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Peritendinous injection of platelet-rich plasma to treat tendinopathy: A retrospective review

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ABSTRACT

Objective: The aim of this study was to determine factors associated with the likelihood of a better clinical outcome after the peritendinous injection of PRP for the treatment of chronic tendinopathy and identify whether PRP represents an effective treatment option for chronic tendinopathies.
Methods: The study included 214 patients (86 males and 128 females; mean age: 39.3 (18–75) years) who received PRP injections for tendinopathy refractory to conventional treatments. The mean duration of symptoms at the moment of the PRP treatment was 8.3 months. Primary outcome measurement was perceived improvement in symptoms for each anatomic compartment for upper and lower limbs at 6 months after treatment. Also, a visual analog scale (VAS) score (pain intensity on a 0–10 scale) was used for pain scoring questionnaire before treatment, 6 weeks and 6 months following the PRP injection(s). To identify factors associated with the likelihood of a better clinical outcome, patients were categorized on the basis of their perceived improvement in symptoms 6 months after the PRP injection(s)—that is, as lower (less than 50% global improvement) or higher (more than 50% global improvement).
Results: A visual analogue scale score and perceived improvement in symptoms were significantly lower after peritendinous injection in 6-week and 6-month follow-ups compared with the baseline ($P < 0.001$) except for peroneal and Achilles tendons. Overall, 83% of patients indicated moderate to complete improvement in symptoms. The most common injection sites were the lateral epicondyle, Achilles, and patellar tendons. Furthermore, 30% of patients received only 1 injection, 30% received 2 injections, and 40% received 3 or more injections. A total of 85% of patients were satisfied (more than 50% global improvement) with the procedure. In addition, upper limb tendons, increase in the age, and female gender were associated with a higher likelihood of perceived improvement in symptoms.
Conclusions: In the present retrospective study assessing PRP injections in the treatment of chronic tendinopathy, a moderate improvement (>50%) in pain symptoms was observed in most of the patients. Our research found that results were most promising with patellar and lateral epicondylar tendinopathy in the short to medium term. Female patients, patients with upper extremity tendinopathy and older patients appeared to benefit more from PRP injection.
Level of evidence: Level IV, Therapeutic study.

Introduction

Tendon pain is frequently observed in professional and recreational athletes, in addition to sedentary individuals.[1,2] Tendon injuries are classified as tendinitis in the acute inflammatory process and tendinosis in the case of the chronic impairment of healing, indicated by the scarcity of inflammatory cells in the tissue, collagen degeneration, abnormal tissue repair, thickening of the tendon, and neovascularization.[2] The term tendinopathy is used by

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clinicians at an increasing rate for the purpose of referring to tendon disorders without indicating a particular pathology and chronic tendinopathy for cases that are hard to treat by means of conventional treatments.

Ice, rest, activity modification and anti-inflammatory medications are generally included in the current mode of management. The reasons for the above-mentioned treatments have been questioned in recent times. An increase in the activity of the collagen-degrading enzymes, indicating a detrimental impact on tendon healing, was demonstrated in a study conducted on the impact of ibuprofen on rat Achilles tendon cells.[3] Peritendinous injection of corticosteroid is widely used for the treatment of tendinopathy, although inflammation is absent in the above-mentioned condition and there is the risk of tendon atrophy or secondary rupture.[4]

Platelet-rich plasma (PRP) is being utilized at an increasing rate for the promotion of musculoskeletal healing by stimulating angiogenesis, cell proliferation, and chemotaxis.[5] It has been demonstrated that PRP promotes healing in cases of tendinous and ligamentous injury and muscular strain,[6–8] and it has been utilized for the purpose of shortening the recovery period and return to play (RTP) duration.[9]

It has been suggested that platelet-rich plasma (PRP) injections are a promising option for the treatment of tendinopathies. In tendinopathy, the failed-healing hypothesis suggests that repetitive stresses lead to small injuries within the tendon that fail to heal before further trauma occurs. Difficulties in achieving healing arise in tissues characterized by a low cell number and low extracellular matrix turnover.[10] Thus, broadly speaking, tendon regeneration can be achieved by increasing cell numbers and/or enhancing tendon cell anabolism (collagen synthesis).

