

## CLINICAL ASSESSMENT OF THE THERAPEUTIC OPTIONS FOR ALOPECIA TREATMENT

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### Abstract

Baldness has been a major aesthetic issue for men in general and solutions to solve this problem have been tried for several hundred years. Although there are cases in which alopecia is the result of a specific pathology (which can be treated accordingly), for many years baldness has been thought to be idiopathic or genetic and without treatment. Our study aims to evaluate different treatments: a topical mixture of finasteride and minoxidil, PRP (platelet rich plasma) infiltrations and oral medicine to stop hair loss and improve hair density and follicle diameter. The study was conducted on a series of patients exhibiting hair loss with or without a known medical cause.

### Rezumat

Calviția reprezintă o problemă estetică majoră pentru bărbați, în general, iar soluții pentru rezolvarea acestei probleme au fost încercate de-a lungul timpului. Deși există cazuri în care alopecia este generată de o patologie specifică (care poate fi tratată corespunzător), o lungă perioadă de timp aceasta a fost considerată ca fiind o problemă genetică, idiopatică și fără soluții terapeutice. Studiul nostru are drept scop evaluarea diferitelor tratamente: un amestec topic de finasteridă și minoxidil, infiltrații locale cu PRP (plasmă bogată în trombocite) și medicație orală pentru stoparea căderii părului, îmbunătățirea densității părului și a diametrului foliculului pilos. Studiul a fost realizat pe o serie de pacienți care au prezentat acest diagnostic, cu sau fără o etiologie medicală cunoscută.

**Keywords:** hair loss, minoxidil, finasteride, PRP - platelet rich plasma, hair transplant

### Introduction

Hair loss is a common problem both in men and women around the world. Only in the USA, according to the National Institute of Health, there are 30 million women and 50 million men suffering from AGA (androgenic alopecia) [1]. Although quite frequent and with an important psycho-social impact, the pathogenesis of this aesthetic problem is to this day not well understood. Male pattern baldness (MPB), also known as AGA, is reported in 20% of men aged 20 - 30 years, and the incidence increases with 10% *per* decade according to Liu *et al*; furthermore, it is stated in the same study that AGA in the Asian and African-American populations is lower in prevalence and severity compared to AGA in the European population [2]. There are several hormonal, genetic, nutritional, environmental or psychological factors that should

be considered as they are involved in a series of pathological complications, among which hair loss is a relevant one [3-5].

Cortisol, which is a stress hormone, has been incriminated in perturbing the cyclic regulation of the hair follicle. Thom *et al.* have demonstrated that high levels of cortisol reduce the synthesis of 2 important elements of the skin (proteoglycans and hyaluronan) by 40% [6]. There is an important difference between normal hair loss (during the hair cycle) and pathological hair loss, which is not connected to this cycle. Every follicle will normally follow the 3 phases of the hair cycle – anagen, catagen and telogen. The first phase – anagen – is the period of active growth and it can take between 2 and 7 years (by some authors up to 10 years). The catagen phase represents a transitional period of 2 - 3 weeks, while the telogen phase lasts approximately 100 days. 80 - 90% of the hair follicles on the scalp are

in anagen phase at any time, 2% of all hair follicles are in catagen phase, while the rest of the hair follicles (8 - 18%) are in telogen phase [7].

At the end of the telogen phase, the shaft is eliminated, permitting a new hair follicle to enter in the anagen phase. Normal telogenic hair can be estimated by doing a "telogen count" on a trichogram using a flock of hair which is forcibly removed from the scalp. A normal "telogen count" is between 6% and 13%, while a percentage higher than 20 is considered to be pathological [7].

In terms of evaluating hair disorders and alopecia, there are several methods which can be used; these methods can be divided into 3 groups – invasive, semi-invasive and non-invasive. The invasive method is the biopsy for histopathology analysis. The semi-invasive are the trichogram and the unit areatrachogram, while the non-invasive methods are: dermoscopy, laser scanning microscopy, electron microscopy, hair count, global hair counts, weighing shed hair and phototrichogram [8].

