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Platelet-Rich Plasma in the Treatment of Androgenetic Alopecia: An Equation with Many Unknowns

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Abstract

The article deals with the use of platelet-rich plasma in the treatment of androgenetic alopecia: effectiveness, problems and prospects. Androgenetic Alopecia (AGA) is one of the most common types of non-scarring hair loss. Baldness affects the psycho-emotional state of a person, which significantly reduces the quality of life. An opinion deviating from generally accepted standards exists that with a normal level of androgens in the blood, AGA in men is a normal biological phenomenon, and not a disease. Regardless of how their condition is classified, people with AGA perceive it as a deviation from the norm, unacceptable from a psychosocial point of view, and turn to a doctor for treatment.

Keywords: Platelet rich plasma• Androgenetic alopecia • Evaluation• Minoxidil

Description

Despite the high prevalence of AGA, the first European recommendations for treatment were published in 2011 [1], where minoxidil and finasteride were proposed as the main methods of treatment, having level 1 evidence. The drugs have a number of disadvantages associated with contraindications for use, side effects, etc., the search for alternative methods of treatment remains relevant. Platelet-rich plasma therapy (PRP-therapy) in terms of the effect on the Hair Follicle (HF) was at the stage of research, the main studies were carried out in vitro. The first pilot studies of its clinical efficacy were published later.

Since this is a controversial topic in the 2013 ISHRS meeting in San Francisco was organized a round table session on the use of PRP in hair loss. Famous doctors who were actively using PRP-therapy at that time took part. Despite the fact that different treatment protocols were used, even then the general opinion about the effectiveness was positive and the experts came to a common opinion: the method is best used in the early stages of AGA; subjective improvement is noted in about 80% of cases; the effect of treatment appears after 4-6 months; randomized placebo-controlled clinical trials are needed.

The number of articles evaluating PRP efficacy in AGA have exponentially increased during the last decade, and in 2018, in updated guidelines for the treatment of AGA attention was paid to this method, but indicated that clinical data on PRP therapy is still insufficient for its good evidence base [2].

In 2020, several systematic reviews and meta-analysis of randomized controlled trials were published, where the assessment of the effect of PRP treatments on hair density and hair thickness was performed. In one of the reviews, out of 30 studies involving 687 patients [3], 29 studies reported beneficial results, and 24 studies reached statistical significance on a measured outcome. 10 randomized controlled trials were included. Another review included twelve original studies [4], only two of which (with two PRP sessions in one study and only one session in the other) showed no statistically significant improvement in the outcomes assessed. The analyzed information highlights the positive effects of PRP on AGA without major side effects and thus can be considered a safe and effective alternative procedure to treat hair loss.

Comparison of the treatment effects of PRP and minoxidil is of undoubted interest. In the studies [5-7], in all cases it was noted that PRP-therapy in some parameters gave an effect superior to the effect of minoxidil. Of particular interest is the result of the combined use of PRP and standard treatment methods. Studies have shown that the use of PRP in combination with minoxidil or finasteride demonstrates a more pronounced clinical effect, confirmed by trichoscopy, compared with monotherapy alone [7,8]. PRP and minoxidil seem to potentiate each other's actions. Data on the specific effect on the pathogenesis of AGA have not been obtained, the mechanism of action of minoxidil, as well as PRP, is not fully understood. PRP has been shown to be effective in the treatment of patients with AGA who are resistant to minoxidil and finasteride therapy [9], which suggests the presence of some other mechanisms of action in PRP, in addition to those that are already known to us. It is assumed that the effectiveness of treatment with minoxidil also depends on the activity of sulfotransferase, which catalyzes the transition of minoxidil to the sulfate form, which is 10-15 times more effective than minoxidil. It was previously shown that platelets (PLT) exhibit minoxidil sulfotransferase activity [10]. Is there a relationship between the sulfotransferase activity of PLT and the high efficiency of PRP in combination with minoxidil? Determination of the concentration of sulfotransferase in PLT, correlation with their activity in HF, and randomization according to these criteria could provide answers to these questions.

It is worth noting that almost in all cases the researchers, using different protocols for the preparation of PRP and different treatment regimens, noted a positive effect. An important point at all stages of PRP preparation is to maintain the integrity and viability of the PLT. Some protocols suggest a soft spin and a single centrifugation, arguing that significant acceleration can be traumatic some blood cells can be mechanically destroyed. Other protocols suggest acceleration over 3000g for better platelet concentration and do not fear cell destruction. Existing systems offer protocols that allow obtaining both low platelet concentration (2.5-3 times higher than the baseline level) and high (5-9 times higher than the baseline blood level) [11]. The number of platelets in PRP of about 1 million/L is considered the "standard for therapeutic PRP", while all manufacturers, despite the difference in concentration, declare the adequacy of their protocols and kits to all the requirements for the effectiveness and safety of PRP therapy. The optimal

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concentration of platelet cells in PRP for solving specific problems and the possible dependence of the therapeutic effect on it are currently being investigated. The first results show no relationship between platelet count, Platelet-Derived Growth Factor (PDGF), Epidermal Growth Factor (EGF) and Vascular Endothelial Growth Factor (VEGF) and clinical improvement [12] .Another study showed that the manual double-spin method had a higher platelet capture efficiency resulting in a higher platelet concentration as compared to the automated device. Though there was a significant interindividual variation in the platelet yield in the PRPs produced by both methods, results were more consistent with the manual method [13].