However, there are a limited number of scientific studies demonstrating the effective treatment of tendinopathy by means of PRP injections. The majority of studies are case series reports with small sample sizes, and contradictory results have been obtained in randomized control trials.[6,8,11,12] This study aims to identify whether peritendinous injection of PRP can be used effectively to chronic tendinopathy and also to determine factors associated with the likelihood of a better clinical outcome. The identification of patient characteristics that predict clinical outcome can be helpful in the development of patient-specific treatment strategies. It will also help provide better information and more realistic expectations for various tendinopathies.

Patients and methods

In this retrospective, single-site, descriptive study, we analyze the clinical results of the peritendinous PRP injection for the treatment of tendinopathies. The Institutional Ethics Board approved this study. 248 consecutive patients with persistent tendinopathy who referred to our institution for a PRP treatment after the initial conservative treatment failure between January 2010 and September 2014 were included in the study. The medical records of all patients were reviewed retrospectively. The following inclusion criteria were determined: male and female subjects with a diagnosis of tendinopathy for more than 3 months that had not resolved by applying conventional treatments, such as oral medications, physiotherapeutic modalities, and eccentric exercises (those involving slow, controlled lengthening of the muscle/tendon unit), among others. To make a diagnosis, the patients should have documented pain upon palpation over the tendon, pain with resisted activation of the tendon, and ultrasound or magnetic resonance imaging findings should have been consistent with tendinopathy. The exclusion criteria were additional treatment after PRP injection during follow-up (either medical or surgical), incomplete data, or loss to follow-up. A total of 214 patients (86 males and 128 females) matched these criteria.

PRP preparation and injection technique

20 ml of peripheral blood in total was drawn from all patients into four 5 ml trisodium citrate tubes, and the preparation of a PRP concentrate was performed by a validated method leading to a 29–39 fold increase in platelet concentration without leucocytes.[13] Centrifugation of tubes was conducted with a single spin, at 460 g for the period of 8 min. Under laminar airflow, the plasma fraction exactly above the buffy coat (1.5 ml) was aspirated from all tubes and dispensed into an empty tube. The addition of 22.8 mM of calcium chloride into the solution was performed before the injection. Following this, the activated concentrate was injected as the needle was gradually withdrawn towards the skin into the peritendinous area before coagulation.

The determination of the number of PRP injections had to be performed in accordance with the certain criteria. In case of (1) 80% global improvement stated by the patient, no further injection was suggested; (2) less than 80% global improvement stated by the patient but improvement still continuing, no further injection was suggested; and (3) less than 80% global improvement and plateaued in progress, further injections were suggested.

Lateral and medial epicondyle

The prepared 3 ml of PRP was injected with an 18-gauge needle into the common extensor or flexor tendon as well as the insertions into bone, using a peppering technique. This technique involved a single skin portal followed by 5 penetrations of the fascia while injecting equal amounts of platelet-rich plasma. Injections were administered at the point where maximal pain was present.

Patellar tendon

Approximately 2 ml of PRP was injected directly into the area of maximum tenderness. Then the remaining 2 ml PRP was injected by the investigator using an 18-gauge needle into the patellar tendon origin on the patella with a peppering technique. This technique involved a single skin portal and then five penetrations of the tendon.

Rotator cuff

Approximately 5 ml of PRP was injected under the posterolateral aspect of the acromion, directly into the subacromial space. No repeated needling (tenotomy) was done.

Achilles

Approximately 3 ml–5 ml of PRP was injected into the Achilles tendon using a peppering technique always in local anesthesia, with patient prone. This technique involved a single-skin portal followed by five penetrations of the tendon.

Hamstring

The patient was positioned in a lateral decubitus or prone position. An 18-gauge spinal needle was inserted through the skin. The needle was directed toward the ischial tuberosity using direct palpation. The needle was then withdrawn a few millimeters, and approximately 3 ml–5 ml of PRP was administered into the muscle origin.

