International Journal of Dermatology, Vol. 31, No. 12, December 1992

Pharmacology and Therapeutics

ElectroTrichoGenesis: Further Evidence of Efficacy and Safety on Extended Use

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Abstract
These data represent a subset of data from the original 36-week study conducted by Maddin et al.,[1] which was in itself a preliminary study of a pulsed electrical stimulation device in male subjects alone. The extension phase of this study, which is summarized here, was undertaken to gather data on longer-term efficacy and safety and to study clinical effects in control subjects who were then switched to active treatment. Thirteen subjects had active treatment for 70 weeks, and 14 subjects were included in the crossover group, which had sham treatment for 36 weeks followed by active treatment for 30 additional weeks. On average, terminal hair counts increased from 82 to 276 in the active treatment group. Among those in the crossover group, a mild increase, from 124 to 160, was observed during the sham treatment period and a more notable increase, from 160 to 249, occurred during the subsequent active treatment period. The results presented here provide evidence of the efficacy and safety of this device during extended use; however, the generalizability of these findings is limited by the small subset of subjects for whom complete data are available.
Int J Dermatol 1992; 31:878-880

The application of pulsed electrical stimulation has excited considerable research interest in recent years for the treatment of a variety of clinical indications. This paper on electrotrichogenesis aims to provide longer term evidence of efficacy and safety in a novel approach to the management of a common clinical entity notably refractory to treatment.

Materials and Methods

In a comparative controlled study, Maddin et al.[1] reported on 73 white men with male pattern baldness in severity class III vertex or IV on the Hamilton Scale. Subjects were given either (active) treatment or sham treatment (control) with a pulsed electrical simulation device, on a predefined treatment schedule. Terminal hairs were counted in a designated 1 inch diameter circle on the scalp vertex to measure clinical improvement. Data were available for 56 subjects (30 treatment and 26 control) collected over 36 weeks.

Participants in the initial 36-week trial were offered the opportunity to continue in the program in an arrangement whereby treatment subjects continued on the same treatment regime and control subjects were crossed to actual treatment. Twenty-two subjects declined to participate in the extended trial leaving 34 (15 treatment and 19 cross-over subjects) available for further study. Data were collected for 25 subjects (13 treatment and 14 crossovers) who completed 70 weeks and 66 weeks respectively. The balance of seven subjects were classified as dropouts for such reasons as subject relocation and erratic attendance.

Results

There was little difference between those subjects who entered the extension phase and those who discontinued after 36 weeks; however, some differences were found between those who completed the entire extension phase and subjects who dropped out during this phase. The two groups were equivalent for all characteristics except bald spot diameter and hair count; the differences in these two measures indicate that dropouts had greater severity of baldness than those who completed the extension phase. These findings should be given consideration in regard to the generalizability of conclusions from this study; however, they do not impact on the primary analysis to be presented, which is directed at the 27 subjects who completed the study, with comparisons over time within the treated and crossover groups as the main focus.

Baseline comparisons of the 13 subjects in the treatment group and 14 subjects in the crossover group are presented in Table 1. These comparisons yield no significant differences (all P-values > 0.05) and verify the homogeneity of the treated and crossover subjects. These findings support the validity of between-group hair regrowth comparisons which follow.

Table 1. Baseline Comparability of Treatment versus Crossover Group for Subjects Who Completed the Extension Phase

	Treatment Group (N=13)		Crossover Group (N=14)	
Age (yr)>	39	(1.1)	37	(2.1)
Weight (lb)	158	(2.5)	170	(6.2)
Pulse rate (/min)	67	(1.1)	67	(1.9)
Alcohol usage (drinks/week)	4.3	(0.70)	6.7	(1.50)
Duration baldness (yr)	9	(1.3)	12	(1.5)
Bald spot diameter (cm)	2.8	(0.27)	2.5	(0.24)
Bald spot hair count	82	(15)	124	(21)

Values given are the mean (±S.E.).

Table 2 presents mean hair counts, and their associated standard errors, for treated and crossover subjects who completed the extension phase. For the 13 "treatment group" subjects, there was substantial hair regrowth during both phases (mean change from 82 to 150 during the first 36 weeks with a final mean hair count equal to 276 at the end of 70 weeks of treatment). Among the 14 "crossover group" subjects who had the sham treatment initially followed by active treatment after week 36, there was a mild improvement in hair count during the first 36 weeks (mean change of 124 to 160) followed by a very substantial improvement through week 66 (final mean hair count of 249). A similar improvement during the placebo-controlled period was noted in pooled data from topical minoxidil studies in male subjects.[2] It should also be mentioned that although the crossover treatment group started out with a higher (but non-significant) mean hair count at baseline, this difference was made up by the active treatment group whose final mean hair count at the end of the extension period was the higher of the two.

Table 2. Summary of Terminal Hair Counts for Subjects Who Completed the Extension Phase

	Treatment Group* (N=13)		Crossover Group* (N=14)	
Baseline	82	(15)	124	(21)
Week 12	106	(16)	114	(20)
Week 24	130	(25)	133	(24)
Week 36	150	(20)	160	(21)
Week 52/48**	180	(31)	156	(21)
Week 64/60**	238	(39)	219	(28)
Week 70/66**	276	(45)	249	(31)

Values given are the mean (±S.E.).
*During extension period (beyond week 36) all subjects received active treatment.
**During extension phase assessments were made at weeks 48, 60, and 66 for the crossover group and

weeks 52, 64, and 70 for the treatment group.

