Platelet-rich Plasma for Androgenetic Alopecia Treatment: A Randomized Placebo-controlled Pilot Study

Paul GRESSENBERGER[1], Gudrun PREGARTNER[2], Thomas GARY[3], Peter WOLF[1] and Daisy KOPERA[1]
[1]Department of Dermatology and Venereology, [2]Institute for Medical Informatics, Statistics and Documentation, and [3]Department of Internal Medicine, Division of Angiology, Medical University of Graz, Graz, Austria

Platelet-rich plasma injections have been presented as an effective treatment for androgenetic alopecia; however, reliable study data concerning this therapy are lacking. The current randomized, placebo-controlled pilot study explored this novel therapy in 30 healthy male subjects with androgenetic alopecia. Five platelet-rich plasma treatments, at intervals of 4–6 weeks, and 2 follow-up examinations were performed. Twenty subjects were injected intracutaneously with platelet-rich plasma and 10 with physiological saline. Treatment efficacy was assessed by changes in hair number and diameter, measured with the TrichoScan system. A secondary objective was to assess clinical improvement, which was evaluated by an independent reviewer using patient photographs and a 5-point Likert scale. In addition, subject satisfaction was assessed by survey. No improvements were seen over the course of the trial, using TrichoScan measurements or visual assessment. In conclusion, these results suggest that treatment with platelet-rich plasma as a monotherapy does not improve hair growth in men with androgenetic alopecia.

Key words: platelet-rich plasma; androgenetic alopecia; hair restoration.

Accepted Jul 9, 2020; Epub ahead of print Jul 31, 2020

Acta Derm Venereol 2020; 100: adv00247.

Corr: Paul Gressenberger, Department of Dermatology, Medical University of Graz, Auenbruggerplatz 8, AT-8036 Graz, Austria. E-mail: paul.gressenberger@medunigraz.at

SIGNIFICANCE

Androgenetic alopecia is a common form of hair loss, which can have a significant impact on an individual's overall appearance. Although platelet-rich plasma has been presented as a novel treatment approach for the management of androgenetic alopecia, robust study data demonstrating efficacy of this therapy are lacking. The current study comprised 30 male subjects with untreated androgenetic alopecia. Twenty subjects were treated with platelet-rich plasma and 10 with physiological saline. No hair growth promoting effect was observed. Despite these results, the majority of subjects in both groups declared themselves at least partially satisfied with the result.

Androgenetic alopecia (AGA), also known as male-pattern hair loss, is a genetically determined individual sensitivity of hair follicles to androgens, presenting with a varying severity of hair loss, and progressing with age (1). It is the most common form of hair loss (2) and can affect both men and women (3). A change or loss of hair is visible and can have a major impact on an individual's overall appearance (4). While many people consider AGA to be part of the normal ageing process, many men find it difficult to cope with (5–7). Voluminous hair is associated with health and youthfulness and is closely linked with personal identity and style (4–9). The desire of men to maintain a young and attractive appearance has increased in recent years and may play a greater role now than in previous decades (8–10). Unfortunately, approved drugs for the treatment of AGA are limited (i.e. minoxidil, finasteride) (11). These drugs may have side-effects and do not always provide satisfactory results (11–13). A lack of treatment options is a common clinical complaint for patients with AGA. Although hair transplantation generally gives good results and can lead to permanent improvement, because of its invasive nature and high price, it is not a viable option for many patients.

Injection of platelet-rich plasma (PRP), a novel treatment approach for the management of AGA, has recently become increasingly popular (14, 15). PRP injections are presented as an effective and low-side-effect option for treatment of AGA (16). Several clinical trials have been published, all with relatively small cohorts showing rather positive outcomes (17–38). While the most positive results were shown in methodologically weak trials (26–38), the number of randomized controlled trials is few (17–25). Furthermore, due to differences in the design of those studies, direct comparison of their results is difficult (17–38).

In this pilot study, the effect of PRP on hair growth was tested in a single-centre, blinded, placebo-controlled setting in 30 subjects with AGA.

MATERIALS AND METHODS

Study design and population

The study protocol conformed to the ethics guidelines of the Declaration of Helsinki 1975, as reflected by approval by the ethics committee of the Medical University of Graz (EK 28-576 ex 15/16). Informed consent was obtained from each participant. Thirty healthy male subjects with untreated AGA, aged 18–52 years, were enrolled in this single-centre, randomized, placebo-controlled, blinded pilot study in a 2:1 ratio between 2016 and 2019. Selected subjects had an AGA Norwood-Hamilton score

