doi: 10.21823/2311-2905-2019-25-3-67-69

Comment to the Article "PRP-Therapy for Tendinopathies of Rotator Cuff and Long Head of Biceps"

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The article is devoted to the actual problem of treating patients with tendinopathies of the rotator cuff and the biceps long head of the shoulder. This pathology is widespread both among young people with a physically active lifestyle, and in the age group over 45 years old, which is due to the peculiarities of the anatomical structure of the acromion, the coraco-acromial ligament, supraspinatus and infraspinatus tendons, united by a "rotator cable", inside of which there is plot of tendon tissue with reduced blood flow. It is in this section of the sickle-shaped tendon tissue that, with a certain combination of external and internal circumstances, inflammation and degeneration develop, leading, in the absence of adequate treatment, to the formation of its partial and full-layer rupture. The traditional approach to the conservative treatment of this pathology using hormonal drugs does not have proven clinical efficacy with long-term follow-up.

Platelet-rich plasma (PRP) injections are increasingly used in orthopedic practice [1, 2, 3]. P. Randelli published the first report on the clinical use of PRP in the treatment of the rotator cuff in 2008 [3].

The studies of the effect of PRP on human tenocytes of the shoulder rotator cuff with degenerative lesions *in vitro* have shown that platelet-derived growth factors enhance cell proliferation and promote extracellular matrix synthesis [1, 2]. The autologousness, safety and ease of reproduction of PRP make this method attractive for treating patients with both the initial stages of osteoarthritis and tendinopathies of various locations. It should be noted that the options used in world practice of PRP vary significantly, and the optimal drug for the treatment of various pathologies of the musculoskeletal system has not yet been determined. To date, the popularity and frequency of clinical use of various options for PRP therapy has significantly exceeded the evidence base confirming the effectiveness of its use [4]. Obviously, with the advent of the biological method of influencing the degenerative processes occurring both inside the tendon tissue and inside the joint with osteoarthritis using PRP, there is a need for evidence-based clinical studies of the effectiveness of this type of treatment.

The authors of the commented article investigated the clinical efficacy of the mono-injection therapy with one of the many options for PRP (Rusvisk). Encouraging early

• *Comment on the Article*

Malanin D.A., Norkin A.I., Tregubov A.S., Demeshchenko M.V., Cherezov L.L. [PRP-Therapy for Tendinopathies of Rotator Cuff and Long Head of Biceps]. *Travmatologiya i ortopediya Rossii* [Traumatology and Orthopedics of Russia]. 2019;25(3):57-66. (In Russian). doi: 10.21823/2311-2905-2019-25-3-57-66.

Cite as: Dokolin S.Yu. , Kuz'mina V.I. [Comment to the Article "PRP-Therapy for Tendinopathies of Rotator Cuff and Long Head of Biceps"]. *Travmatologiya i ortopediya Rossii* [Traumatology and Orthopedics of Russia]. 2019;25(3): 67-69. (In Russian). doi: 10.21823/2311-2905-2019-25-3-67-69.

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results were obtained, expressed in a decrease in the level of pain and an improvement in the functionality of the upper limb. As the undoubted advantages of the presented study, a sufficient number of observations in groups, their homogeneity, and the prospective nature of the study can be noted.

The clinical studies in this topic have different designs and levels of evidence that range from 1 to 4 [5, 6, 7, 8]. The heterogeneity of the blood processing methods used to prepare PRP, as well as the lack of complete information on the basic characteristics and compositions of the preparations obtained during processing, is the main obstacle to understanding the clinical effects of PRP [4]. The vast majority of existing clinical trials for evaluating PRP drugs do not provide sufficient information to allow an adequate assessment of their protocols. This circumstance complicates the general interpretation of the results of such scientific works and makes it almost impossible to compare the studies [4, 5, 6].

Currently, there is no comprehensive and generally accepted system in the world for classifying PRP and other autologous blood products [4]. The researches have shown that the effectiveness of PRP therapy depends on the volume of autologous blood used, the speed and time of centrifugation, the method of injections, the activating agent, the amount of PRP and platelet concentration, the presence or absence of leukocytes in the administered drug [9].

Today there are different PRP-therapy techniques abroad [4]. In Russia, PRP variants are used obtained both by centrifugation and using special dividing gels-activator for whole blood. However, the use of gels-activator leads to an increase in the cost of consumables and reduces the autologousness of this type of PRP: «Regenlab» systems (Switzerland) and Endoret PRGF (Spain). The most widely used are two competing systems of the so-called "pure" (autologous) PRP. The first system is promoted by the «Rusvisk» company and having the commercial name «Ycellbio». The second plasma-based system was developed by «Arthrex» and has the commercial name «ACP» (A — autologous, C — Conditioned, P — Plasma). It should be noted that with the declared by the manufacturers of these technologies their universal effectiveness in patients with both osteoarthritis and with tendinopathies of different localization, the creators of each of these PRP systems diametrically opposite answer questions about the optimal concentration of platelets and the presence/absence of leukocytes in the excreted drug for achieve maximum clinical effect. For example, the advantages of «ACP» technology are based on three scientific hypotheses. The first indicates that only a certain amount of growth factors secreted by platelets stimulates proliferation. An excess of growth factors is not used and eventually degrades in the tissues, and the maximum platelet count for saturating all available cell receptors and inducing the maximum cellular response is twice their concentration [10]. The second hypothesis states that platelet concentration based on the light layer of a blood clot is excessive for maximum physiological response. With more than four-fold excess of platelet concentration relative to the initial level, a paradoxical inhibition of cell proliferation develops — the so-called "overfilled glass" effect [11]. The third is based on the assumption of the negative impact of certain types of leukocytes on reparative processes [12].

Of course, all of the hypotheses listed need to be repeatedly verified and confirmed by experimental and clinical studies for patients with osteoarthritis and with tendinopathies of various localizations. Today, there is a need to develop a universal classification of PRP, which should combine the following properties: to be easy to use, reproducible and focused on characteristics that are relevant to the prognosis and choice of treatment tactics for patients with

orthopedic pathology. The proposals on the clinical use of cell therapy options to improve the healing of tendons to the proximal humerus are interesting. Stem cells can be a promising solution for restoring the structure of the site of attachment of the rotator cuff on the tubercles of the humerus due to the mechanism of triple action: direct participation in the recovery response, stimulation of local cells through a "paracrine" reaction and immunomodulation activity [1]. Further experimental and clinical work in these areas, of course, has prospects for modern orthopedic practice.

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