

Study of the Platelet-Rich Plasma Injections for the Treatment of Achilles Tendinopathy after Failure of Conservative Treatment

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Achilles tendon disorders, chronic degenerative tendon disorders (tendinopathy) are a frequent pathology in the Orthopaedic ward and quite difficult to treat. The authors present the case of a number of 25 patients (18 females and 7 male), with mean age of 37.2 years, a group of young and active patients, with chronic unilateral Achilles tendinopathy (at least 6 months of symptoms) refractory to conservative treatment, including physical rest and physical therapy. All study patients have no surgical treatment performed at the Achilles tendons, or any corticosteroids infiltrations in this region. Patients were treated with 3 PRP injections at one week interval. The patients were evaluated clinically and with the ultrasound at baseline, at 1 month and at 6 months, further results will be evaluated at 1 year and early after that. Scores used for evaluation were: Visual Analog Scale (VAS) and VISA A score. The study group that included 25 patients male and females were evaluated using the VAS score and the VISA A questionnaire referring to Achilles tendinopathy, pain symptoms and functionality. Results were assessed at 1 month and at 6 months, both scores improved significantly, and also the ultrasound imaging findings. The majority of the patients were symptoms free after the 3 step PRP local infiltrations showing stable results at 6 months, while 5 of the patients showed no clinical improvement of symptoms. The overall findings in our study show that repeated PRP injections for Achilles tendinopathy obtained good results in term of clinical symptom improvement and also stable results in time at the 6 months evaluation. On this study group discussion refer mainly to the small group of patients, only 25, and to the short term follow up period, 6 months, with future data to be analysed at 12 months and 24 months on this study group.

Keywords: PRP, Growth factors, Achilles tendinopathy, Injections, The Visual Analogue Scale, Musculoskeletal Ultrasound

Achilles tendon disorders, chronic degenerative tendon disorders (tendinopathy) are a frequent pathology in the Orthopaedic ward and quite difficult to treat.

Pain in the Achilles tendon is relatively common in recreational exercisers and individuals active in sports and also pain has been reported in inactive individuals. It is seen most commonly in the mid-portion of the tendon, but can occur at the bone-tendon junction [1-6].

The great incidence of tendon injuries in the population as well as the failure rate of up to 25% [7] of the available conservative treatments has made this field one of the most interesting for alternative biological approaches.

There are currently a number of therapeutic options and the local administration of growth factors is an emerging treatment strategy. Platelet-rich plasma (PRP) is a widely used way to provide a local regenerative stimulus for tendon healing [1-6].

The aim of this study was to document the short/mid-term results obtained after treating recalcitrant Achilles tendinopathy with injections of high concentrate, leucocyte-rich PRP.

Experimental part

The study group included a number of 25 patients (18 females and 7 male), with mean age of 37.2 years, a group of young and active patients, with chronic unilateral Achilles tendinopathy refractory to conservative treatment, including physical rest and physical therapy. All patients have no surgical treatment performed at the Achilles tendons, or any corticosteroids infiltrations in this region. Patients were treated with 3 PRP injections at one week interval. Evaluation was done clinically, also using the ecography and also completing the scores. Then patients were evaluated at baseline, at 1 month and at 6 months, further results will be evaluated at 1 year and early after that. Scores used for evaluation were: Visual Analog Scale (VAS) and VISA A score. All the patients signed an informed consent approved by the Ethics Committee, in accordance with some published models [8-10].

The local Platelet Rich Plasma infiltrations technique consisted of a 8 mL blood sample harvested for each treatment. The sample was centrifuged once at 2700 rpm

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for 10 min and for each sample an approximate quantity of 4 mL enriched plasma was used for local infiltrations. Local PRP infiltrations for Achilles tendinopathy was administered at 1 week a part, with a number of 3 injections per patient.

Platelet rich plasma (PRP) is an increased concentration of autologous platelets suspended in a small amount of plasma after centrifugation. The advantages of this technique is the lack of reactivity to the infiltration substance without a danger of immune reaction or disease transmission [11].