doi: 10.2340/00015555-3609
Acta Derm Venereol 2020; 100: adv00247

of ≥III. Exclusion criteria were previous or ongoing treatment for AGA (finasteride, minoxidil), previous hair transplantation, malignancy, haematological disorders, thyroid dysfunction, malnutrition, and other dermatological disorders contributing to hair loss. Five treatments were performed at intervals of 4–6 weeks. Twenty subjects were treated with PRP ("verum" group) and 10 with physiological saline ("placebo" group). The subjects were blinded to treatment and therefore were asked to wear goggles during the treatment sessions. Randomization of the subjects was performed using an online randomizer tool (randomizer.at). Standardized photographs of the affected AGA areas were taken in front of a grey photograph wall with a Nikon D300 12.3-megapixel camera (Nikon Corporation, Japan) in a fixed position. Hair density documentation using TrichoScan technology (TRICHOLOG GmbH, Germany), a computer-assisted method for determining hair density and hair root status, was performed at 3 time-points: baseline (BL) and at follow-up visits 4 weeks and 6 months after the last treatment (FU1 and FU2, respectively). To facilitate precise identification of the treated areas at clinical control examinations, a point was tattooed in a shaved area of the scalp with an 18-gauge cannula and sterile black ink before the first treatment.

Study procedure

At each treatment, 20 ml of each subject's blood was collected in a tube containing sodium citrate to stop clotting. Platelet-poor plasma (PPP) and red blood cells were removed from the blood using "Yes" PRP kits, centrifuging at 2,800 RPM for 9 min (single-spin procedure) and the resulting PRP was extracted into a syringe. During the same session, depending on the degree of AGA, approximately 3–4 ml of the concentrated PRP or saline, respectively, was used to intracutaneously deliver 0.1 ml injections into the affected areas of the scalp. The injections were delivered with a 30-gauge needle at approximately 1 cm intervals in a grid-like pattern.

Outcome measures

The main outcome measures were hair number per square centimetre and hair diameter (μm), both measured using the TrichoScan system. Briefly, images of a shaved area of the scalp (1 cm^2) were taken with a digital microscope camera and evaluated with the TrichoScan software for determination of the essential parameters of hair growth. The secondary objective was the clinical improvement, which was evaluated by an independent reviewer using patient photographs. For this purpose, changes from baseline were evaluated on a 5-point Likert-type scale (much worse (1), somewhat worse (2), no change (3), somewhat better (4), much better (5)) at each of the follow-ups. Another blinded investigator, who was not involved in the enrollment and treatment procedure, evaluated the TrichoScan measurements at baseline and each of the follow-ups. In addition, subject satisfaction was assessed by survey after the final treatment. Subjects provided the perceived level of pain, clinical improvement, willingness to pay for each procedure, and whether they would recommend the treatment to others with AGA.

Statistical analysis

The study was performed as a pilot study in order to test PRP as a novel therapy for AGA. Due to the sample size of this study, only large effect sizes (Cohen's d: 1.12) could be detected with a sample size of 30 (power 80%, 2-sided significance level 5%). The 2 primary outcomes, hair number and hair diameter, were summarized in each group at the 3 time-points using standard statistical measures. Differences between baseline and each of the follow-up measurements were calculated. Furthermore, differences between the groups regarding these calculated changes from baseline were determined. Due to the non-normal nature of the data, which was assessed visually using quantile-quantile plots, the data is presented as medians and ranges (minimum to maximum) and Mann–Whitney *U* tests were performed. The results of visual improvement on a 5-point Likert-type scale and patient satisfaction are presented as absolute and relative frequencies. Differences between the groups were determined by Mann–Whitney *U* test for visual improvement and Fisher's exact test for items of satisfaction. Missing values are due to the refusal of some subjects to submit to the TrichoScan follow-up examination or technical problems (e.g. picture files or TrichoScan measurements could not be opened). A p-value of <0.05 was considered statistically significant. All statistical analyses were performed using R version 3.6.1.

RESULTS

Twenty-eight of the 30 enrolled subjects (93%) completed all treatments. Two subjects dropped out of the study before completion. One subject dropped out of the verum group after the fourth treatment and did not take part in the follow-up examinations. One subject dropped out of the placebo group after the first treatment, and did not appear for further scheduled visits. The following report is based on the 28 participants who completed all treatments.

Hair number

The median (range) hair number per square centimetre at baseline (BL) was 59.0 (15.0–133.0) in the treated group and 30.0 (11.0–92.0) in the placebo group (**Table I**). At the first follow-up visit 4 weeks after the last treatment (FU1), differences to baseline were –6.5 (–38.0–4.0) in the treated group and –9.0 (–15.0–2.0) in the placebo group; these differences were not statistically significant ($p=0.817$). At the second follow-up visit 6 months after the last treatment (FU2), differences to baseline were –9.0 (–27.0–8.0) in the treated group and –12.0 (–30.0–3.0) in the placebo group; these differences were also not statistically significant ($p=0.366$) (**Table II**).