A pharmacological treatment for exceeding hair loss is represented by a topical solution of minoxidil. Minoxidil is a peripheral vasodilator in which the mechanism of action that causes hair growth is not yet known. The medicine was first utilized as a treatment for hypertension but due to its side effect (hypertricosis), it became an important drug used for hair growth [1, 9] and is a FDA approved medicine for MPHL (male pattern hair loss). In Europe, minoxidil is also approved by the European Medicines Agency (Procedure no.: PSUSA/00002067/201510) as topical formulation [10].

Finasteride is another drug frequently used for the treatment of androgenetic alopecia. Finasteride is a 5- $\alpha$  reductase inhibitor, an enzyme which converts testosterone into dihydrotestosterone. Dihydrotestosterone is associated with male baldness therefore finasteride prevents the synthesis of this hormone. Finasteride is not only used for male pattern hair loss, but also for benign prostate hyperplasia [11].

A new therapeutic approach for alopecia is the treatment with platelet-rich plasma (PRP), a serum which contains a high concentration of thrombocytes and growth factors and is obtained by centrifuging the patient's own blood. PRP is an autologous remedy used for many medical disorders – skin ulcers, bone defects, eroded cartilage, skin rejuvenation, nerve regeneration and hair restoration [12-15].

Hair transplant surgery is the last option when all other treatments have failed or when the patient wants a permanent result without using continuous pharmacologic therapies. There are several techniques used in hair transplant, the 2 most important being the follicular unit transplantation (FUT) and the novel follicular unit extraction (FUE) [16].

The follicular unit transplantation (FUT) consists of removing an elliptical strip of hair-bearing tissue from

the donor site which is then divided into follicular units (groups of hair follicles). The donor area is then closed primarily using sutures and the follicular units are transferred as skin grafts to the recipient area. This technique leaves a linear scar at the donor area, which will be masked by the surrounding hair. The follicular unit extraction (FUE) implies harvesting small individual follicular units, without leaving the linear scar at the donor site; the units can be then directly transferred at the recipient site [17, 18].

The aim of this study was to evaluate and compare 2 types of treatments in terms of preventing hair loss and achieving hair regeneration – topical treatment and PRP infiltrations. The 2 therapeutic options were evaluated both alone and in combination with one another.

## Materials and Methods

This is a retrospective observational study conducted on a number of 35 patients experiencing hair loss. All patients were examined *via* trichoscopy prior to the treatment. The trichoscope used was Dino-Lite digital microscope. The area selected for trichoscopy were the vertex area and the fronto-parietal region (in case of unspecific hair loss). The trichoscope was set at a magnification of 50x.

The two variables recorded for each patient in the study were the hair follicle diameter and the hair follicle density. These variables were recorded prior to treatment as well as 4 months after the beginning of the therapy. The program used for measurement was DinoCapture 2.0. When assessing hair follicle diameter, the focus was placed on the hair shaft. When counting the hair follicles, the focus was set on the scalp, at the emerging site of the follicle.

The hair density was performed by counting the number of follicles (both with one, 2 or 3 shafts of hair). The surface area for counting was standard for all measurements – 7.8/5.8 mm at a magnification of 50x. For hair shaft diameter, an average between the 3 thinnest and the 3 thickest hair follicles was calculated and noted before and after the treatment.

The magistral prescription of the foam consisted of minoxidil 5% and finasteride 0.5%, which was to be applied twice daily on the scalp. The composition of the foam is: minoxidil 5 mL, finasteride 25 mL, transcutool, lactic acid *qsad* pH 4.5, incorporation base *qsad* 100 mL. The composition for the incorporation base is: thyme extract, rosemary extract, nettle extract, tocopherol, niacinamide, panthenol, inositol, purified water, denatured alcohol, propylene glycol, lactic acid, hydrogenated castor oil, glycerine, potassium sorbate, BHT, phenoxyethanol and isopropyl alcohol.

