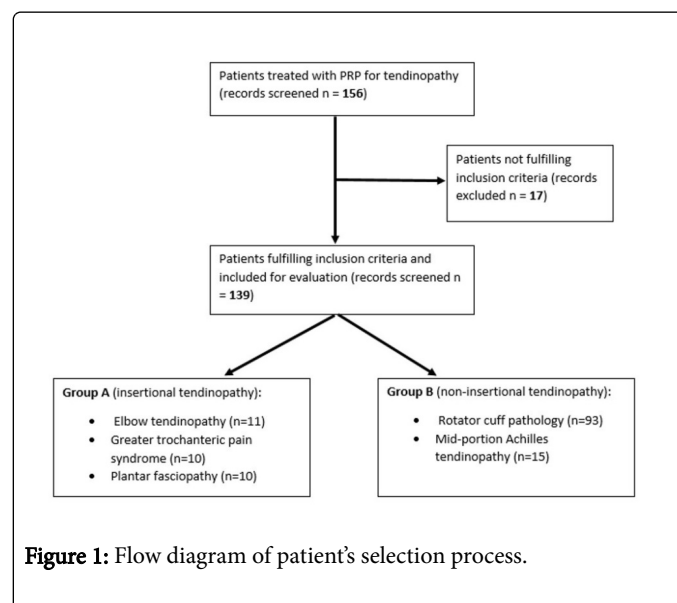
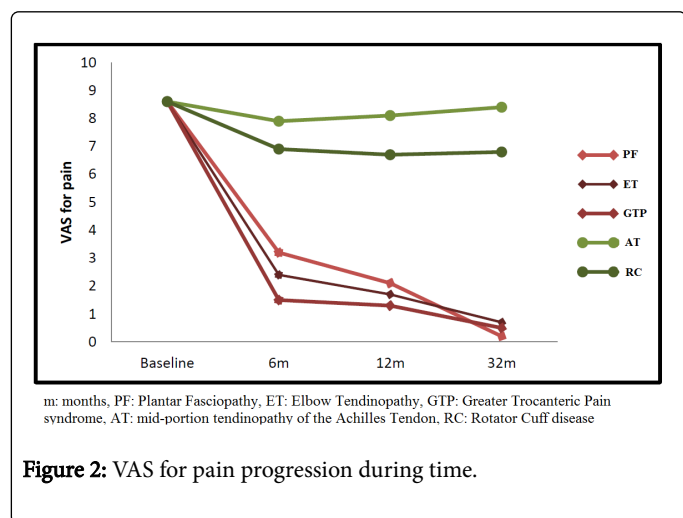


Figure 1: Flow diagram of patient's selection process.