The Visual Analogue Scale (VAS) consists of a straight line with the endpoints defining extreme limits such as no pain at all and pain as bad as it could be. The patient is asked to mark his pain level on the line between the two endpoints. The distance between no pain at all and the mark then defines the subject's pain. This tool was first used in psychology by Freyd in 1923. If descriptive terms like mild, moderate, severe or a numerical scale is added to the VAS [12]. In a Numerical Rating Scale (NRS), patients are asked to circle the number between 0 and 10 that fits best to their pain intensity. Zero usually represents no pain at all whereas the upper limit represents the worst pain ever possible. In contrast to the VAS, only the numbers themselves are valuable answers, meaning that there are only 11 possible answers in a 0-10.

The VISA A score evaluates severity index of Achilles tendinopathy, and is mainly referring to pain symptoms, we conclude that from our group of 25 patients with unilateral Achilles tendinopathy 5 patients had no improvement of the baseline scores (mean baseline score was 527 per all questionnaires), and in the other 20 patients, signs of improvement in terms of pain in the Achilles region appeared after the first PRP local injection, and major improvement after the third local administration with evaluation at 1 month (mean score was 1440) after baseline. We observed that the remission of the symptoms remained stable at 6 months and in some cases we documented even more improvement than before (mean score for all study patients was 1980) in terms of symptoms related to sports and physical activity. Patients performed physiotherapy as a method of conservative treatment before any local mini invasive treatment like infiltrations were performed, as per the following table 1.

Table 1

PREVIOUS TYPES OF TREATMENTS THAT PATIENTS INCLUDED IN THE STUDY PERFORMED (No. of patients)

Laser therapy	15
TENS therapy	18
Ultrasound therapy	20
External Shock Wave therapy	10
Rehabilitation programme (for a minimum of 4 weeks)	20

Ultrasonography is an initial imaging of choice for evaluation of symptomatic Achilles tendon disorders. Diagnostic accuracy reaches 85% [2-6].

Patients were evaluated using Musculo-skeletal Ultrasound at baseline, and with a re-evaluation at 1 month and at 6 months. The echography findings at baseline showed: alterations in the structure of the Achilles Tendons like fusiform focal thickening, relatively homogeneous ecostructure, interrupted by hyperrecognized areas, possibly hemorrhagic focus and calcifications without any modifications that advocate for tenosynovitis and also no tendon ruptures (figs. 1-4).

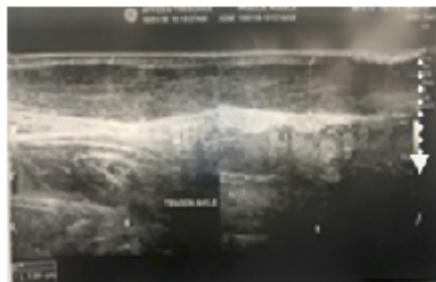


Fig. 1. Echography image showing an Achilles tendon with local modifications

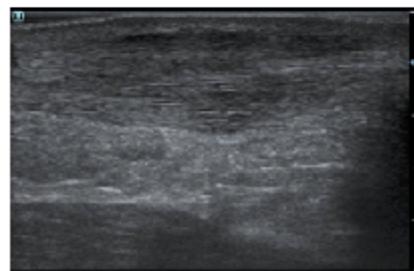


Fig. 2. Ultrasound longitudinal view at baseline of the Achilles tendon showing tendinopathy alterations: arrow shows the modified region

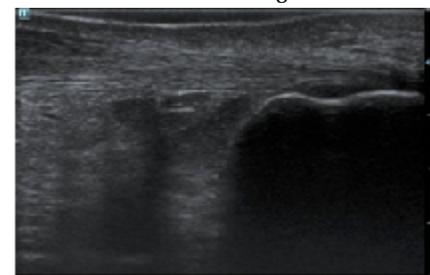


Fig. 3. Ultrasound longitudinal view at baseline of the Achilles tendon showing tendinopathy alterations: arrows show the modified region



Fig. 4. Ultrasound transverse view at baseline of the Achilles tendon showing tendinopathy alterations

The local Platelet Rich Plasma infiltrations, a quantity of 4 mL enriched plasma, were administered at 1 week a part, with a number of 3 injections per patient.

Results and discussions

The study group that included 25 patients male and females, were evaluated using the VAS score and the VISA A questionnaire referring to Achilles tendinopathy, pain symptoms and functionality [14-16]. Results were assessed at 1 month and at 6 months, both scores improved significantly, the majority of the patients were symptoms free after the 3 step PRP local infiltrations showing stable results at 6 months, while 5 of the patients showed no clinical improvement of symptoms.

No local reaction, complications or adverse events were observed during or after this treatment for this study group (figs. 5-7).