Hair diameter

The median (range) hair diameter at baseline (BL) was 66.0 (47.5–81.9) micrometres in the treated group and

Table I. Baseline characteristics

Variables	Verum ($n=19$)	Placebo ($n=9$)
Age, years, median (range)	29 (25–52)	29 (24–33)
Sex, male, *n* (%)	19 (100)	9 (100)
Norwood Hamilton, *n* (%)		
III	10 (52.6)	2 (22.2)
IV	4 (21.1)	4 (44.4)
V	3 (15.8)	3 (33.3)
VI	1 (5.3)	
VII	1 (5.3)	
Hair number, per cm^2, median (range)	59.0 (15.0–133.0)	30.0 (11.0–92.0)
Hair diameter, μm, median (range)	66.0 (47.5–81.9)	64.6 (55.8–72.0)

Table II. Outcome parameters; follow-up measurements and differences to baseline

	Verum ($n=19$)	Placebo ($n=9$)	p-value
Hair number per cm^2, median (range)			
FU1	46.5 (8.0–127.0)	20.0 (2.0–94.0)	
BL-FU1	–6.5 (–38.0–4.0)	–9.0 (–15.0–2.0)	0.817
FU2	54.0 (12.0–133.0)	18.0 (0.0 –95)	
FU2-BL	–9.0 (–27.0–8.0)	–12.0 (–30.0–3.0)	0.366
Hair diameter µm, median (range)			
FU1	66.4 (44.5–74.8)	67.0 (47.9–74.2)	
BL-FU1	1.7 (–20.5–14.2)	1.1 (–7.9–9.6)	0.523
FU2	64.5 (34.2–74.8)	67.9 (60.8–73.1)	
FU2-BL	–0.6 (–18.7 –12.9)	– 0.4 (–2.1–12.2)	0.630
Likert scale, n (%)			
FU1			
Somewhat worse	4 (22.2)	4 (44.4)	0.824
No change	11 (61.1)	2 (22.2)	
Somewhat better	3 (16.7)	3 (33.3)	
FU2			
Much worse	4 (23.5)	1 (14.3)	0.131
Somewhat worse	7 (41.2)		
No change	3 (17.6)	4 (57.1)	
Somewhat better	3 (17.6)	2 (28.6)	

Differences between the groups were assessed with the Mann–Whitney U test or Fisher's exact test.
BL: baseline; FU1: follow-up 1; FU2: follow-up 2; BL-FU1: difference from baseline to follow-up 1; BL-FU2: difference from baseline to follow up 2.

64.6 (55.8–72.0) in the placebo group (Table I). At the first follow-up visit 4 weeks after the last treatment (FU1), differences to baseline were 1.7 (–20.5–14.2) in the treated group and 1.1 (–7.9–9.6) in the placebo group; these differences were not statistically significant ($p=0.523$). At the second follow-up visit 6 months after the last treatment (FU2), differences to baseline were –0.6 (–18.7–12.9) in the treated group and –0.4 (–2.1–12.2) in the placebo group; these differences were also not statistically significant ($p=0.630$) (Table II).

Visual improvement

None of the patients was scored "much better" compared with baseline at either of the 2 follow-up visits. At the first follow-up visit (FU1), in the verum group 4 subjects (22.2%) were rated "somewhat worse", 11 subjects (61.1%) were rated "no change" and 3 subjects (16.7 %) were rated "somewhat better". In the placebo group, 4 subjects (44.4 %) were rated "somewhat worse", 2 subjects (22.2%) were rated "no change", and 3 subjects (33.3%) were rated "somewhat better" (Table II).

At the second follow-up visit (FU2), 4 subjects (23.5%) were scored "much worse" compared with baseline in the treated group, whereas 1 subject (14.3 %) was scored "much worse" in the placebo group. In the treated group, 7 subjects (41.2 %) were rated "somewhat worse", 3 subjects (17.6%) were rated "no change", and 3 subjects (17.6%) were rated "somewhat better". In the placebo group, 4 subjects (57.1 %) were rated "no change" and 2 subjects (28.6%) were rated "somewhat better". There were no statistically significant differences between the groups at either follow-up ($p=0.824$ and $p=0.131$, respectively) (Table II).

Subject satisfaction survey results

In the verum group, 13 subjects (68.4%) rated the clinical outcome at the end of the study as better, while 6 subjects (31.6%) did not notice any change. In the placebo group, 4 subjects (44.4%) reported an improvement, while 4 subjects (44.4%) did not notice any change, and 1 (11.1%) subject rated a worsening of hair loss. Most subjects reported mild to moderate pain during treatments, however, only one subject in the placebo group reported severe pain. In the verum group, the majority of subjects (73.7%) stated that they would be willing to pay for the treatments, while 5 subjects (26.3%) stated they would not. In the placebo group, 5 subjects (55.6%) stated that they would be willing to pay for the treatments and 4 subjects (44.4%) stated that they would not be willing to pay anything for the treatments. Sixteen subjects in the verum group (84.2%) vs 5 subjects in the placebo group (55.6%) would recommend the treatment for other individuals with AGA. None of these differences were statistically significant (**Table III**).

No serious adverse events were reported during or after treatment in either group. Common, but fully reversible, side-effects included swelling, redness, minor bleeding in treated areas, haematoma and pain.