Gluteus medius

Point of maximal tenderness identified on the lateral aspect of the greater trochanter. A 22-gauge spinal needle was advanced perpendicular to the skin to the level of bony contact, then withdrawn 2 mm; approximately 3 ml–5 ml of PRP were injected.

Hip adductor

Point of maximal tenderness identified on the medial aspect of the groin. A 22-gauge spinal needle was advanced perpendicular to the skin to the level of bony contact, then withdrawn 2 mm; approximately 3 ml–5 ml of PRP were injected.

Peroneal tendons

The peroneal tendons were localized by palpating along the posterior aspect of the inferior lateral malleolus. An 18-gauge spinal needle was then introduced in a superior to inferior direction, parallel to the long axis of the peroneal tendons, approximately 3–4 cm proximal to the distal tip of the fibula. The needle was advanced until the tip penetrated the superficial aspect of the peroneal tendons. Then approximately 3 ml of PRP were injected.

Outcome measures

The primary outcome measurement was the perceived improvement in symptoms at 6 months after the PRP injection(s). This perception was scored from 1 to 5 by means of the Likert-type scale presented below: 1 = Not at all, 2 = Slightly, 3 = Moderately, 4 = Mostly, and 5 = Completely.[14] Also, A visual analogue scale (VAS) score (pain intensity on a 0–10 scale) was used for pain scoring questionnaire before treatment, 6 weeks and 6 months following the PRP injection(s). Moreover, pain level during and immediately after the PRP injection was assessed using a VAS on a 0–10 scale. Local complications (at the site of tendinitis) that might have occurred after the PRP injection to assess tolerance were noted.

To identify factors associated with the likelihood of a better clinical outcome, patients were categorized on the basis of their perceived improvement in symptoms 6 months after the PRP injection(s)—that is, as lower (less than 50% global improvement) or higher (more than 50% global improvement). The effects of patient age (continuous), gender, tendinopathy location (lateral epicondyle, patella, Achilles, rotator cuff, hamstring, gluteus medius, medial epicondyle, hip adductor, peroneal tendons), metabolic comorbidities (such as diabetes mellitus or thyroid dysfunction) and the number of injections (once or twice) on the likelihood of a better clinical outcome were evaluated. Patient age and tendinopathy location were dichotomized as <35 years old versus ≥35 years old and upper limbs versus lower limbs, respectively, based on suggestions in the literature.[15,16]

Statistical analysis

Means, standard deviations, ranges, frequencies, and proportions were used to describe the study sample. The level of significance was determined to be $p < 0.05$. The SPSS software package (version 17.0 for Windows; SPSS, Chicago, IL, USA) was used for performing all analyses. Differences in clinical outcome measures within the tendon groups were examined by the Friedman test with post-hoc Dunn's test. The study sample was grouped into those with more than 50% global improvement (moderate to complete resolution of symptoms) and less than 50% global improvement (slightly or no resolution of symptoms) 6 months after the PRP injection(s). Categorical x^2 tests were performed to compare categorical variables, and the analysis of variance (ANOVA) compared continuous variables between patients who had more than 50% global improvement and those who did not have. A generalized linear model, adjusting for hospital clustering, was performed using logit link and binomial distribution. Odds ratio (OR), 95% confidence interval (CI), and Wald x^2 P values are provided.

Results

A total of 214 patients (86 males and 128 females) were included the study. The mean age of the patients was 39.3 years (range, 18–75 years), and the mean duration of symptoms at the moment of the PRP treatment was 8.3 months (range, 3.3–16.8 months). Table 1 presents the distribution of the different tendons treated and demographic data of the patients.

The VAS scores at the end of the 6 weeks after the PRP injection(s) were significantly better than before the injection in the majority of the tendon groups; however, there were not significantly better scores for the peroneal and Achilles tendons (Table 2). The scores did not change significantly based on the time of the final follow-up; thus, no clinical deterioration occurred during this time interval and the improvements observed were not simply because of the spontaneous resolution of symptoms. Regarding pain during and immediately after the PRP injection, the VAS mean scores were 1.6 ± 0.3 and 0.8 ± 0.2, respectively. Aside from the transitory local pain that required analgesic oral treatment in 22 patients, no major side effects or complications after the PRP injection were encountered. No clinical complications were reported during the early follow-up.