The combined finasteride and minoxidil solution is then placed in special foam bottles with exact dosing. One push releases a volume of 0.5 mL which equates to 25 mg of minoxidil and 2.5 mg of finasteride. The

recommended dose for patients with AGA was 1 mL, twice *per* day. The number of PRP sessions differed, ranging from 1 *per* month to 1 every three months. The protocol for PRP involved drawing 8 mL of blood into a special PRP tube. The blood was then centrifuged for 5 minutes at 4000 rpm. The platelet rich plasma was then extracted (about 5 mL plasma) from the tube using a 10 mL syringe (containing calcium citrate as activator) and then injected into the scalp using 1 mL syringes with 30 G x 1/6" luer lock needles. Injections were spaced out in the thinning area, which is typically along the hairline, part, vertex and crown of the scalp. Prior to treatment, the patients receive a topical anaesthetic (either 3 puffs of lidocaine 10% or topical application of eutectic mixture of lidocaine and prilocaine – EMLA).

The patients opted for surgery in order to improve the density of the hair follicles in a shorter period of time. The equipment used for FUE transplant was a manual punch, a motorized punch for the follicular unit extraction and multiple Choi implanters used for seeding the small grafts.

35 patients who began treatment for hair loss received a survey with multiple questions regarding the treatment followed, possible cause of their hair loss, history of hair loss (both personal and family history), treatment they used and period of time they used the treatment or the number of PRP sessions they had, side-effects of the treatment and degree of satisfaction after hair loss therapy. All the study participants signed an informed consent for the inclusion in the study. The study was conducted in accordance with the Declaration of Helsinki, and the protocol was approved by the Ethics Committee.

31 patients were included in the study, based on the treatment they underwent (topical solution, PRP infiltration or combination of the 2). 4 patients were excluded from our study, 3 patients for using only vitamins and one patient for using as treatment only oral finasteride.

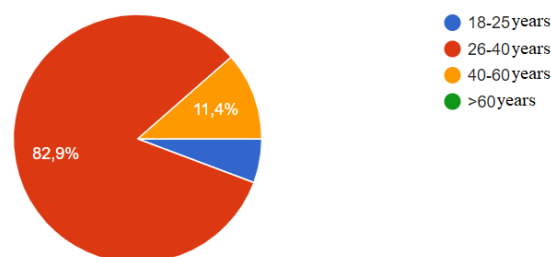
The remaining 31 patients were divided into 3 groups. **Group 1.** Enrolled 16 patients and they received topical treatment with PRP. From the 16 patients who used a combination of topical treatment and PRP infiltrations, 13 used the combination of finasteride and minoxidil while 3 used minoxidil without finasteride as topical treatment. 2 patients in the first subgroup also used in their previous medical history oral treatment with finasteride.

**Group 2.** Enrolled 9 patients who received topical treatment without PRP. 9 patients used topical treatment without PRP (6/9 used a combination of minoxidil and finasteride for topical used, while 3/9 patients used minoxidil). Among the 3 patients who used minoxidil as topical treatment, 1 patient also had oral treatment with finasteride.

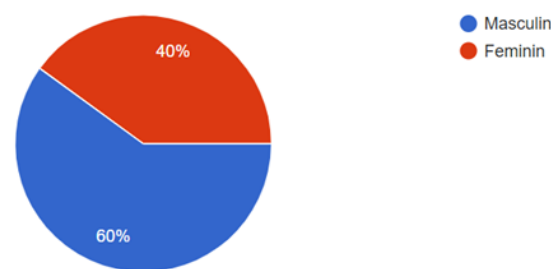
**Group 3.** Enrolled 6 patients treated with PRP without topical treatment.

In the 3 groups, some patients also had additional treatments (Dermapen®, hair transplant, vitamins or oral medication with finasteride) prior or during the main treatment. In the group of 35 patients, a total of 10 patients used vitamins, 4 patients also underwent hair transplant in their history (2 of which were performed in our clinic) and 2 patients opted for an additional treatment with Dermapen®.