DISCUSSION

In recent years, PRP has become an increasingly popular treatment modality for various dermatological and aesthetic indications, including hair restoration (39, 40). Numerous clinical trials have reported the promotion of hair growth by PRP (17–38), indicating that PRP may offer hope to those affected by hair loss. However, the best results observed to date have been from methodologically weak trials (26–38), giving reason for caution when drawing conclusions (41). More robust data generated from randomized controlled trials is notably lacking (17–25). In this regard, results from the current blinded,

Table III. Subject satisfaction at end of study

Variable	Verum ($n=19$) n (%)	Placebo ($n=9$) n (%)	p-value
Pain			
Severe	0 (0)	1 (11.1)	0.482
Moderate	10 (52.6)	4 (44.4)	
Mild	9 (47.4)	4 (44.4)	
Clinical outcome			
Much better	3 (15.8)	0 (0)	0.272
Somewhat better	10 (52.6)	4 (44.4)	
No change	6 (31.6)	4 (44.4)	
Somewhat worse	0 (0)	1 (11.1)	
Willing to pay, €			
100–200	1 (5.3)	2 (22.2)	0.135
Up to 100	13 (68.4)	3 (33.3)	
Nothing	5 (26.3)	4 (44.4)	
Recommendation			
Yes	16 (84.2)	5 (55.6)	0.165
No	3 (15.8)	4 (44.4)	

Group differences were assessed using Fisher's exact test.

placebo-controlled trial, wherein no hair growth promoting effect of PRP was observed, are rather sobering. There are many factors that may have influenced the outcome of this trial in comparison with other reports. In fact, there is no general consensus in the field regarding several potentially critical aspects of PRP treatment for hair restoration (42). These include the method used for preparing PRP for injection, and which characteristics of the PRP itself, such as platelet concentration, are critical, the number of treatments to administer, how frequently to administer treatment, the best mode of administration, and the volume of PRP injected per unit area (17–38). Other unknowns include the effect of co-treatments, such as concurrent or alternating use of medical treatments with PRP treatments, or the use of mechanical stimulation methods, such as microneedling in conjunction with PRP administration (36–38, 43–46). There has also been some indication that certain patients are better candidates for PRP treatment for hair loss than others; i.e. some patients may simply be non-responders (47), which may confound trial observations. Finally, other variables, which may account for differences in results reported from various trials, are the methods used in and the timing of clinical outcome assessment (17–38). Some of these topics are discussed in more detail below.

The best mode of preparation of PRP for use in the treatment of hair loss, as well as its composition, have not been well defined. As illustrated by the large variety of PRP preparation methods and range of platelet concentrations that have been reported (48–54), no consensus has yet been reached in the field (42). For example, while 1 study reported that 1.5 million platelets per microliter was the most therapeutically effective concentration (54), other studies have recommended lower platelet concentrations (48–53). Rodrigues et al. (18) analysed the potential correlation between platelet count and growth factor levels in PRP and hair growth following subcutaneous PRP injections, but none was found. In a recent review, Evans et al. (16) emphasized that use of a double-spin procedure gave better results (providing PRP with higher platelet concentrations), while studies using a single spin procedure, such as the current study, did not impart statistically significant results. According to the supplier of the "Yes" PRP kit utilized for PRP preparation in the current study (https://yesprpkit.com/yes-prp-kit-2/test-results/), the PRP preparation should comprise 6–10 times more platelets than at baseline. The normal range for platelets in healthy Caucasians is 150,000–450,000 per microliter (55). With regard to the absolute numbers of platelets being so different, it seems to be difficult to find a standardized preparation method that produces a product for each patient that has the same platelet count. Perhaps there is the need for an individual manufacturing process for each patient depending on their baseline platelet count. In sum, the field is currently lacking a standard with regard to preparation methods and platelet concentration in PRP for AGA treatment.

In published studies, the frequency of PRP treatment, as well as the total number of PRP treatment sessions, have varied substantially. The frequency of treatments has ranged from weekly to monthly to bimonthly administration (17–38). Similarly, the total number of treatment sessions range from only 1 to up to 6 (17–38). While several groups have reported positive results with 4-week treatment intervals, such as Cervelli et al. (22) and Gentile et al. (21), it should nonetheless be noted that others have reported negative results with 4-week and 2-week treatment intervals (23, 24). We chose to administer 5 treatments at 4- to 6-week intervals for the current trial, which, in order, is roughly in line with the regiments of other studies.