To date, the issue of platelet activation remains under discussion. Some protocols are activated exogenously by calcium ions (the addition of calcium gluconate or calcium chloride to PRP), which stimulate the formation of fibrin gel, adsorption of platelets on it, their activation and degranulation. Other protocols exogenously do not activate PRP, suggesting more physiological endogenous activation.

The effects of PRP containing a buffy coat are characterized by additional biological activity than PRP, in which it is absent. Neutrophils and monocytes contained in the a buffy coat, which have phagocytic activity, play a role in balancing the pro-inflammatory and anti-inflammatory aspects of healing and can influence the regeneration processes in different ways [14]. When studying the antibacterial action of PRP against strains of Staphylococcus aureus and Staphylococcus epidermidis, it was revealed that the drug has a strong bacteriostatic effect on these microorganisms, especially, the first 4 hours after application. The addition of a buffy coat to PRP does not increase the bacteriostatic potential of plasma, but more likely slows the inflammatory process locally [15]. The relevance of a buffy coat in PRP protocols continues to be debated.

If we talk about specific changes in the condition of hair when using PRP, then a decrease in the intensity of hair loss (a decrease in the number of telogen hairs) is noted already 2 months after the start of treatment. The prolongation of the anagen phase is attributed, in part, to the anti-apoptotic action of PRP, and Autologous Activated PRP (AA-PRP) has been proposed as one of the most important factors in stimulating hair growth through Bcl-2 protein activation (anti-apoptotic effect) and Akt signaling, improving survival dermal papilla cells during the hair growth cycle. In addition, it has been suggested that activation of Fibroblast Growth Factor-7 (FGF-7) /β-catenin signaling pathways in A-PRP treatment stimulates hair growth by inducing differentiation of hair follicle stem cells as well as prolonging the anagen phase. It also appears to stimulate the perifollicular vascular plexus by increasing levels of Vascular Endothelial Growth Factor (VEGF) and Platelet Growth Factor (PDGF), which have angiogenic potential. Approximately 4-8 months after the start of treatment, an increase in hair density and thickness is noted. The duration of the treatment effect ranges from several months to several years and is individual.

It is worth noting the differences are not only in the methods of obtaining PRP and treatment regimens, but also in the criteria for evaluating the clinical result obtained. This makes it difficult to come to a common denominator in the use of PRP in AGA and in the assessment of hair condition in general.

Some researchers operate exclusively with subjective assessment methods: tension test, satisfaction questionnaires, global photos; others use objective assessment methods such as morphometry (trichoscopy) using digital equipment and software from different manufacturers. When assessing the morphometry of hair, there are also no generally accepted norms, since the morphometric characteristics of hair in people of different races and living in different regions of our planet are different.

When we talk about the stimulating effect of PRP on cell proliferation, the question naturally arises about the possible initiation of malignant transformation. In PRP, all growth factors are natural in their biologically determined relationship. The secreted growth factors from PRP are not mutagenic and act by stimulating the normal physiological process, it just happens much faster. Growth factors PRP bind to receptors of cell membranes, and do not penetrate into the cell or its nucleus. The normal sequence of reactions in the processes of cell proliferation and normal gene expression are triggered, and not abnormal, as in cancer. PRP also features plasma components, which are cell adhesion molecules that support cell migration. Theoretically, this implies that PRP does not have the ability to induce tumor formation [16].

As for our personal experience, we have performed more than 4000 procedures, including the treatment of more than 300 men with AGA of II–IV degree on Hamilton-Norwood severity scale and duration of the disease up to 12 years, with a good clinical result. Based on the results of our observations and research, we came to the following conclusions:

1. For the treatment of androgenetic alopecia up to grade IV, it is advisable to use PRP-therapy both as monotherapy and in combination with the use of a 5% solution of minoxidil 2 times a day.

2. PRP injections should be performed once every 4 weeks, at least 4 procedures per course. The course can be repeated once a year.

3. The choice of treatment tactics depends on: the degree of AGA, the duration of the anamnesis, the presence of trichoscopic (morphometric) signs of disease progression. Patients with degree I-IV of AGA with anamnesis of no more than 5 years with signs of progression gave a more noticeable clinical response to PRP monotherapy, in contrast to patients with a more pronounced stage of the stabilized form of AGA and a duration of the anamnesis.

Conclusion

PRP therapy has a sufficient theoretical, scientific and clinical basis to support its use in hair restoration, given its autologousness, safety, efficacy, and availability. The lack of standards in the use of PRP (a reference protocol regarding the preparation method, frequency of use and the amount of PRP administered) and the lack of standards in the methods for assessing the results obtained significantly reduce the possibility of an objective assessment of the therapeutic potential of this treatment method. The main limitation in interpreting the evidence for the effectiveness of PRP continues to be the lack of comparability of studies.

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