The results of the questionnaire addressed to all 35 patients are presented below.

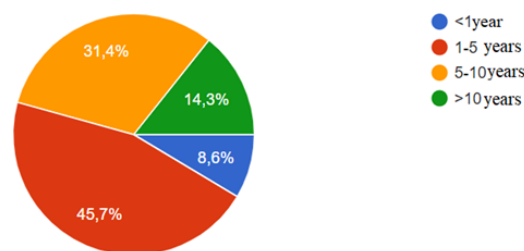


**Figure 1.**  
Age distribution



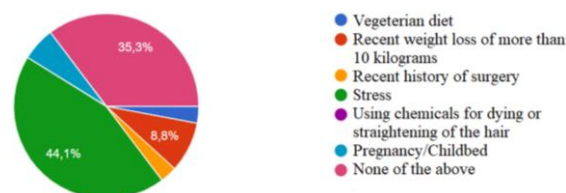
**Figure 2.**  
Sex distribution

For how long have you had a hair loss problem?



**Figure 3.**  
Period with hair loss problems

Previos to the hair loss debut (1-6 months), were you in one of these situations?



**Figure 4.**  
Other causes for hair loss

Do you have a known medical cause for hair loss?

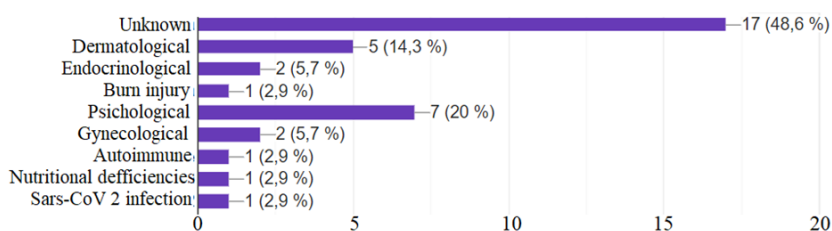


Figure 5.

Medical conditions for hair loss

Family history of alopecia

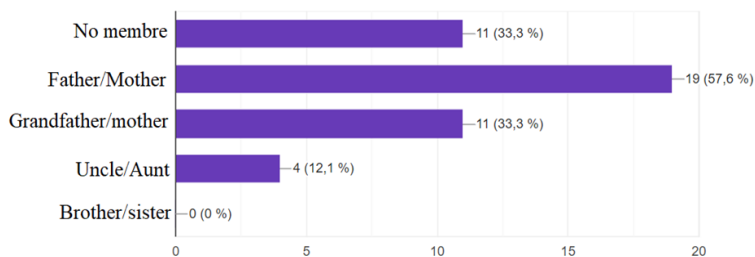


Figure 6.

Family history of alopecia

For how long have you been using topical treatments?

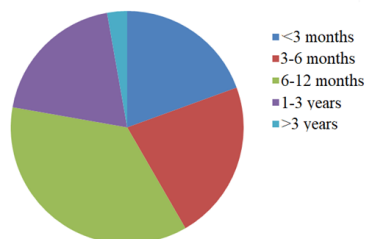


Figure 7.

Time intervals for using topical treatments

How many PRP sessions have you had?

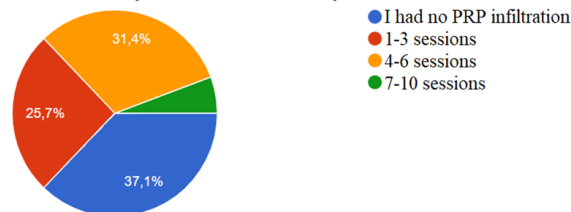


Figure 8.

Number of PRP infiltration sessions

What were the outcomes after using the treatment?