The results of some studies have suggested an effect of the degree of alopecia in individual subjects in the outcome of PRP treatment. Dicle et al. (19) performed a randomized placebo-controlled crossover study on 25 male patients with AGA (grades III–V) with treatments of PRP and placebo. The study randomized patients into 2 groups. In the first phase of the study, group 1 patients received 3-monthly PRP treatments, while group 2 patients received monthly saline injections. After a washout period of 3 months, the groups were switched and each group received a further 3 treatments. TrichoScan measurements were assessed at baseline, at month 4, and again at month 9. No statistically significant increase in hair growth in group 1 was detected at the follow-up examinations, thus the primary endpoint of the study was not met. Interestingly, in the group that received saline in the first phase (control group), hair growth was detected after PRP injections in the second phase when comparing month 9 with month 4 and baseline (secondary endpoint). The authors concluded that a greater proportion of patients with low-grade alopecia in the control group may have influenced this outcome. In a similar finding, a recent study from Qu et al. (30) has also suggested that PRP may be more beneficial for low-grade AGA patients. Juhasz et al. (47) recently speculated that the apparent lack of efficacy of PRP treatment may be due to a high number of non-responders. In this regard, it would be of interest to determine which patients have the best likelihood of benefitting from PRP treatment.

The best mode of PRP delivery is generally considered to be intradermal injection (56) as the proposed therapeutic mechanism of PRP is the activation of stem cells which, in turn, target the hair bulge and dermal papilla cells located in the dermis (39, 40). Interestingly, Rodrigues et al. (18) achieved hair growth by subcutaneous injections, suggesting that mechanical stimulation alone may also promote hair growth. Similarly, other studies have reported hair growth promoting effects after microneedling (43–46) or after inserting threads into the scalp (57–60), observations that further support this

hypothesis. Moreover, several studies (34–38) used PRP as a co-adjuvant in combination with other treatment modalities, such as microneedling, topical minoxidil or oral finasteride, which may gain additive or synergistic effects and probably significantly influence the outcome, but gives no information regarding the effect of each individual drug.

Another aspect that has varied widely among published studies is the timing of follow-up examinations after treatment (17–38). In the current trial, 4-week and 6-month follow-up time-points were chosen to assess short-term and long-term improvements, respectively. The selection of these time-points was loosely based on observations from a previous study by Gkini et al. (29), which reported observable hair growth both early in the study (6 weeks after the first PRP injection) as well as 6 months after the last PRP injection. Interestingly, other studies using similar time-points have shown apparently conflicting results. For example, Schiavone et al. (33), Singhal et al. (26), Alves & Grimalt (20) and Rodrigues et al. (18) all demonstrated hair growth 3 months after the last injection, whereas Ayatollahi et al. (24) reported negative results at the same time-point. Other studies, such as those reported by Cervelli et al. (22), reported hair growth using short-term follow-up time-points directly after the last treatment, whereas Mapar et al. (23) did not observe a hair growth promoting effect directly after the last treatment. With the exception of one study, no long-term follow-ups were performed. In this study from Gentile et al. (21), progressive hair loss was observed in 20 percent of subjects 12 months after PRP injections. This seems to be a logical outcome, as AGA is a chronic progressive condition and therefore subsequent treatments may be required to maintain the effect. This observation is of some clinical significance, as the high cost of PRP treatment precludes its use over longer time periods for many patients (61). In sum, the disparity in published results underscores the difficulty of finding appropriate time-points for evaluation.

It should be noted that the inconclusive nature of some PRP studies may not be due only to follow-up timing. For example, across published studies, there is also a lack of systematic evaluation of hair growth parameters (e.g. TrichoScan measurements) (27–34). Furthermore, several trials have assessed hair growth using only a single method, such as the hair-pull test or before and after pictures, to evaluate treatment efficacy, rather than collecting multiple measurements (27–34). Half-head studies are common in the literature (17, 19–21); however, this design may be problematic due to the risk of potential carry-over effects, as each patient is included in both the treatment and control groups. Other general limitations of PRP trials have included small sample sizes (17–38) or the absence of control groups (27–34). With regard to the current study, the small sample size was only one of the limitations. In addition, the area measured for hair density and thickness was quite small; and it cannot be excluded that assessment of a larger scalp area (though unlikely) or using another treatment protocol may have revealed at least a modest PRP treatment effect.

Interestingly, out of the 3 published randomized controlled PRP trials reporting no improvement after PRP injections (23–25), 2 noted patient satisfaction despite the negative results (24, 25). A similar observation was made in the current study. Although PRP treatment provided no measurable improvement, the majority of subjects in both the placebo and PRP treatment groups were at least partially satisfied with the result and indicated a willingness to pay for the treatment and to recommend the treatment to others. This positive assessment despite no measurable improvement is likely attributable to the placebo effect, a complex neurobiological phenomenon described in several research articles (62–64).

In conclusion, our results suggest that treatment with PRP as a monotherapy does not improve hair growth in men with AGA. Although numerous trials have suggested that PRP benefits at least a subset of AGA patients, substantial differences in trial design has made it difficult to draw concrete conclusions about its clinical efficacy. Furthermore, the development of a reliable clinical protocol has not yet been possible. Parameters for further development in the field include the process for preparing PRP, eligible subjects, mode of delivery, timing of treatment and usefulness of combination therapy. Thus, PRP and a standardized treatment protocol for its use, in light of the current low level of evidence, must be further evaluated in a large, randomized, placebo-controlled multicenter study.