The good clinical outcome may be attributed to: the stimulus produced by the needling of the tendon at the time of injection which could cause and inflammatory

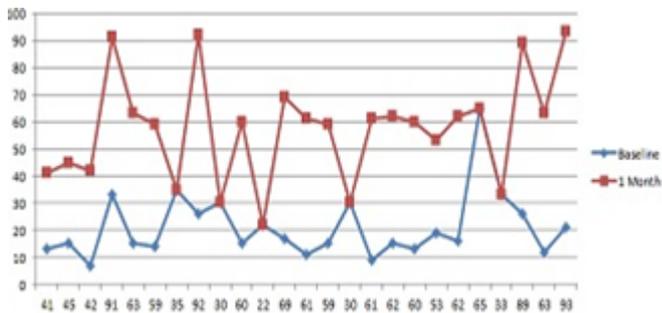


Fig. 5. Results of the VISA A Questionnaire at Baseline and at 1 month per each patient

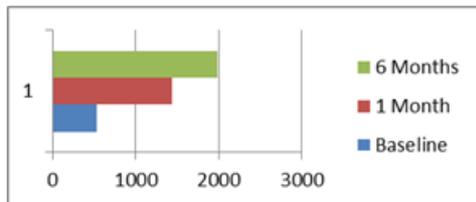


Fig. 6. Results of the VISA A Questionnaire at baseline, 1 month and 6 months

response and a healing effect, the biological impact of the platelet-derived growth factors stimulating gene expression of matrix molecules, collagen production and tendon cell proliferation; and the activation of circulation-derived cells [17], promoted by PRP releasate, which play a crucial role in the tissue healing process [18].

The ultrasound evaluation showed local improvement of the Achilles tendon structure in terms of reduction of the thickness and general improvement of the tendon echostructure. Timing and number of injections are also important details that should be further investigated since they might have an influence on clinical outcome (fig. 8).

A study by Monto *et al.* [19] confirmed the positive clinical outcome in the studies in a larger series of patients: they treated 30 patients affected by chronic tendinopathy refractory to at least 6 months of traditional non-operative management. Each patient received a single US-guided injection of autologous PRP. The clinical results were positive, with a significant improvement with respect to the first evaluation, and this improvement was confirmed up to the final follow - up at 24 months.

Deans *et al.* [20] published their results of treating 26 patients with recalcitrant Achilles tendinopathy with one injection of autologous-conditioned plasma combined with exercise and therapeutic ultrasonography. At the short-term evaluation at 6 weeks, the patients were.

Ferrero *et al.* [21] showed in his studies good results at the 6-month evaluation in 24 patients treated with a single injection of PRP. Besides the good clinical outcome, follow-up US scans were also performed and revealed a widespread improvement in the fibrillar echo texture of the tendon and reduced hyper vascularity as shown by power Doppler [22-25].

Conclusions

The overall findings in our study show that repeated PRP injections for Achilles tendinopathy obtained good results in term of clinical symptom improvement and also stable results in time at the 6 months evaluation.

With regards to the research performed on this study group discussions refer mainly to the small group of patients, only 25, and to the short term follow up period, 6 months, with future data to be analysed at 12 months and 24 months on this study group.

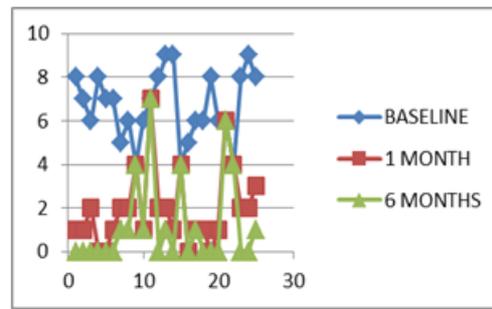


Fig. 7. Results of the VAS score at Baseline, 1 Month and 6 Months timeline



Fig. 8. Achilles tendon at baseline ultrasound evaluation (longitudinal view with measurement)