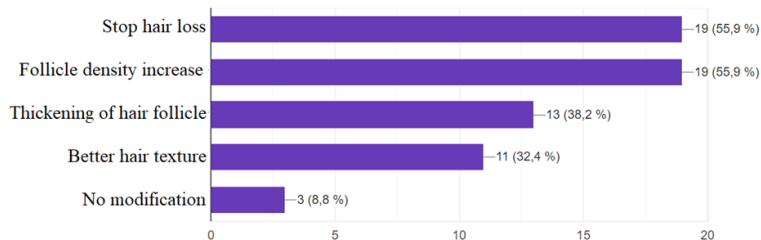


Figure 9.

Results after treatment

Did you experience side effects after using minoxidil?

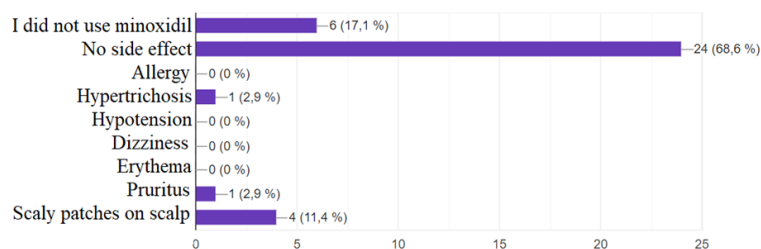


Figure 10.

Side effects after minoxidil

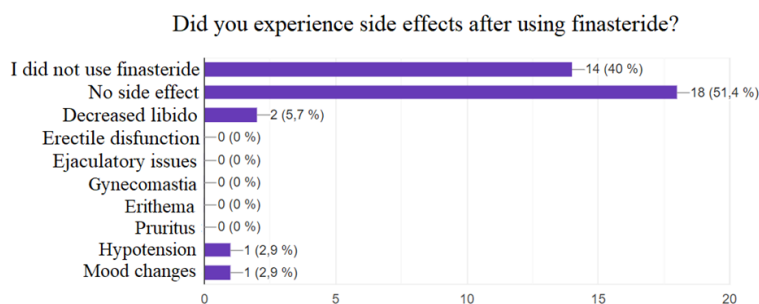


Figure 11.

Side effects after finasteride

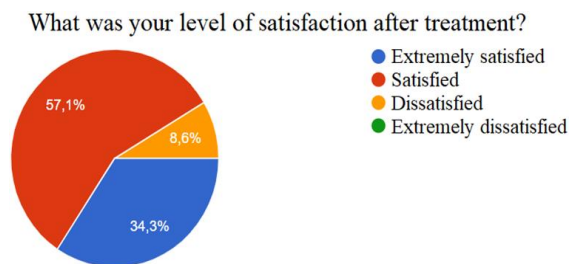


Figure 12.

Satisfaction level after treatment

### Results and Discussion

Prior to treatment initiation, all patients were evaluated using trichoscopy. The density of the hair follicles and the average hair shaft diameter were recorded before and after treatment.

A descriptive analysis of the first 3 groups (31 patients) was performed using IBM SPSS Statistics 26. The variables used were follicular density and hair thickness, measured before and after treatment. Wilcoxon Signed Ranks tests were performed in order to evaluate whether the treatment used improved the 2 parameters.

Table I

Mean and median determinations for follicular density and hair thickness before and after the treatment in the 3 groups

Group		Follicular density T0	Follicular density T1	Hair thickness T0 (µm)	Hair thickness T1 (µm)
Topic + PRP (n = 16)	Mean (SD)	33.75 (11.705)	41.19 (9.181)	46.69 (18.135)	59.63 (19.609)
	Median (IQ)	34 (24)	39.50 (15)	51 (32)	64.50 (31)
Topic (n = 9)	Mean (SD)	35.33 (11.203)	42.11 (10.191)	55.22 (20.999)	65.11 (23.23)
	Median (IQ)	37 (16)	42 (19)	61 (42)	74 (46)
PRP (n = 6)	Mean (SD)	26.83 (10.704)	28.83 (11.737)	36.00 (19.016)	37.83 (17.612)
	Median (IQ)	25 (23)	25 (23)	29.50 (35)	32.50 (34)

In the Topical + PRP group, the Wilcoxon signed rank test revealed a statistically significant difference in hair density after applying the treatment. ( $p = 0.001$ ). There was also a statistically significant improvement in hair thickness in the Topical + PRP group after treatment ( $p < 0.001$ ).