The authors have no conflict of interest to declare.

REFERENCES

1. Miranda BH, Charlesworth MR, Tobin DJ, Sharpe DT, Randall VA. Androgens trigger different growth responses in genetically identical human hair follicles in organ culture that reflect their epigenetic diversity in life. FASEB J 2018; 32: 795–806.
2. Vañó-Galván S, Saceda-Corralo D, Blume-Peytavi U, Cucchía J, Dlova NC, Gavazzoni Dias MFR, et al. Frequency of the types of alopecia at twenty-two specialist hair clinics: a multicenter study. Skin Appendage Disord 2019; 5: 309–315.
3. Lolli F, Pallotti F, Rossi A, Fortuna MC, Caro G, Lenzi A, et al. Androgenetic alopecia: a review. Endocrine 2017; 57: 9–17.
4. Titeca G, Goudetsidis L, Francq B, Sampogna F, Gieler U, Tomas-Aragones L, et al. The psychosocial burden of alopecia areata and androgenetica': a cross-sectional multicentre study among dermatological out-patients in 13 European countries. J Eur Acad Dermatol Venereol 2020; 34: 406–411.
5. Kim BK, Lee S, Jun M, Chung HC, Oh SS, Lee WS. Perception of hair loss and education increases the treatment willingness in patients with androgenetic alopecia: a population-based study. Ann Dermatol 2018; 30: 402–408.
6. Lee HJ, Ha SJ, Kim D, Kim HO, Kim JW. Perception of men with androgenetic alopecia by women and nonbalding men in Korea: how the nonbald regard the bald. Int J Dermatol 2002; 41: 867–869.
7. Han SH, Byun JW, Lee WS, Kang H, Kye YC, Kim KH, et al. Quality of life assessment in male patients with androgenetic alopecia: result of a prospective, multicenter study. Ann