The insertion of the common extensor tendon at the lateral epicondyle and patellar tendon represent the two tendons treated most frequently. 6 months after the injection(s), the perceived change in symptoms was classified as completely in the lateral epicondyle group (mean, 3.86) and mostly in the patellar tendons (mean, 3.86).

In terms of the number of PRP injections administered to patients, only 1 injection was administered to 30% of patients, 2 injections were administered to 30% of patients, and 3 or more injections were administered to 40% of patients.

Regarding the primary outcome, moderate-to-complete resolution of symptoms was reported by 83% of patients after administering only 1 injection, by 82% of patients after administering 2 injections, and by 76% of patients after administering 3 or more injections.

Adjusted generalized linear models showed that the upper limb tendons were 1.46 (95% CI, 1.24–1.71) times more likely to have a higher perceived improvement in symptoms than lower limb tendons during a 6-month follow-up (Table 3). For each year increase in the age of the patient, the likelihood of a higher perceived improvement in symptoms increased by 4% (95% CI, 4%–5%). Female gender was 1.68 (95% CI, 1.39–2.04) times more likely to have a higher perceived improvement in symptoms than male gender (Table 3).

Discussion

It was determined in the current study that PRP utilized for the treatment of chronic tendinopathy in various part of the body had clinical effects on improving subjective patient complaints and pain, except for peroneal and Achilles tendons. Adjusted models showed that older patient age, female gender, and upper limb tendinopathies were all independently associated with a higher likelihood of improvement in symptoms.

Contrary to the other studies in the literature that have examined only the reaction of a specific tendon to PRP, in the present study, the reaction of multiple tendons treated in the whole body was examined, and the overall improvement in symptoms was identified. In spite of the possible differences in etiology, it was proved that the underlying tissue pathology among the above-mentioned tendinopathies was similar in the case of utilizing advanced imaging techniques. Considering the heterogeneity of

Table 1
Descriptive parameters for patients.

Tendon group	Number of patients	Gender, n		Age, yrs	Duration of symptoms, mo
		Female	Male		
Lateral epicondyle	73	47	26	42.2 ± 14.6 (18–75)	8.4 ± 3.0 (3.3–16.8)
Patella	37	23	14	33.2 ± 14.4 (18–75)	6.9 ± 2.1 (3.8–11.3)
Rotator cuff	27	15	12	42.9 ± 17.9 (18–75)	8.3 ± 2.4 (4.5–13.3)
Achilles	18	6	12	44.3 ± 15.1 (18–67)	10.8 ± 3.4 (6.5–16.8)
Hamstring	17	7	10	35.6 ± 8.6 (18–56)	8.3 ± 1.7 (4.5–11.3)
Medial epicondyle	16	11	5	37.9 ± 17.4 (18–75)	7.6 ± 2.7 (3.8–14.3)
Peroneal tendons	12	8	4	38.6 ± 13.2 (19–64)	9.0 ± 2.7 (4.8–13.5)
Gluteus medius	7	5	2	37.7 ± 9.7 (18–47)	8.6 ± 1.2 (6.9–10.8)
Hip adductor	7	6	1	33.3 ± 14.5 (21–60)	7.9 ± 2.7 (5.3–11.8)
Total	214	128	86	39.3 ± 15.0 (18–75)	8.3 ± 2.8 (3.3–16.8)

Data are presented as mean ± standard deviation (range), if not otherwise specified.