For the topical treatment, the Wilcoxon signed rank test showed that between the 2 determinations of hair density (before and after treatment), there was a statistically significant improvement. Indeed the median hair density after treatment was higher than before treatment. ( $p = 0.011$ ).

The analysis for the topical treatment showed that between the 2 determinations of hair thickness (before and after treatment), there was a statistically significant improvement. The median hair thickness after treatment was bigger than before treatment. ( $p = 0.008$ ).

In the PRP group, no improvement in hair density after treatment. ( $p = 0.084$ ). Also, regarding the hair thickness after treatment. ( $p = 0.131$ ).

In terms of clinical aspect, the before/after pictures below depict the hair improvement in a series of patients

who used a topical mixture of finasteride and minoxidil and PRP infiltration (alone or in combination).

Before any hair treatment, a physician must study the patient's history in order to exclude any pathological causes for hair loss. During the first consult, a series of blood analysis should also be requested in order to evaluate if there are any biological imbalances. Vitamin A, B, C, D, E, inosine, iron, zinc and selenium – all play an important role in non-scarring alopecia [19, 20]. Moreover, an evaluation of the follicles should be performed using trichoscopy before treatment initiation [21].

There are multiple types of hair (based on shaft thickness): terminal hair: above 70 µm in diameter; intermediate hair: between 30 and 70 µm diameter and vellus hair: below 30 µm in diameter.

Shaft diameter may depend on particular characteristics: race (African hair is generally thicker), shape (curly hair has a coiled springlike structure) [22] or physiologic stage. Hair density also varies in different races: Caucasians (60 - 100 follicular units/cm<sup>2</sup>), Asians (100 follicular units/cm<sup>2</sup>) and Africans (60 follicular

units/cm<sup>2</sup>). A normal growth rate for a hair follicle located on the scalp is 0.35 mm/day in length, which adds up to 1 - 1.2 cm/month [23].

PRP combined with a mixture of finasteride and minoxidil represents a minimal invasive treatment, which can constitute an alternative for hair transplant. The treatment is affordable, but requires regular interventions in order to achieve and maintain results. All patients in our study were recommended for a maximum regeneration result a combination between PRP infiltrations and topical solution – which explains the majority of the patients in the first group. The group with PRP infiltration without topical treatment had the smallest number of patients due to the fact that it is a minimal invasive treatment which may cause discomfort such as local pain and swelling and most patients who endured the PRP treatment were therefore also compliant with the topical treatment (and included in the first group). Currently, minoxidil is undergoing studies for female pattern hair loss (FPHL). Minoxidil exists in 2 forms – one 2% which is indicated for women (twice daily), while for men it is used in a concentration of 5%, twice a day. 5% minoxidil can also be used by women administered once *per* day. There are ongoing studies of oral intake of minoxidil for patients who are not compliant or have had side effects when using topic solution of minoxidil. The side effects encountered in the topical use of minoxidil are contact dermatitis and hypertrichosis, while the oral treatment with minoxidil (0.25 - 1 mg/day) can also cause hypotension and lower limb oedema [24].

As for finasteride, Olsen *et al.* have proven that 5 alpha reductase inhibitors improve scalp hair growth in men with male pattern hair loss [25]. This therapeutic option can also be used in advanced stages of male baldness when there are not enough follicles to be transplanted, although with limited results. This treatment is ideally to be used in the period when the hair starts falling and has limited results when the hair is completely gone for more than a year. Unlike minoxidil, however, the use of finasteride is somewhat controversial, as there are studies which show that the oral administration of finasteride may cause sexual side-effects such as erectile dysfunction, decreased libido and ejaculation problems [26]. Mood disturbance is one more side effect which has been described in patients using this drug.