Pain

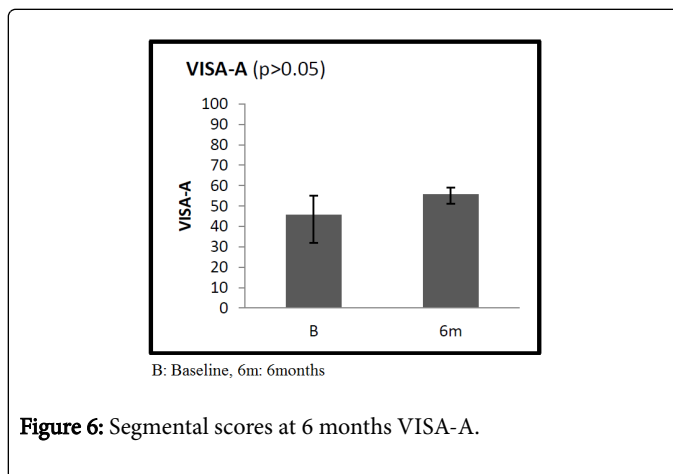
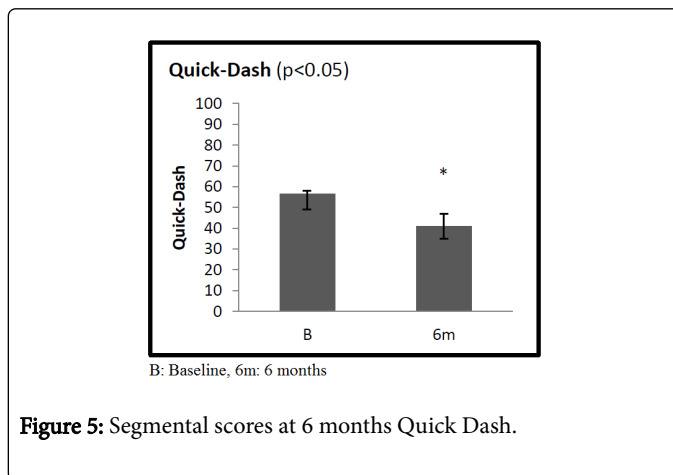
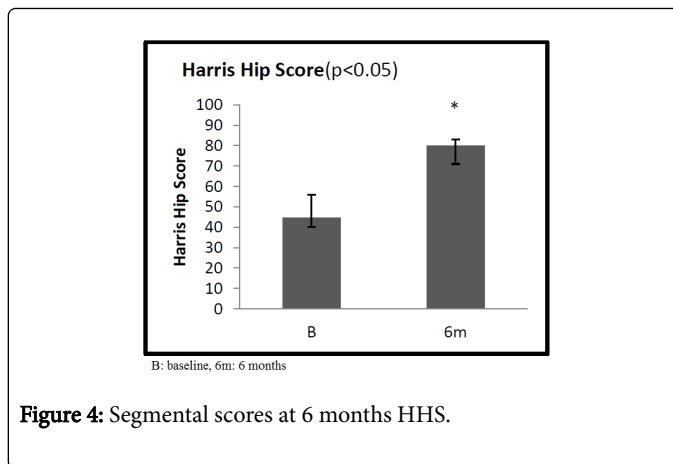
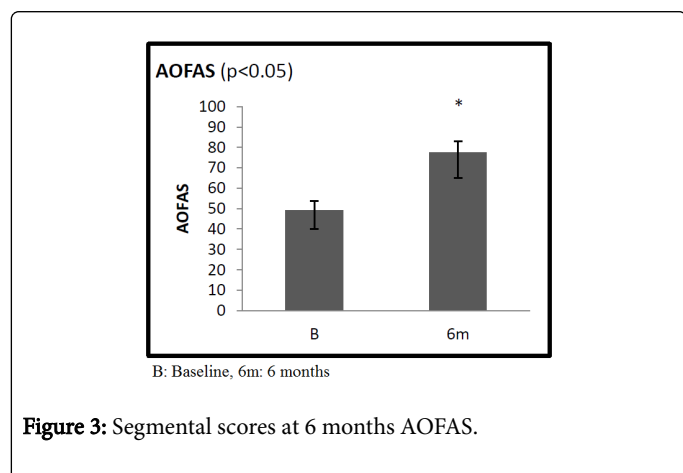
At baseline the overall average VAS was 8.6 (range 8.0-9.1). At 6 months, in the Group A, VAS values were significantly improved ($p < 0.05$). Specifically, the average VAS was 3.2 in patients with plantar fasciopathy (range 1-4, 95% C.I. 1.5-2.4), 2.4 in those elbow tendinopathy (range 1-5, 95% C.I. 0.9-2.9), and 1.5 in those with greater trochanteric pain syndrome (range 0-2, 95% C.I. 1.7-2.2). In the Group B, at 6 months, the VAS improvement was not significant ($p > 0.05$). The average VAS was 7.9 (range 6-9, 95% C.I. 0.2-3.7) in patients with Achilles tendinopathy, and 6.9 (range 5-8, 95% C.I. 0.7-1.8) in those with rotator cuff disease. At 1 year follow-up, in the Group A, the average VAS was 2.1 (range 0-6, 95% C.I. 1.8-2.2) in patients with plantar fasciopathy, 1.7 (range 1-3, 95% C.I. 1.3-2.7) in those with elbow tendinopathy, and 1.3 (range 1-3, 95% C.I. 1.8-2.2) in patients with greater trochanteric pain syndrome. At 1 year, in the Group B, the VAS value averaged 8.1 (range 4-10, 95% C.I. 1.3-2.6) in patients managed for Achilles tendinopathy and 6.7 (range 5-8, 95% C.I. 1.8-1.9) in those managed for rotator cuff disease. Therefore, the inter-group differences were statistically significant ($p < 0.001$). At 3 years, in the Group A, the average VAS was 0.2 (range 0-3, 95% C.I. 1.9-2.0) in patients with plantar fasciopathy, 0.7 (range 0-2, 95% C.I. 1.8-2.1) in those with elbow tendinopathy, and 0.5 (range 0-2, 95% C.I. 1.9-2.0) in patients with greater trochanteric pain syndrome. In the Group B, the VAS value averaged 8.4 (range 6-9, 95% C.I. 0.8-3.1) in patients with Achilles tendinopathy and 6.8 (range 5-9, 95% C.I.

1.7-3.1) in those with rotator cuff disease. At 3 years, the inter-group differences were statistically significant ($p < 0.001$; Figure 2).