To further quantify the degree of hair regrowth during each phase, a slopes analysis was carried out by fitting a trend line for each subject and then summarizing across subjects. For each subject a trend line from week 0 to week 36 together with an allowance for a different trend from week 36 to week 66 or 70 was fitted by ordinary least squares using a piecewise regression model.*

**A statistical appendix on slopes analysis methodology is available upon request from the authors.*

The following schematic illustrates the type of overall trend pattern that was fitted to each subject.

Allowance for Change in Trend

Week 0 **Week 36** **Week 66 or 70**

Then the numerical values of the slopes from weeks 0 to 36 and from weeks 36 to 66 or 70 were analyzed with two objectives in mind: (1) Did the treatment group continue to improve in hair regrowth beyond week 36? (2) Did the crossover group experience enhanced hair regrowth when crossed to actual treatment?

The slopes analysis provides a per subject estimate of the regression coefficient (slope) of the change in hair counts during weeks 0 to 36 and beyond week 36; to best summarize the overall trends in each group the average (median) slope was computed across all subjects. Using these average slope estimates statistical tests were carried out to answer the two questions listed above.

The average slope estimate for the treated group was 1.3 during weeks 0 to 36 and was 3.4 beyond week 36; both were statistically significant ($P < 0.01$) indicating that there was significant improvement in hair growth during each treatment period; furthermore, the regrowth trend was significantly greater ($P = 0.01$) beyond week 36 than it was from baseline to week 36.

For the crossover group the average slope during the first 36 weeks (sham period) was 0.8, which was not statistically significant ($P = 0.10$) and thus indicates no significant improvement in hair regrowth (despite the apparently large increase in Table 2 from 124 to 160). During the period beyond week 36 (treatment period) the average slope was 2.8 which was statistically significant ($P = 0.01$), thus indicating significant improvements in hair regrowth during this period. The change in slope between the two periods was also found to be statistically significant ($P = 0.04$) indicating that for the crossover group there was a significant improvement in hair regrowth after switching from the sham to the active treatment.

Between group comparisons of the slope values in each period indicate that there was no significant difference between the treated and crossover groups in either time period ($P > 0.15$).

Predicted values were derived to describe the average hair regrowth trend during each period. These values, which are plotted in Figure 1, clearly illustrate the patterns described above and, in particular, the greater improvement in hair regrowth during the extension phase as compared to the initial treatment phase, for both groups.

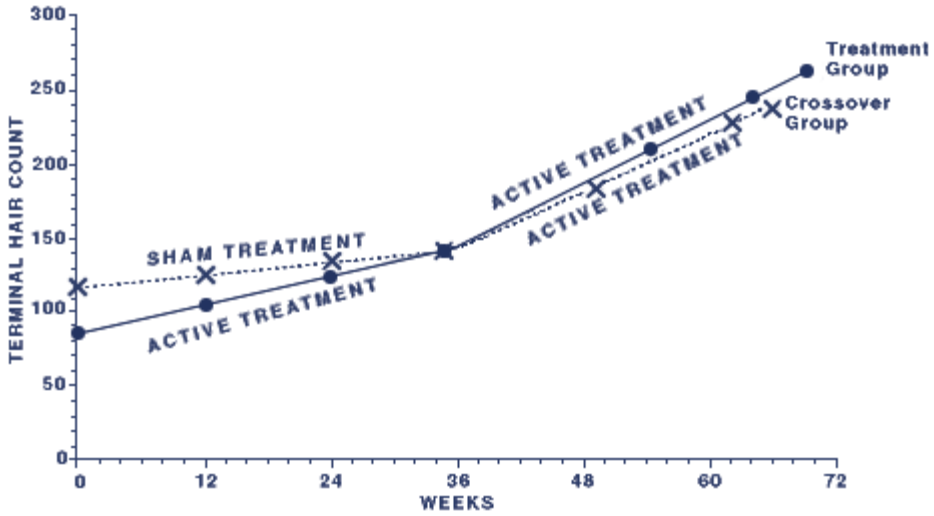

Figure 1. Predicted mean terminal hair counts by treatment group for subjects who completed the extension phase.

Discussion

The overall conclusions of the slopes analysis are: (1) the treatment group had a significant improvement in hair regrowth between weeks 0 to 36, and a significant and continued improvement in hair regrowth, beyond week 36 and through week 70; (2) the crossover group did not show a significant improvement in hair regrowth between weeks 0 to 36 (while on sham treatment), but did show significant regrowth beyond week 36, when the subjects were crossed from sham treatment to actual treatment, and through week 66; and (3) the treatment group exhibited enhanced improvement in hair regrowth beyond week 36, as compared with weeks 0 to 36; the same was true for the crossover group, i.e., hair regrowth during the active treatment (extension) phase was significantly better than the sham treatment phase.

No adverse effects were reported by any of the subjects participating in the extension phase.

These data serve the purpose of providing supportive evidence for further study of this device. Presently under way are multicenter controlled trials in both men and women, with large sample sizes and utilizing computer assisted hair counts rather than visual counts. It is expected that these new studies will complement the results of the study reported here in documenting the efficacy and safety of the pulsed electrical stimulation device in hair regrowth.

References

1. Maddin WS, Bell PW, James JHM. The biological effects of pulsed electrostatic field with reference to hair. Int J Dermatol 1990; 29:446-450.

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Support by a grant from Current Technology Corporation, Vancouver, BC, Canada.

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