Table 2
VAS outcomes measures of the patients pre-operatively and at various follow-up intervals following PRP injection.[a]

Tendon group	VAS			
	Pre-injection	6-wks	6-mo	Time effect (*p* value)
Lateral epicondyle	6.86 ± 0.38 (6.00–7.00)	1.29 ± 0.49 (1.00–2.00)	0.57 ± 0.53 (0.00–1.00)	**0.000**
Patella	6.29 ± 0.49 (6.00–7.00)	3.86 ± 0.38 (3.00–4.00)	2.86 ± 0.38 (2.00–3.00)	**0.021**
Rotator cuff	4.71 ± 1.11 (3.00–6.00)	1.57 ± 0.53 (1.00–2.00)	1.14 ± 0.69 (0.00–2.00)	**0.001**
Achilles	6.00 ± 0.82 (5.00–7.00)	3.43 ± 0.98 (2.00–5.00)	6.71 ± 0.49 (6.00–7.00)	0.782
Hamstring	5.00 ± 0.82 (4.00–6.00)	3.43 ± 0.98 (2.00–5.00)	2.43 ± 0.98 (1.00–4.00)	**0.001**
Medial epicondyle	4.00 ± 1.00 (3.00–6.00)	2.71 ± 0.49 (2.00–3.00)	2.14 ± 0.69 (1.00–3.00)	**0.020**
Peroneal tendons	5.86 ± 0.69 (5.00–7.00)	3.00 ± 0.82 (2.00–4.00)	4.00 ± 0.00 (4.00–4.00)	0.065
Gluteus medius	6.29 ± 0.49 (6.00–7.00)	3.43 ± 0.98 (2.00–5.00)	1.14 ± 0.38 (1.00–2.00)	**0.001**
Hip adductor	4.00 ± 0.00 (4.00–4.00)	1.14 ± 0.38 (1.00–2.00)	1.43 ± 0.53 (1.00–2.00)	**0.000**

[a] Data are presented as mean ± standard deviation (range), if not otherwise specified. VAS, visual analogue scale. Time effect; differences within the treatment groups examined by means of the Friedman test with post-hoc Dunn test. Bolded P values express <.05 and therefore significant.

Table 3
Variables associated with the likelihood of higher improvement in symptoms.

	OR	95% CI	P value
Location, upper limb vs lower	1.46	1.24–1.71	<0.**001**
Gender, male vs female	1.68	1.39–2.04	<0.**001**
Age, per-year increment	0.96	0.95–0.96	<0.**001**
Number of injections, one vs two	0.96	0.83–1.10	0.549
Metabolic comorbidities, yes vs no	1.03	0.90–1.17	0.688

OR, odds ratio; CI, confidence interval. Bolded p values (Wald x^2) express <.05 and therefore significant.

tendinopathies, we have classified tendon studies according to anatomic locations.

A successful treatment for lateral epicondylitis is deemed to decrease pain and enhance function in daily activities. The best response was determined in the lateral epicondylitis group, in which at least moderate improvement was reported by all patients and mostly to complete improvement was reported by 96% of patients. As a result of the present study, a considerable improvement in symptoms was observed in patients, with 82% of patients stating at least moderate improvement in their symptoms. When comparing leukocyte-platelet-rich plasma (L-PRP) with corticosteroids in a controlled randomized trial, Peerbooms et al presented positive results 6 and 12 months and 24 months after the treatment.[8,12] In contrast, 2 other studies did not find significant differences 6 weeks or 3 months after the treatment.[17,18] However, these results are of a limited clinical value because these studies were presumably underpowered.

One of the tendons treated most frequently, rotator cuff had the moderate rate of success. Rotator cuff degeneration is prevalent, and repair is challenging because of the complex biomechanical environment of the shoulder; moreover, the need to modify diverse intrinsic and extrinsic factors most often may require combinatory approaches such as arthroscopic surgery and PRP. Flat acromions may not need surgical decompression and thus are better treated conservatively. In a randomized controlled trial carried out by Rha et al, they compared L-PRP plus dry needling with dry needling alone but were unable to demonstrate the superiority of L-PRP after 6 months.[19] Kesikburun et al compared a single infiltration of 5 ml of L-PRP into the subacromial space plus exercise versus exercise alone in 20 patients but could not find differences in terms of the quality of life, disability, pain, and range of motion.[20] Rotator cuff pathology is challenging, patients are diverse, and different biological interventions or combinations may be indicated for different subgroups. The intrinsic healing potential of the rotator cuff may depend on the surrounding stem cells that, once activated, may drive tendon healing.[21–23] As an illustration, bone marrow stimulating techniques have been assayed in a recent clinical trial; although there were not significant differences in structural integrity, the sub-group analysis showed better healing in the microfracture group.[24] As shown in the knee, microfractures can be improved when associated with PRP injections.[25] Thus, PRP injection(s) administered to patients with rotator cuff tendinopathy and aimed at stem cell activation may possibly improve the outcome.