Specific outcome scores

At 6 months, Specific scores were significantly better than at baseline. Specifically, in patients with plantar fasciopathy, the AOFAS score improved from an average value of 49.3 (range 40-53) to 77.4 (range 65-83, 95% C.I. 5.6-7.8) ($p < 0.05$); the average Quick DASH improved from 56.6 (range 49-58) to 40.9 (range 35-47, 95% C.I. 6.9-12.7) ($p < 0.05$) in patients with elbow tendinopathy; the average Harris Hip score improved from 44.7 (range 40-56) to 79.8 (range 71-83, 95% C.I. 13.2-16.8) ($p < 0.05$) in patients with greater trochanteric pain syndrome. In the Group B, at 6 months, the average UCLA score was slightly increased compared to the average value at baseline, increasing from 16.3 (range 7-29) to 18.1 (range 10-31, 95% C.I. 4.6-16.9) ($p > 0.05$) in patients with rotator cuff disease. Similarly, the average VISA-A score improved from 45.6 (range 32-55) at baseline to 55.6 (range 51-59, 95% C.I. 8.8-13.6) ($p > 0.05$) at 6-month follow-up (Figures 3-6). At one year, the UCLA score averaged 21.5 (range 8-25, 95% C.I. 3.8-9.5); it decreased to 16.5 (range 8-20, 95% C.I. 3.5-7.8) at 3 years (Figure 7).



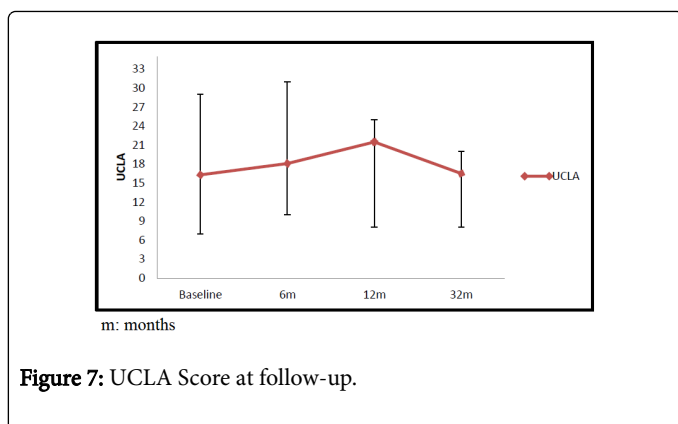


Figure 7: UCLA Score at follow-up.

Discussion

The use of PRP has been widely shown in patients with cartilage lesions, but there is no consensus on its effectiveness in terms of cartilage repair. On the other hand, the role of PRP in the field of tendon healing as management of tendinopathy is still controversial. According to the literature, proper guidelines should be defined when referring to the application of PRP, and well-designed clinical trials are needed [3]. Even though many studies have reported outcomes after application of PRP in tendinopathy, this is the first study showing that PRP injections provide different outcomes in relationship to the tendon involved and the site injected. To the best of our knowledge, this is the first study that compares outcomes of patients who had PRP injections for tendinopathy of the body of the tendon vs insertional tendinopathy. Few studies have investigated the use of PRP for management of tendinopathies [3], focusing on patients with rotator cuff disease [9,16-19], elbow tendinopathy [12,20,21], and patellar tendinopathy [13,22,23]. Even though reported outcomes were satisfying, none of these studies clearly stated that PRP is effective, reasonably because the sample sizes were relatively small. In addition, the methods of preparation, the number of PRP injections, and the quantity of the product have not been standardized yet. Different preparations of PRP are available. Specifically, the L-PRP is used for injections, the PRP fibrin matrix is used intra-operatively, during arthroscopic procedures. The fact that different methods of preparation of the whole blood have been proposed induces many bias, making it difficult to compare available data, and perform meta-analysis on outcomes after PRP administration. The steps of administration of PRP should be standardized to allow the surgeon to define the indications to these products, the quantity of PRP to inject, and the time of injection. These injections should be performed under ultrasound guidance. In the present study, clinical and functional outcomes were significantly different between patients with tendinopathy of the body of the tendon and those with insertional tendinopathy. Pain improved at the first follow-up in both groups, not significantly in patients with tendinopathy of the body of the tendon. On the other hand, no recurrences occurred during the follow-up period, showing that PRP injections relieve pain and are a viable option of management of tendinopathy. It would be interesting to extend this study to a population of athletes, considering the return to sport. This study has some limitations: the number of patients is small to draw definitive conclusions on the effectiveness of PRP in tendinopathy, there is no control group of patients, and results are heterogeneous as tendinopathies affected different districts. In addition, US was used to inject superficial tendons, not to perform sub

acromial injections, and no imaging methods were used to assess the tendon healing. On the other hand, as strengths of the study, a standardized Regen lab method produced by a specialist in hematology in a specialized Transfusion Medicine and Cellular Therapy Centre has been used to prepare PRP products, the same orthopedic surgeon performed all the injections, and an independent investigator blinded to the site of tendinopathy and number of injections collected data collection and performed the statistical analysis. As growing point for the future, given the concern on the PRP formulation, future studies should compare different formulations of PRP.

Conclusion

This is a pilot study comparing outcomes after injection of PRP for management of insertional tendinopathy and tendinopathies of the main body of the tendon, with better results in patients with insertional tendinopathy.

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