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Review Article

The efficacy of using platelet-rich plasma (PRP) in the treatment of androgenic alopecia: a literature review

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Abstract

Androgenetic alopecia (AGA) is currently the primary cause of hair loss in both men and women. It is characterized by a progressive thinning of the hair follicles due to a shortening of the anagen phase of the hair growth cycle. The pathophysiology mainly involves the accumulation of dihydrotestosterone (DHT), a metabolite of testosterone, and a chronic perifollicular inflammatory process. The objective of this study is to evaluate, through a literature review, the validity, protocols, and efficacy of the use of platelet-rich plasma (PRP) in the treatment of patients with AGA. It is a review conducted in the first half of 2024, using the PubMed and BVS databases, employing Descritores em Ciência e Saúde (alopecia, plasma rico em plaquetas, terapia) and Medical Subject Headings (alopecia, platelet-rich plasma, therapy). Inclusion criteria consisted of: a) articles published between 2022 and 2024; b) written in Portuguese or English; c) full-text articles available for free; d) research focused on PRP therapy for the treatment of androgenetic alopecia in men. Twelve articles were included in the synthesis. Overall, the articles indicated that despite the need for standardized protocols, the use of PRP as a treatment for AGA shows promising results in the current context. The therapy demonstrated improvements in hair density and patient satisfaction, suggesting its potential as a viable option for managing androgenetic alopecia. Besides being a safe option with minimal side effects, its combination with other therapies, such as minoxidil, has brought beneficial outcomes for patients with this condition.

Keywords: Alopecia, Platelet-Rich Plasma, Therapy

INTRODUCTION

The hair growth cycle is a process that involves interaction between the epidermal and mesenchymal cells of the hair follicle. These cells come together, proliferate, and go through various distinct phases known as anagen, catagen, and telogen. During the anagen phase, the hair fiber is formed and elongates, being retained in the catagen phase. Finally, in the telogen phase, the hair fiber is eliminated in a process called exogen, the moment of hair shedding. Although the linear growth rate of the hair remains relatively constant throughout life, it is the duration of the anagen phase that emerges as the primary determinant of hair length.[2]

Androgenetic alopecia (AGA) is currently the leading cause of hair loss in both men and women, affecting between 30% and 50% of the male population. It is characterized by progressive thinning of the hair shaft due to a shortening of the anagen phase of the cycle, a process genetically determined and also influenced by androgenic hormones.[3]

There are several perspectives seeking to explain the pathogenesis of AGA, as it is a multifactorial condition. Among the most accepted hypotheses, the influence of oxidative stress (OS) and the individual's inflammatory response explain the development of AGA.[3]

OS occurs as a result of increased expression of pro-inflammatory cytokines associated with chronic perifollicular microinflammation. In genetically predisposed individuals, OS acts in conjunction with high levels of androgens and various environmental factors, such as exposure to environmental toxins (atmospheric pollutants and chemicals present in food, water, and personal care products) and lifestyle factors, including diet, physical activity, and sleep patterns that can interfere with the corticotropin-releasing hormone and cortisol pathway, contributing to AGA. Additionally, exposure to high levels of OS on the skin results in the accumulation of reactive oxygen species (ROS), such as superoxide and hydrogen peroxide, in the hair follicles, overwhelming the follicular antioxidant defense capacity and leading to premature and dysfunctional human dermal papilla cells (hDPCs).[3]

Another theory is based on the relationship between the accumulation of dihydrotestosterone (DHT) and the body's inflammatory response. The accumulation of DHT results from the inhibition of testosterone metabolism by 5α-reductase. Thus, the presence of perifollicular inflammatory infiltration and the involvement of inflammatory genes, such as caspase-7 and tumor necrosis factor (TNF), increase the sensitivity of androgen receptors and support the inflammatory hypothesis in contributing to the development of AGA. Therefore, there is no single central mechanism involved in the pathology, but rather a network of complex processes that interconnect and need to be addressed simultaneously to bring efficacy in treatment.[3]

Platelet-rich plasma (PRP) has emerged as a new treatment strategy for AGA. PRP was first described in hematology as a

volume of plasma with higher concentrations of platelets than in peripheral blood, initially used as a transfusion product for the treatment of thrombocytopenia. However, after years of study, it was revealed that PRP contains a varied number of growth factors and cytokines that can accelerate wound healing and tissue restoration, being the reference in the therapeutic approach to hair loss.[1]