The favorable reaction was observed in the patellar tendon group, with at least moderate improvement reported by all patients and moderate to mostly improvement reported by 96% of patients. PRP combined with needling was superior to dry needling at 12 weeks but not at 26 weeks. However, the PRP group at 26 weeks included merely 9 patients.[26] Another randomized trial included a total of 46 patients administered with 2 injections of pure PRP every other week; 3 extracorporeal shockwave therapy sessions were used as a comparator.[27] This study showed VISA-P improvement 6 and 12 months but not 2 months after the treatment. The

rate of responder patients was higher for PRP than extracorporeal shockwave therapy. In terms of the number of injections administered, only 1 or 2 injections were administered to 89% of these patients, while 3 PRP treatments were used for patellar tendinopathy in previous studies. In one case series report, the outcome of 20 athletes was examined after administering 3 consecutive patellar PRP treatments, and a statistically significant improvement was observed in knee function and quality of life, with 80% of athletes finally returning to their previous sports activity level.[28] In another case-control trial conducted by the same researchers, patients administered with 3 PRP injections and physiotherapy were compared with patients administered with physiotherapy only. 39% improvement in sports activity level was reported in the PRP group in comparison with 20% improvement in the control group.[6] The outcome may have been improved as a result of administering an additional PRP injection to our patients with patellar tendinopathy.

The findings of the present study support that PRP will be a reasonable non-operative addition to the selection of treatment modalities for proximal hamstrings tendinopathies, especially for those in which traditional conservative treatment has failed. In the present study, symptom resolution was observed in all patients administered with PRP, and they returned to sport 4.5 months on average after the treatment. Furthermore, a statistically significant decrease in the VAS pain scores and NPRS functional outcomes measurements was observed only in the patients in the PRP group.

In the study of Wetzel et al, 15 patients with 17 proximal hamstring injuries were examined retrospectively, and a PRP injection at the muscle origin was administered to 12 injuries in which conventional treatments failed.[29] A significant decrease on a visual analog scale and the Nirschl phase rating scale not found in patients treated with traditional conservative methods was observed in the above-mentioned patients.

Of our tendons treated most frequently, the lowest rate of success was reported in Achilles tendons. Furthermore, pain level during and immediately after the PRP injection was the highest. Two randomized clinical trials (1 pilot) have compared PRP with an eccentric loading program versus saline solution injections with an eccentric loading program.[11,30] As expected, the pilot randomized study confirmed feasibility but was underpowered (10 patients per group) and thus was not able to show efficacy.[30,31] The completed randomized clinical trial, involving 27 patients per group, showed non-superiority of buffered L-PRP plus eccentric exercises over saline solution plus eccentric exercises.[11] Eccentric exercise therapy represents an effective treatment method of Achilles tendinopathy; thus, as anticipated, significant differences between the 2 effective treatments could not be determined in head-to-head comparisons. In fact, it may be better to indicate PRP treatment for recalcitrant tendinopathies that may necessitate operative intervention once conservative treatments have been exhausted. What is more, the authors did not find any tendon change in vascularity or echogenicity, as assessed by US, 12 months after PRP.[11] This is in sharp contrast to the case series of tendinopathic Achilles tendons (recalcitrant to conservative treatments), in which 2 US-guided injections along with extensive scarification had an impact on decreasing pain, improving function, and enhancing the structure of the tendon as evaluated by US.[32] We may infer that more than 1 injection is necessary to recover a degenerated tissue and that a single PRP injection is insufficient to reduce symptoms and modify tendon structure. It was possible to manage most Achilles tendons (81%) with a single injection of 3–4 ml of L-PRP (platelet enrichment 4× to 8×).

