Double-Blind, Placebo-Controlled Pilot Study on the Use of Platelet-Rich Plasma in Women With Female Androgenetic Alopecia

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BACKGROUND Platelet-rich plasma (PRP) has been suggested as a therapeutic intervention for female androgenetic alopecia.

OBJECTIVE To perform a pilot study on the effect of PRP scalp injections in women with female androgenetic alopecia.

MATERIALS AND METHODS This double-blind, multicenter, placebo-controlled study compared the effect of PRP with that of saline placebo as scalp injection. The endpoints were hair count and hair mass index (HMI), along with patient-opinion survey responses. Platelet-rich plasma was manufactured from patients' blood using the Angel PRP system.

RESULTS Hair mass index or hair count did not statistically significantly differ between the study and placebo groups. However, 13.3% of the treatment subjects (vs 0% of the placebo subjects) experienced substantial improvement in hair loss, rate of hair loss, hair thickness, and ease of managing/styling hair, and 26.7% (vs 18.2% of the placebo group) reported that their hair felt coarser or heavier after the treatment.

CONCLUSION Platelet-rich plasma failed to demonstrate any statistically significant improvement in HMI or hair count in women with congenital female pattern hair loss. The patient survey results suggest a therapeutic advantage of PRP as perceived by patients but not according to hair count or HMI.

Angel PRP and all the soft goods for making the PRP were provided by Cytomedics. The authors have indicated no significant interest with commercial supporters.

For the last 7 to 8 years, the benefits of the use of platelet-rich plasma (PRP) to facilitate wound healing, collagen development, and hair growth have been advocated.[1–3] Indeed, recent discoveries about the long-term role of PRP in wound healing and tissue remodeling,[4–6] and the concentration of growth factors in PRP that may influence the hair growth cycle, such as transformation growth factor beta (TGF-beta), vascular endotheial growth factor (VEGF), fibroblastic growth factor b (bFGF), and platelet derived growth factor (PDGF)[5,7] suggest that PRP may affect the hair cycle and encourage hair regrowth.[8,9]

Although much has been discussed, written, and even attempted clinically regarding this topic, no placebo-controlled blinded study has been attempted.[10–12]

Methods

The purpose of this prospective, double-blind, placebo-controlled study was to evaluate the effect of PRP on hair growth, as assessed based on hair count and hair mass index (HMI), in women with Ludwig Type II female pattern hair loss. The research questions

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guiding this study were (1) "Is there a statistically significant mean difference in hair count between the study and placebo groups?" and (2) "Is there a statistically significant mean difference in HMI between the study and placebo groups?"

Research Design and Sampling

Study Population

A randomized sample of 26 women (treatment group, $n = 15$; placebo group, $n = 11$), at least 18 years of age, diagnosed with Ludwig II female androgenetic alopecia through history taking, physical examination, and either biopsy or strong family history of female pattern hair loss as defined by 2 or more female relatives known to have a similar Ludwig pattern of hair loss, without known disease, were included in this study. None of the patients received other hair loss treatments during the study and for 60 days before the study.

Preparation of Study Solutions

Two solutions were applied for treatment in this study. The patients were randomly assigned to receive 10 mL of one of the following study solutions:

(1) Nonactivated (no thrombin added) Angel PRP manufactured from the patient's blood just before injection using the Angel PRP system (Cytomedix).
(2) Normal saline (placebo).

All the patients had 60 mL of blood sample drawn, centrifuged in a sterile, closed, single-use Angel PRP system. The highly concentrated PRP from the 60 mL of blood sample was diluted with platelet-poor plasma to obtain 10 mL of low-concentration, leukocyte- and erythrocyte-free PRP for injection, this resulted in roughly a 2.75 to 3.4X platelet concentration for injection. Platelet-rich plasma hematocrit concentrations were set at 2%. The Angel centrifuge system allows the user to control the hematocrit concentration (RBC concentration) of the PRP product. Hematologic stem cells, the size, and weight of RBCs circulating in the blood were found. Many authors believed that these hemotologic stems cells may contribute to the effect PRP on wound healing and hair growth. A hematocrit concentration of 2% captures many of these circulating stem cells. The injection solution was mixed the day of the procedure and concealed from the treating physician and the study photo evaluators. The placebo and study syringes were wrapped in light-blocking tape, but the syringe gradations were minimally visible so that the correct injection dose could be administered. The randomization of the aforementioned samples was performed by constructing a randomization solution list for each of the participating sites. The patients were randomized within and across the participating sites.