Dermatol 2012; 24: 311–318.
8. Montes JR, Santos E. Evaluation of men's trends and experiences in aesthetic treatment. J Drugs Dermatol 2018; 17: 941–946.
9. Calvo Peretti M, Caballero Uribe N, Régnier A, Trüeb RM. Look at your hair the way you look at your face: concept of total facial skin and hair care. Skin Appendage Disord 2020; 6: 67–76.
10. Rossi AM. Men's aesthetic dermatology. Semin Cutan Med Surg 2014; 33: 188–197.
11. Blumeyer A, Tosti A, Messenger A, Reygagne P, Del Marmol V, Spuls PI, et al. Evidence-based (S3) guideline for the treatment of androgenetic alopecia in women and in men. J Dtsch Dermatol Ges 2011; 9: 1–57.
12. Pallotti F, Senofonte G, Pelloni M, Cargnelutti F, Carlini T, Radicioni AF, et al. Androgenetic alopecia: effects of oral finasteride on hormone profile, reproduction and sexual function. Endocrine 2020; 68: 688–694.
13. Traish, AM. Post-finasteride syndrome: a surmountable challenge for clinicians. Fertil Steril 2020; 113: 21–50.
14. Alsalhi W, Alalola A, Randolph M, Gwillim E, Tosti A. Novel drug delivery approaches for the management of hair loss. Expert Opin Drug Deliv 2020; 6: 1–9.
15. Dervishi G, Liu H, Peternel S, Labeit A, Peinemann F. Autologous platelet-rich plasma therapy for pattern hair loss: a systematic review. J Cosmet Dermatol 2020; 19: 827–835.
16. Evans AG, Mwangi JM, Pope RW, Ivanic MG, Botros MA, Glassman GE, et al. Platelet-rich plasma as a therapy for androgenic alopecia: a systematic review and meta-analysis. J Dermatolog Treat 2020; 26: 1–14.
17. Kachhawa D, Vats G, Sonare D, Rao P, Khuraiya S, Kataiya R. A Spilt head study of efficacy of placebo versus platelet-rich plasma injections in the treatment of androgenic alopecia. J Cutan Aesthet Surg 2017; 10: 86–89.
18. Rodrigues BL, Montalvão SAL, Cancela RBB, Silva FAR, Urban A, Huber SC, et al. Treatment of male pattern alopecia with platelet-rich plasma: a double-blind controlled study with analysis of platelet number and growth factor levels. J Am Acad Dermatol 2019; 80: 694–700.
19. Dicle Ö, Bilgic Temel A, Gülkesen KH. Platelet-rich plasma injections in the treatment of male androgenetic alopecia: a randomized placebo-controlled crossover study. J Cosmet Dermatol 2020; 19: 1071–1077.
20. Alves R, Grimalt R. Randomized placebo-controlled, double-blind, half-head study to assess the efficacy of platelet-rich plasma on the treatment of androgenetic alopecia. Dermatol Surg 2016; 42: 491–497.
21. Gentile P, Garcovich S, Bielli A, Scioli MG, Orlandi A, Cervelli V. The effect of platelet-rich plasma in hair regrowth: a randomized placebo-controlled trial. Stem Cells Transl Med 2015; 4: 1317–1323.
22. Cervelli V, Garcovich S, Bielli A, Cervelli G, Curcio BC, Scioli MG, et al. The effect of autologous activated platelet rich plasma (AA-PRP) injection on pattern hair loss: clinical and histomorphometric evaluation. Biomed Res Int 2014; 2014: 760709.
23. Mapar MA, Shahriari S, Haghighizadeh MH. Efficacy of platelet-rich plasma in the treatment of androgenetic (male-patterned) alopecia: a pilot randomized controlled trial. J Cosmet Laser Ther 2016; 18: 452–455.
24. Ayatollahi A, Hosseini H, Shahdi M, Ahmad Nasrollahi S, NassiriKashani M, Yadangi S, et al. Platelet-rich plasma by single spin process in male pattern androgenetic alopecia: is it an effective treatment? Indian Dermatol Online J 2017; 8: 460–464.
25. Puig CJ, Reese R, Peters M. Double-blind, placebo-controlled pilot study on the use of platelet-rich plasma in women with female androgenetic alopecia. Dermatol Surg 2016; 42: 1243–1247.
26. Singhal P, Agarwal S, Dhot PS, Sayal SK. Efficacy of platelet-rich plasma in treatment of androgenic alopecia. Asian J Transfus Sci 2015; 9: 159–162.
27. Verma K, Tegta GR, Verma G, Gupta M, Negi A, Sharma R. A study to compare the efficacy of platelet-rich plasma and minoxidil therapy for the treatment of androgenetic alopecia. Int J Trichology 2019; 11: 68–79.
28. Butt G, Hussain I, Ahmed FJ, Choudhery MS. Efficacy of platelet-rich plasma in androgenetic alopecia patients. J Cosmet Dermatol 2019; 18: 996–1001.
29. Gkini MA, Kouskoukis AE, Tripsianis G, Rigopoulos D, Kouskoukis K. Study of platelet-rich plasma injections in the treatment of androgenetic alopecia through a one-year period. J Cutan Aesthet Surg 2014; 7: 213–219.
30. Qu Q, Shi P, Yi Y, Fan Z, Liu X, Zhu D, et al. Efficacy of platelet-rich plasma for treating androgenic alopecia of varying grades. Clin Drug Investig 2019; 39: 865–872.
31. Anitua E, Pino A, Martinez N, Orive G, Berridi D: The effect of plasma rich in growth factors on pattern hair loss: a pilot study. Dermatol Surg 2017; 43: 658–670.
32. Gupta S, Revathi TN, Sacchidanand S, Nataraj HV: A study of the efficacy of platelet-rich plasma in the treatment of androgenetic alopecia in males. Indian J Dermatol Venereol Leprol 2017; 83: 412.
33. Schiavone G, Raskovic D, Greco J, Abeni D: Platelet-rich plasma for androgenetic alopecia: a pilot study. Dermatol Surg 2014; 40: 1010–1019.
34. Khatu SS, More YE, Gokhale NR, Chavhan DC, Bendsure N. Platelet-rich plasma in androgenic alopecia: myth or an effective tool. J Cutan Aesthet Surg 2014; 7: 107–110.
35. Ferrando J, García-García SC, González-de-Cossío AC, Bou L, Navarra E. A Proposal of an effective platelet-rich plasma protocol for the treatment of androgenetic alopecia. Int J Trichology 2017; 9: 165–170.
36. Jha AK, Vinay K, Zeeshan M, Roy PK, Chaudhary RKP, et al. Platelet-rich plasma and microneedling improves hair growth in patient of androgenetic alopecia when used as an adjuvant to minoxidil. J Cosmet Dermatol 2019; 18: 1330–1335.
37. Jha AK, Udayan UK, Roy PK, Jha Amar AK, Chaudhary RKP. Platelet-rich plasma with microneedling in androgenetic alopecia along with dermoscopic pre- and post-treatment evaluation. J Cosmet Dermatol 2018; 17: 313–318.
38. Shah KB, Shah AN, Solanki RB, Raval RC. A Comparative study of microneedling with platelet-rich plasma plus topical Minoxidil (5%) and topical Minoxidil (5%) alone in androgenetic alopecia. Int J Trichology 2017; 9: 14–18.
39. Emer J. Platelet-rich plasma (PRP): Current applications in dermatology. Skin Therapy Lett 2019; 24: 1–6.
40. Alves, R, Grimalt R. A review of platelet-rich plasma: history, biology, mechanism of action, and classification. Skin Appendage Disord 2018; 4: 18–24.
41. Mao G, Zhang G, Fan W. Platelet-rich plasma for treating androgenic alopecia: a systematic review. Aesthetic Plast Surg 2019; 43: 1326–1336.
42. Harrison P, for the subcommittee on platelet physiology. The use of platelets in regenerative medicine and proposal for a new classification system: guidance from the SSC of the ISTH. J Thromb Haemost 2018; 16: 1895–900.
43. Fertig RM, Gamret AC, J Cervantes J, Tosti A. Microneedling for the treatment of hair loss? J Eur Acad Dermatol Venereol 2018; 32: 564–569.
44. Dhurat R, Sukesh M, Avhad G, A Dandale, Pal A, Pund P. A randomized evaluator blinded study of effect of microneedling in androgenetic alopecia: a pilot study. Int J Trichology 2013; 5: 6–11.
45. Dhurat R, Mathapati S. Response to microneedling treatment in men with androgenetic alopecia who failed to respond to conventional therapy. Indian J Dermatol 2015; 60: 260–263.
46. Bao L, Gong L, Guo M, Liu T, Shi A, Zong Ha, et al. Randomized trial of electrodynamic microneedle combined with 5% minoxidil topical solution for the treatment of chinese male androgenetic alopecia. J Cosmet Laser Ther 2020; 22: 1–7.
47. Juhasz MLW, Sukhdeo K, Lo Sicco K, Shapiro J. Stratifying clinical response to adjuvant platelet-rich plasma in patients with androgenetic alopecia. Br J Dermatol 2020 Apr 5. doi: 10.1111/bjd.19064.
48. Butt G, Hussain I, Ahmad FJ, Choudhery MS. Stromal vascular fraction-enriched platelet-rich plasma therapy reverses the effects of androgenetic alopecia. J Cosmet Dermatol 2020; 19: 1078–1085.