The procedure involves preparing concentrated platelets from the patient's own blood. All PRP preparation protocols follow a generic method, starting with the collection of venous blood of approximately 10 to 60 mL from the patient and placing it in tubes containing an anticoagulant, acid citrate dextrose or sodium citrate solution to prevent coagulation and premature secretion of alpha granules. Subsequently, the whole blood is centrifuged and divided into 3 layers based on specific gravity. The bottom layer contains red blood cells (RBCs) with leukocytes, the middle layer is the PRP, and the top layer is low-platelet plasma (PPP). There are several types of commercial PRP kits that alter platelet concentrations, the presence of leukocytes, and platelet activator to diversify the concentration of growth factors and increase the variability of PRP clinical benefits.[1]

Moreover, many studies have shown that platelets not only affect the hemostatic system but also interfere with the inflammatory system, angiogenesis, stem cell induction, and cell proliferation through the release of many different growth factors and cytokines. Platelets activated in PRP release numerous growth factors and cytokines from their alpha granules, including platelet-derived growth factor (PDGF), transforming growth factor β (TGF-β), fibroblast growth factor-2 (FGF-2), vascular endothelial growth factor (VEGF), epidermal growth factor (EGF), insulin-like growth factor-1 (IGF-1), glial cell-derived neurotrophic factor (GDNF), which play an important role in stimulating hair growth through cell proliferation, differentiation, and angiogenesis.[1]

GDNF can stimulate cell proliferation and protect the hair follicle from premature catagen transition, VEGF acts as a potent hair growth stimulator by inducing angiogenesis, and IGF-1 stimulates the proliferation of Ki67+ basal keratinocytes cyclically to induce and prolong the anagen phase of the hair growth cycle. Additionally, PRP can also induce the proliferation of dermal papilla cells (DP) by activating extracellular signal-regulated kinase (ERK), fibroblast growth factor 7 (FGF-7), beta-catenin, and Akt signaling (an anti-apoptotic signaling molecule).[1]

In summary, the effects of PRP use as a treatment for AGA have been widely studied, with promising results. It not only increases the survival of hair follicle cells through anti-apoptotic effects but also stimulates hair growth, prolongs the anagen phase of the hair cycle, and induces cell proliferation.

MATERIAL AND METHODS

This is a review conducted in the first semester of 2024, aiming to answer the following guiding question: "What is the effectiveness of Platelet-Rich Plasma therapy in the treatment of Androgenetic Alopecia?". For this, articles found in the PubMed and BVS databases were used, covering the period from 2022 to 2024. The MeSH terms used were Alopecia, Platelet-Rich Plasma, Therapy, along with their respective Portuguese versions on DeCS. The combination of these descriptors was performed using the boolean operator AND.

The inclusion criteria adopted were: a) articles published between 2022 and 2024; b) written in Portuguese or English; c) freely available full articles; and d) research related to PRP therapy focusing on the treatment of androgenetic alopecia in men. Exclusion criteria were: a) studies predating 2022; b) studies that did not meet inclusion criteria b, c, and d.

Initially, 544 articles were identified, which were filtered to consider only full texts in English and Portuguese, published between 2022 and 2024. Thus, 98 publications remained for analysis. After reading the abstracts, 86 articles were manually excluded due to theme inadequacy, duplication, and being paid, resulting in 12 articles included in this review.