Finasteride is also described to have a teratogenic effect on the unborn male. Treatment with finasteride is contraindicated for patients with family history of breast cancer [24]. The side effects in topical use of finasteride are the same as in oral administration; furthermore, when using a topical solution, there is also a risk of contamination of family members.

Hair transplant, on the other hand is a fast way for obtaining hair coverage on small bald areas. It is recommended after one year of local or oral treatment for hair loss, to enrich hair density. Hair transplant is

however dependent on the hair density at the donor site area (and there are patients who might have a relative contraindication to hair transplant due to low density follicles in the donor area). Furthermore, to obtain natural results with hair transplant, the technique is important, as well as the donor area (because the hair follicles must be similar to those at the recipient area).

In our study, the topical treatment (finasteride and minoxidil) combined with PRP infiltrations offered results which are clinically obvious. The topical treatment alone also improved follicular density and hair thickness, while PRP alone did not achieve statistical significance in improving these parameters. We need, however, to take in the consideration the limitations of the study: the small sample and non-parametric data. A similar study conducted by Satyendra *et al.* for male type baldness showed that the combination of topical minoxidil and PRP infiltrations is more effective in increasing hair density compared to PRP infiltrations or topical minoxidil administered separately. The study also demonstrated that PRP infiltrations have better results than topical treatment with minoxidil [27]. Another randomized trial compared PRP infiltrations with topical minoxidil foam on 20 women exhibiting androgenic alopecia (AGA) [28]. The conclusions of the study were that PRP is an efficient treatment for hair regrowth in women but the results were better for the treatment with minoxidil. However, the same study revealed an improved quality of life after PRP, which was not noted after minoxidil.

Pakhomova *et al.* conducted a study on 69 men to evaluate PRP, minoxidil and their combination and the results were analysed both clinically and immunohistochemical [29]. PRP therapy was found to be more effective than minoxidil, while the combination of the 2 treatments had better results than each treatment used separately.  $\beta$ -catenin, Ki67+ and CD34 expression area increased after PRP, which represent a sign of proliferative activity of the hair follicle.

A more comprehensive, systematic review that compared PRP to minoxidil, finasteride and adult stem cell-based therapy was performed by Gnetile *et al.* [30]. In 17% of these studies, the PRP had no effect in treating AGA, while the rest of the studies reported positive results without significant side effects.

Other therapeutic options which were isolated used by some of the patients in our study (oral medication with finasteride or vitamins, Dermapen®, hair transplant and mesotherapy) need further investigations to prove their value in hair loss treatment.

In our study, 2 patients underwent hair transplant in our clinic with good results. However, due to the small number, the 2 patients could not be included in a separate group. A comparison between the surgical and the medical treatment for alopecia could constitute a new research project once a significant number of patients who opt for hair transplant is reached.

However, taking into consideration that most patients undergoing hair transplant have previously had PRP infiltrations and/or topical solutions, this could constitute a bias in interpreting final results. Hair transplant could be a fast solution for achieving hair coverage, but this should not exclude the use of long-term local hair treatments to prevent the remaining follicles from falling.

### Conclusions

Hair loss is a major aesthetic problem both in men and women and there are several treatment options available to address this issue. Although not all hair loss is clearly related to a specific cause, there are multiple problems (both medical and non-medical) which if corrected could improve the scalp appearance. In our study, the combination of treatments including PRP infiltration and a mixture of finasteride and minoxidil has proven his utility in hair regeneration, both from the perspective of hair density and follicle diameter. Similarly, the application of the topical solution statistically improved hair density and thickness, but PRP alone didn't achieve statistical power in improving the 2 parameters due to the small number of patients included in this group.

### Conflict of interest

The authors declare no conflict of interest.

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