Appropriate blood samples obtained from all the patients in the treatment arm of the study were sent to a local laboratory for platelet counting. The platelet count was recorded on the baseline data form. Proper sterilization techniques were adhered to at all times.

Post-Treatment Data Collection

The patients were examined every 4 weeks to verify for possible complications or problems occurring after the treatment. At 26 ± 1 week, final data points were collected from the same sites on the scalp from which the baseline data were collected using the same methods as applied in the baseline data collection. At 26 weeks, the patients also completed a patient survey. The data collection end points consisted of the following:

(1) Hair count (through photography);
(2) Hair mass index (measured using the Cohen hair check system); and
(3) Patient survey.

All photographs were forwarded to the primary investigator, who had the hair counting performed by an experienced hair restoration technician trained in working with strip graft dissection and slivering, and did not participate in any of the patient treatments. The hair counts were tracked by study identification (ID) number and date only. The date of the photograph was used to determine whether the count was made before or after the treatment.

Data Collection Procedures

The board-certified hair restoration surgeon from each of the participating sites was responsible for collecting

(1) patient baseline and follow-up data and (2) performing all patient injections according to the following procedures:

Pretreatment

All the patients underwent a comprehensive history taking and physical examination before enrollment in this study. After the application of the inclusion and exclusion criteria, specific data regarding past medical treatments for hair loss was sought and recorded.

Baseline Data

Hair mass was measured on the midline scalp using the Cohen hair check system, and the exact distance from the glabella was recorded. Hair within the 4-cm^2 hair check data box was then clipped to a length of 1 mm, and the hair check data box was photographed using Dermalight 1-cm reticule for independent hair count analysis. Photographs in .jpg format were labeled with the patients' study ID and the date they were obtained. The complete blood count along with platelet count was determined at the time blood samples were drawn from the patients to make PRP.

Post-Treatment

The patients were anesthetized using a ring block method. This block was achieved by injecting a 50:50 mixture of 2% lidocaine and 0.5% bupivicaine 4 cm from each side of the hair check data box. This created a treatment area of 10×10 cm in the central scalp. The exact anesthetic volume in milliliters for each participant was recorded. Subcutaneous injection of 10 mL of either the study solution or the placebo solution was injected in the hair check data box and within 10×10 cm of the immediate surrounding area.

Results

Hair Count

The results of the 2-tailed independent *t*-test indicate no statistically significant mean difference in patient hair count 26 weeks after the treatment between the study and placebo groups ($t[24] = 0.680$, $p = .503$).

Hair Mass

The results of the 2-tailed independent *t*-test indicate no statistically significant mean difference in patient hair mass 26 weeks after the treatment between the study and placebo groups ($t[24] = 1.258$, $p = .220$).

Survey Results

Although statistically significant mean differences in patient hair count and mass were not observed between the treatment and placebo groups, 13.3% of the treatment subjects (vs 0% of the placebo subjects) claimed to have experienced substantial improvement in hair loss, rate of hair loss, hair thickness, and ease of managing/styling hair (Tables 1 and 2). In addition, 26.7% of the patients in the study group (vs 18.2% of the placebo subjects) reported that their hair felt coarser or heavier after the treatment (Table 3).

Discussion

To the authors' knowledge, to date, this is the only placebo-controlled study that investigated the effect PRP had on female androgenetic alopecia. Although the results of this pilot study with a small number of patients failed to demonstrate the efficacy of PRP, some of its findings suggest that PRP, or maybe scalp-needling therapy, may have promise in the treatment of female androgenetic alopecia.