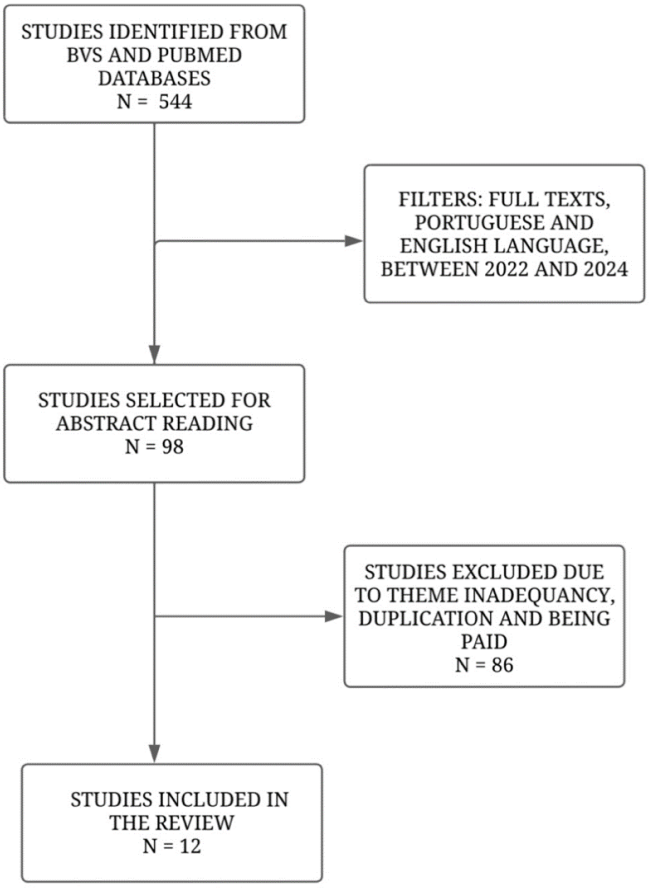

Figure 1. Flowchart of article selection in the PubMed and BVS databases from 2022 to 2024, focusing on the descriptors: Alopecia; Platelet-Rich Plasma; Therapy.

RESULTS

The selected articles are summarized in Table 1 and organized by author and year, sample, objective, method, and results.

Table 1 - Articles obtained from the review, between the years 2022 and 2024, with the theme of the descriptors: Alopecia; Platelet-rich plasma; Therapy

Author and year	Sample	Objective	Method	Results
Paichitrojjana A, Paichitrojjana A 2022	Systematic Review	Studying the definition, classification, mechanism of action, and clinical efficacy of PRP in hair growth.		PRP can be used as a new therapeutic option in AGA, both as monotherapy and in combination.
Wall D *et al.* 2022	Review	Researching therapeutic advances in hair growth.		PRP prolonged the anagen phase and shortened the period between the telogen and anagen phases due to the release of growth factors which stimulated cell proliferation.
Shimizu Y *et al.* 2022	Review	Summarize the main treatment options within regenerative medicine for alopecia.		Both PRP and the use of exosomes appear to be viable forms of treatment for various forms of hair loss.
Georgescu SR *et al.* 2022	Meta-analysis	Evaluate, through a review and meta-analysis, the effectiveness of PRP use in the treatment of AGA		Frequent applications of PRP appear to increase hair density, and starting earlier may lead to better final results.
Elena EP; Irina OS 2022	69 men aged between 18 and 53 years with stages I to V of Norwood-Hamilton scale of Androgenetic Alopecia	Evaluate the effectiveness of using minoxidil, PRP, and the combination of both in the treatment of AGA.	They were divided into 3 observational groups: the main (25 men, receiving minoxidil and PRP), the comparative (22 men, only with PRP), and the control (22 men, only with minoxidil).	The use of combined therapy with minoxidil solution and PRP appeared to be the best therapeutic option for AGA.
Fatima K *et al.* 2023	Systematic review and meta-analysis	Analyze and compare the effectiveness of different treatments for AGA, particularly the use of PRP as a standalone treatment and in combination with other treatments such as minoxidil, finasteride, and microneedling		From an analysis of 9 randomized clinical trials, a significant improvement in hair density was found both in combined therapy and in PRP monotherapy. However, further studies are needed to include combined therapy with PRP in protocols.
Manickam N *et al.* 2023	30 men aged 18 to 50 years with AGA grade II to V (modified Norwood-Hamilton scale)	Evaluate the efficacy of PRP in men with AGA and study any associated adverse effects of this procedure.	The 30 participants received PRP injections every 3 weeks for 4 months	Most patients experienced mild to moderate improvement. Therefore, despite the need for more clinical trials evaluating the long-term sustainability of the method, it appears to be an effective alternative for patients who do not