Still, the results remain controversial due to the scarcity of Level I evidence in this condition. In spite of the fact that clinical and structural improvement was observed in uncontrolled studies with more than 1 PRP injection, this was not corroborated after 1 single injection. Moreover, as reviewed recently, the literature on other injectable treatments for non-insertional Achilles tendinopathy is of low quality and has shown variable results.[33] Currently, PRP cannot be recommended for Achilles tendinopathy given substantial knowledge deficits such as the number of doses, the procedure of application, and the best PRP formulation that fits the demand of the host tissue.

In the current study, the overall primary outcome measurement was compared on the basis of the number of injections administered, and moderate-to-complete resolution of symptoms was reported by more than 80% of patients administered with 1 or 2 injections and by 76% of patients administered with 3 injections. Accordingly, it can be concluded that a second or third injection may be beneficial for patients administered with one injection and having residual symptoms. However, no improvement was observed in a number of patients administered with 3 injections. In terms of the above-mentioned tendency, it is possible to question whether more than 3 injections are required. Furthermore, additional factors, such as hormonal and nutritional factors which were not investigated in the present study and which may have an impact on the potential for improvement with PRP treatment, can be present, preventing a response to PRP treatment in some patients. Further studies are needed for the determination of the optimal number of PRP injections.

We strictly utilized a fixed platelet concentration in PRP (×3) and no adjuvant for the purpose of avoiding adding to the variety of PRP preparations presented in the literature.[13–15] We also used a leukocyte-reduced PRP with systematic counting to minimize the acute inflammatory response as reported in the literature.[34] There is growing interest in optimizing PRP formulations, that is, platelet and leukocyte counts and the balance between these counts, as well as the ratio with respect to plasma proteins. In particular, there is a debate about which factor is pivotal in the formulation. To some extent, this conflict was resolved by the finding that different platelet-leukocyte ratios showed a plateau impact of platelet concentrations, with an adverse effect of increasing platelet concentrations on extracellular matrix synthesis.[35] An increase in the platelet concentration within L-PRP preparations leads to the delivery of more anabolic growth factors and decreased proinflammatory cytokines. However, its biological impact on tendons is decreased metabolism as demonstrated by the decreased synthesis of both COL1A1 and COL3A1. Furthermore, it is suggested that bringing leukocytes in PRP to minimum is more significant when compared to bringing platelet numbers to maximum in terms of reducing inflammation and improving anabolic signaling.

Finally, a lack of histologic evaluation and the absence of a control group constitute the limitations of our study, and it requires future confirmation. No placebo group was formed in our series, but in the literature and in our personal experience, tendinopathy does not evolve naturally toward healing in these patients.[10] However, this study represents an important descriptive pilot study with imaging guidance performed in a musculoskeletal interventional department, exact knowledge of PRP and leukocyte concentration, and reproducible clinical scores to assess PRP efficacy and tolerance.

In conclusion, despite the absence of a placebo group, this research indicates that peritendinous injection of PRP under US guidance ensures quick tendon healing and decrease in clinical complaints in patients presenting with tendinosis and tendon tear, with excellent tolerance. Additional preclinical and randomized clinical studies comparing PRP with other currently used methods will be of great interest to consolidate clinical practice.

PRP injections are deemed to be safe, but we must pay attention to metabolic comorbidities because L-PRP injection provoked an exuberant inflammatory response in a patient with type 1

diabetes.[36,37] In addition, unexpected poor results have been observed in 3 patients with recalcitrant patellar tendinopathy who referred to a clinic after they had received PRP treatment elsewhere.[38]

Conclusions

Considering the heterogeneity in tendons and tendinopathies, we are not ready to determine the usefulness of PRP therapies at present. Our research found that results were most promising with patellar and lateral epicondylar tendinopathy in the short to medium term (ie, up to 6 months). In addition, patient (age and gender) and injury location (upper limb) are associated with a higher likelihood of PRP treatment.

Conflicts of interest

All named authors hereby declare that they have no conflicts of interest to disclose.

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