49. Fadadu PP, Mazzola AJ, Hunter CW, Davis TT. Review of concentration yields in commercially available platelet-rich plasma (PRP) systems: a call for PRP standardization. Reg Anesth Pain Med 2019; pii: rapm-2018-100356.
50. Oudelaar BW, Peerbooms JC, Huis In 't Veld R, Vochteloo AJH. Concentrations of blood components in commercial platelet-rich plasma separation systems: a review of the literature. Am J Sports Med 2019; 47: 479–487.
51. Kramer ME, Keaney TC. Systematic review of platelet-rich plasma (PRP) preparation and composition for the treatment of androgenetic alopecia. J Cosmet Dermatol 2018; 17: 666–671.
52. Rappl LM. Effect of platelet rich plasma gel in a physiologically relevant platelet concentration on wounds in persons with spinal cord injury. Int Wound J 2011; 8: 187–195.
53. Dohan Ehrenfest DM, Rasmusson L, Albrektsson T. Classification of platelet concentrates: from pure platelet-rich plasma (P-PRP) to leucocyte- and platelet-rich fibrin (L-PRF). Trends Biotechnol 2009; 27: 158–167.
54. Giusti I, Rughetti A, D'Ascenzo S, Millimaggi D, Pavan A, Dell'Orso L, et al. Identification of an optimal concentration of platelet gel for promoting angiogenesis in human endothelial cells. Transfusion 2009; 49: 771–778.
55. Eicher JD, Lettre G, Johnson AD. The genetics of platelet count and volume in humans. Platelets 2018; 29: 125–130.
56. Altunel CT, Güleç AT. Comment on "Treatment of male pattern alopecia with platelet-rich plasma: a double-blind controlled study with analysis of platelet number and growth factor levels". J Am Acad Dermatol 2019; 81: e147.
57. Bharti J, Sonthalia S, Patil P, Dhurat R. Scalp threading with polydioxanone monofilament threads: a novel, effective and safe modality for hair restoration. J Eur Acad Dermatol Venereol 2017; 31: e492–e493.
58. Metwalli M, Khattab FM, Mandour S. Monofilament threads in treatment of female hair loss. J Dermatolog Treat 2020 March 3; 1–5. [Epub ahead of print].
59. Shin HJ, Lee DJ, Kwon K, Seo HS, Jeong HS, Lee JY, et al. The success of thread-embedding therapy in generating hair regrowth in mice points to its possibility having a similar effect in humans. J Pharmacopuncture 2015; 18: 20–25.
60. Bharti J, Patil P. Polydioxanone threads in androgenetic alopecia: a novel innovation. J Cosmo Trichol 2016; 2: 24.
61. Piuzzi NS, Ng M, Kantor A, Ng K, Kha S, Mont MA, et al. What is the price and claimed efficacy of platelet-rich plasma injections for the treatment of knee osteoarthritis in the United States? J Knee Surg 2019; 32: 879–885.
62. Peiris N, Blasini M, Wright T, Colloca L. The placebo phenomenon: a narrow focus on psychological models. Perspect Biol Med 2018; 61: 388–400.
63. Tavel ME. The placebo effect: the good, the bad, and the ugly. Am J Med 2014; 127: 484–488.
64. Meissner K, Bingel U, Colloca L, Wager TD, Watson A, Flaten MA. The placebo effect: advances from different methodological approaches. J Neurosci 2011; 31: 16117–16124.