References

1. KOLBER, M.J., SALAMH, P.A., *Strength and Conditioning Journal*, **41**, no. 1, 2019, p. 81.
2. HENNING, P.R., GREAR, B.J., *Current Reviews in Musculoskeletal Medicine*, **11**, no. 4, 2018, p. 616.
3. LIU, C.J., YU, K.'L., BAI, J.B., TIAN, D.H., LIU, G.L., *Medicine*, **98**, no. 16, 2019, Article Number: e15278, DOI: 10.1097/MD.00000000000015278.
4. SCOTT, A., LAPRADE, R.F., HARMON, K.G., FILARDO, G., KON, E., DELLA VILLA, S., BAHR, R., MOKSNES, H., TORGALSEN, T., LEE, J., DRAGOO, J.L., ENGBRETSSEN, L., *American Journal Of Sports Medicine*, **47**, no. 7, 2019, p. 1654. DOI: 10.1177/0363546519837954.
5. KIA, C., BALDINO, J., BELL, R., RAMJI, A., UYEKI, C., MAZZOCCA, A., *Current Reviews in Musculoskeletal Medicine*, **11**, no. 4, 2018, p. 566. DOI: 10.1007/s12178-018-9515-y.
6. NEPH, A., ONISHI, K., WANG, J.H.C., *American Journal of Physical Medicine & Rehabilitation*, **98**, no. 6, 2019, p. 500. DOI: 10.1097/PHM.0000000000001097.
7. LOHRER, H., DAVID, S., NAUCK, T., *BMC Musculoskelet Disord.*, **17**, 2016, p. 207. <https://doi.org/10.1186/s12891-016-1061-4>.
8. AGHEORGHIESEI CORODEANU, D.T., POROCH, V., 6th LUMEN International Conference on Rethinking Social Action Core Values, 16-19 April 2015, Iasi, Romania, Rethinking Social Action. Core Values, p. 33.
9. ROGOZEA, L., REPANOVICI, A., CRISTEA, L., BARTIZ, M., MICLAUS, R., PASCU, A., *Proceedings of the 4th WSEAS/IASME International Conference on Educational Technologies (Edute'08)*, Book Series: Recent Advances in Computer Engineering, Corfu, Greece, 2008, Oct. 26-28, p. 87.
10. POROCH, V., AGHEORGHIESEI, D.T., *Postmodern Openings*, **9**, no. 2, 2018, p. 225.
11. WANG, H.-L., AVILA, G., *Eyr. J. Dent.*, **1**(4), 2007, p. 192.
12. de VOS, R.J., WEIR, A., van SCHIE, H.T., BIERMA-ZEINSTR, S.M., VERHAAR, J.A., WEINANS, H., Tol, J.L., *JAMA*, **303**, no. 2, 2010, p. 144. doi:10.1001/jama.2009.1986.
13. HOGEA, L.M., SAS, I.T., POROCH, V., NUSSBAUM, L.A., SAS, I., SERBAN, D., ERDELEAN, D., FOLESCU, R., ZAMFIR, C.L., BREDICEAN, A.C., SIMU, M.A., *Rev Chim. (Bucharest)*, **69**, no. 4, 2018, p. 934.
14. CHIRIAC, V.D., HOGEA, L.M., BREDICEAN, A.C., *et al, Rom. J. Morphol. Embryol*, **58**, no. 3, 2017, p. 1023.

15. NUSSBAUM, L.A., HOGEA, L.M., FOLESCU, R., et al., Rev. Chim (Bucharest), **69**, no. 4, 2018, p. 965.
16. KAJIKAWA, Y., MORIHARA, T., SAKAMOTO, H., et al., J. Cell. Physiol., **215**, 2008, p. 837.
17. DE MOS, M., VAN DER WINDT, A.E., JAHR, H., et al., Am. J. Sports Med. **36**, 2008, p. 1171.
18. MONTO, R.R., Foot Ankle Int., **33**, 2012, p. 379.
19. DEANS, V.M., MILLER, A., RAMOS, J., J. Foot Ankle Surg., **51**, 2012, p. 706.
20. FERRERO G, FABBRO E, ORLANDI D, J. Ultrasound, **15**, 2012, p. 260.
21. MAFFULLI N., KHAN, K.M., PUDDU, G., Arthroscopy, **14**, 1998, p. 840.
22. ALFREDSON, H., LORENTZON, R., Sports Med., **29**, 2000, p. 135.
23. HOGEA, B.G., ANDOR, B.C., TOTOREAN, A., Rev. Chim.(Bucharest), **69**, no. 12, 2018, p. 3530.
24. HOGEA, B.G., PATRASCU jr., J.M., SANDESC, M.A., Rom. J. Morphol. Embryol, **59**, no. 3, 2018, p. 741.

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