TABLE 1. Treatment Group: 26-Week Post-Treatment Patient Survey

	No Improvement, %	*Some Improvement, %*	*Substantial Improvement, %*
Hair loss	73.3	13.3	13.3
Rate of hair loss (amount of shedding)	60.0	26.7	13.3
Hair thickness	66.7	20.0	13.3
Ease of managing and styling hair	60.0	26.7	13.3

TABLE 2. Placebo Group: 26-Week Post-Treatment Patient Survey

	No Improvement, %	*Some Improvement, %*	*Substantial Improvement, %*
Hair loss	72.7	27.3	0.0
Rate of hair loss (amount of shedding)	63.6	36.4	0.0
Hair thickness	72.7	27.3	0.0
Ease of managing and styling hair	54.5	45.5	0.0

These data show little difference in results between the study and placebo groups. The fact that a similar trend toward positive changes was observed between the 2 groups implies a therapeutic effect of both treatments. The therapeutic component common to both treatments that may have a positive effect on outcome was scalp needling. In a recent work by Stiefsohn and colleagues, postincision endogenous platelet-derived growth factor levels that were similar or exceeded the growth factor levels obtained after growth factor release from PRP[13] reaffirm the need for carefully designed placebo-controlled studies. The study results of Stiefsohn and colleagues imply that injuring the scalp may release more growth factors than the PRP injection. Scalp needling is a minor traumatic event, and the body is most likely to react by shunting PRP to wounded area as part of its natural defense system. This minor trauma may simulate the release of additional growth factors in the scalp that may induce additional hair growth in some patients.

The question is, "Does additional PRP production induced by the body's natural response enhance hair growth?" This pilot study does not answer this, but its research design offered a strictly controlled and limited therapeutic intervention. For example, only 1 treatment was applied, the PRP was diluted with PPP to 10 mL, and the timeline between the PRP injection and post-treatment data collection was 6 months. Would PRP with a higher hematocrit concentration and hence higher hematologic stem cell show different results? A single dose of additional growth factors seems to have no significant effect compared with the placebo, but whether a single dose every 4 to 6 weeks has different results remains to be known. Is the influence of PRP on hair follicles enhanced by adding MatriStem MicroMatrix (A-Cell Inc, Columbia, MD) to the injection? MatriStem MicroMatrix is a sterile, porcine derived, naturally occurring lyophilized extracellular matrix in particle form that maintains and supports a healing environment for wound management. To date, there is no placebo-controlled data to suggest that the addition of extracellular scaffolding will enhance hair growth.

TABLE 3. Nature of the Hair and Scalp After Treatment

	Treatment, %		*Placebo, %*	
	Yes	*No*	*Yes*	*No*
Hair feels coarser or heavier after treatment	26.7	73.3	18.2	81.8
Improved sensitivity of the scalp	6.7	93.3	18.2	81.8

One firm conclusion that can be derived from the survey data of this study is that the study patients perceived positive effects of the treatment (Tables 1–3). Of the study subjects, 13.3% (vs 0% of the placebo subjects) claimed to have experienced substantial improvement in hair loss, rate of hair loss, hair thickness, and ease of managing/styling hair. In addition, 26.7% of them (vs 18.2% of the placebo subjects) reported that their hair felt coarser or heavier after the treatment. These data are not consistent with the HMI and hair count data, suggesting a strong placebo effect or that HMI and hair count are not reliable indicators of patient-perceived improvements.

Conclusion

This double-blind, placebo-controlled study of the effect of PRP, as compared with that of the saline placebo, on female androgenetic alopecia failed to

demonstrate any statistically significant improvement. The positive treatment results obtained from both groups suggest that scalp needling delivers enough PRP growth factors to the scalp to stimulate hair growth. The patient survey responses suggest a therapeutic advantage of the PRP treatment as perceived by the patients but not according to hair count or HMI. Considering the sample size of the study and the fact that the placebo effect of any intervention for hair loss can be achieved in up to 30% of subjects, the present results may be purely due to the placebo effect. Additional controlled studies are needed to confirm that PRP has potential as part of the treatment plan for congenital female pattern hair loss.

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