				respond satisfactorily to Minoxidil or Finasteride
Kaiser MA *et al.* 2023	Systematic review	Evaluate the effects of combined therapy with Minoxidil and PRP in the treatment of AGA.		Most studies demonstrated a superior response in the combined treatment of PRP with Minoxidil; however, there are still limitations in the studies
Pachar S *et al.* 2022	50 men aged between 18 and 54 years with AGA grade II to V (Norwood-Hamilton scale)	Compare the effectiveness of minoxidil 5% and minoxidil 5% combined with PRP in the treatment of AGA in the same patient	Randomized prospective study. The scalp of each patient was divided into two sides for comparison with applications at a one-month interval over a period of 6 months. Clinical improvement was evaluated by hair pull test, photography, patient satisfaction, and trichoscopic assessment	The side with only minoxidil showed a good response in 41%, moderate in 20%, and poor in 29%; while the PRP + minoxidil side obtained a good response in 59%, moderate in 16%, and poor in 25% of patients.
Wei *et al.* 2023	30 men aged between 21 and 49 years with mild to moderate Androgenetic Alopecia	Evaluate the efficacy and safety of PRP prepared by an automatic blood cell separator combined with topical 5% minoxidil therapy in men with AGA.	Randomized, double-blind, controlled study. Patients were divided into two groups, group A received PRP + topical minoxidil, and group B received PRP + topical placebo. Evaluation was performed through trichoscopy, photography, and patient satisfaction	Significant increase in hair density and quantity in all patients after PRP. Although the density/quantity of hair was more pronounced in group A than in group B, this difference was not statistically significant. In terms of clinical efficacy, the satisfaction of group A was superior to that of group B.
Assim M *et al.* 2023	72 patients of both genders aged between 20 and 60 years	Compare the efficacy of PRP therapy and minoxidil for the treatment of AGA in a Pakistani population.	The patients were randomly divided into two groups, group A received PRP, and group B received topical minoxidil. The patients were followed for three months, and the effectiveness of the treatment was assessed by hair pull test.	PRP therapy demonstrates greater efficacy compared to minoxidil in the treatment of AGA
Li C *et al.* 2023	Systematic review	Assess the effectiveness of platelet-rich plasma in the treatment of androgenetic alopecia, establish an effective treatment protocol, and determine the ideal procedure in PRP preparation.		The treatment with PRP for androgenetic alopecia is effective.

DISCUSSION

With technological advances in the medical field, regenerative medicine has gained considerable attention in studies. Its goal is to restore the physiological function of the body through the replacement or regeneration of cells, tissues, or even organs. As a result, therapies based on regenerative medicine are emerging and are currently reported as promising in the treatment of alopecia, including the use of stem cells and PRP.[3]

A recent study comparing hair count and hair density in patients with AGA revealed significant improvements in the scalp treated with PRP compared to the placebo-treated scalp. This is due to the fact that PRP is rich in growth factors known to play important roles in cell proliferation and differentiation.[3]

Moreover, it is a safe source, as it is a minimally invasive and cost-effective procedure, and it has been well-tolerated by patients.[3,6] In a prospective observational study conducted by Manickam and colleagues with 30 patients, the most common side effect observed was temporary pain at the injection site, which was relieved with a single dose of 500 mg paracetamol.[7] In another study published by Dicle and colleagues, only mild side effects were reported, such as temporary pain and swelling at the application site, reinforcing the safety of PRP use.[7,17]

Histological examinations of biopsy samples from PRP-treated areas versus control areas suggest significant changes such as the proliferation of epithelial cells, especially in the dermal papillae of hair follicles, increasing the capillary network and strengthening the basal dermal extracellular matrix. The factors secreted by the platelets present in PRP preparations appear to promote hair growth by stimulating multiple signaling pathways involved in the hair follicle cell cycle, such as the protein kinase B (Akt) pathway.[4,14,15]

In addition, PRP promotes a reduction in micro-inflammation of the hair follicle associated with hair loss during AGA. Growth and transcription factors from PRP signal the follicle to enter the anagen phase of the hair cycle, playing an important role in cellular regeneration and renewal.[4,13,16]

According to a meta-analysis published by Georgescu and colleagues[4], although the total number of PRP treatments and the amount of PRP injected per treatment did not seem to influence the outcome, an increased frequency of application (number of treatments per month) results in greater increases in hair density in patients with AGA. Furthermore, other important factors are the age of the patients and the early start of treatment from diagnosis, with earlier initiation resulting in better outcomes.[4]

Regarding the technique used in this treatment, it is recommended that the volume of PRP be at least 0.05 ml/cm^2 per injection, with a volume of 0.1 ml/cm^2 being the best-reported option. This volume should be adjusted according to each patient's characteristics. Concerning the frequency of application, it was reported that three consecutive treatments at one-month intervals seem to be the best alternative. Benefits have also been demonstrated from a reapplication after 3 to 6 months of the first treatment.[12]

Due to the complexity of AGA pathogenesis, it is recognized that the best scenario for achieving therapeutic success involves a combined multimodal approach. Within this context, studies have been published reporting favorable and promising results when using multiple forms of treatment simultaneously. This strategy achieves different pathological aspects of the condition, such as stimulating blood circulation in the scalp through microneedling and promoting hair growth with minoxidil.[8,11]

Currently, minoxidil therapy, whether in oral or topical form, emerges as a prominent pharmacological intervention in the treatment of AGA and is widely adopted. Minoxidil, known for its vasodilatory properties, promotes increased blood flow to the hair follicles, thus stimulating hair growth.[9,11]

Despite the recognition of minoxidil as a standard therapy for AGA, it is important to note that its isolated use does not always result in complete efficacy for all patients. Some individuals may experience satisfactory results, while others may exhibit a limited response to treatment, in addition to some patients reporting adverse reactions to topical minoxidil such as dermatitis, scalp irritation, and relapse tendencies after discontinuation.[10]

This variation in efficacy highlights the need to explore new therapeutic approaches that can optimize results and meet individual patients' needs. Therefore, studies investigating the combination of minoxidil with other therapies, such as PRP, compared to minoxidil alone, gain significant importance.[10,11]

A randomized prospective study conducted by Sandeep Pachar and colleagues[9] involved 50 male patients, aged 18 to 54 years. Each patient's scalp was divided into two hemispheres, with the right side receiving 5% minoxidil, while the left side received 5% minoxidil combined with intradermal PRP, at monthly intervals, over a period of six months. Minoxidil was applied to both sides in a dosage of 1 mL twice daily.[9]

The clinical improvement was assessed monthly for six months through hair pull tests, photography, patient satisfaction, trichoscopy evaluation, and hair density. Additionally, at the end of the study, the results were classified using a comprehensive questionnaire that assessed a variety of aspects related to the treatment. These included the reduction of baldness, improvement in hair appearance, increased hair density, decreased hair loss, and overall satisfaction after therapy.[9]

The results of the study showed that the side that received only minoxidil had a good response in 41%, moderate in 20%, and poor in 29% of patients; while the side with minoxidil combined with PRP had a good response in 59%, moderate in 16%, and poor in 25% of patients.[9]

Therefore, it is concluded that a combination of these therapies can not only boost hair growth but also may halt the progression of AGA for a considerable period of time. The platelet growth factors present in PRP are likely able to regulate the life cycle of hair bulbs, ensuring better hair growth. Considering its excellent safety profile, PRP combined with 5% minoxidil is a promising treatment option for patients with mild to moderate AGA.[5,9]

CONCLUSIONS

Currently, it is known that AGA (Androgenetic Alopecia) is the main cause of alopecia in both men and women. Various pathophysiological factors are involved in this condition, with the androgenic effect associated with chronic perifollicular inflammation being the main one. The accumulation of DHT, a testosterone metabolite, in the receptors of the hair follicle cells is the key factor in hair follicle miniaturization and consequently in the development of AGA. Thus, studies have emerged to validate therapy using PRP (Platelet-Rich Plasma), given its potential effect on this chronic inflammatory process and the presence of growth factors.

Therefore, it can be concluded that the use of PRP is an effective alternative for AGA treatment, being a safe method well tolerated by most patients. It is also worth noting that it can be used as monotherapy or combined with minoxidil to enhance hair growth, as well as improving hair density and texture. However, it's essential to conduct additional studies to determine the best protocol for preparing PRP treatment, including the ideal dosage, injection technique, quantity, and

frequency of treatment sessions, aiming to achieve maximum therapeutic efficacy.

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