International Journal of Dermatology, July - August 1990, Vol. 29, No. 6

Pharmacology and Therapeutics

The Biological Effects of a Pulsed Electrostatic Field with Specific Reference to Hair

ElectroTrichoGenesis

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Abstract: This comparative, controlled study demonstrates the positive biological effect on hair regrowth of a pulsed electrical field administered according to a regularized treatment schedule over 36 weeks. Mean hair count comparisons within the groups significantly favor the treatment group, which exhibited a 66.1% hair count increase over baseline. The control group increase over baseline was 25.6%. It is notable also that 29 of the 30 treatment subjects (96.7%) exhibited regrowth or no further hair loss. The process is without side effects and untoward reactions. The rationale of this phenomenon is unclear but is considered to be due to an eletrophysiologic effect on the quiescent hair follicle, similar to that documented with respect to bone fracture and soft tissue repair enhancement. The electrical pulse may cause increased cell mitosis through calcium influx, involving both the hair follicle sheath and dermal papilla cells.

For more than 30 years the relationship between electrical effects and the growth of mammalian tissue has been a subject of interest and conjecture. Starting with studies of electrical signals arising from nonexcitable tissues, exogenous signals have been applied to cellular and animal models to determine biologic response, and electrical stimulation has been used clinically to enhance hard and soft tissue repair.1

This study presents data on a hair regrowth method utilizing the proximal application to the scalp of a pulsed electrical field. Previously, Gunn and Lee2 reported an experiment involving four men with early hair loss being treated with a commercially available transcutaneous electrical neural stimulation (TENS) device, resulting in a reduction of shedding, an improvement in hair texture, and a gradual resumption in growth rate. Also, in two open, uncontrolled trials involving 25 and 40 subjects, respectively, Bell3 reported that 84% of the former group and 70% of the latter showed regrowth after 60 days, utilizing the electrical modality being tested in this study. Disciplines within the medical profession are familiar with the use of electrical modalities in a variety of circumstances, but the suggestion of electricity stimulating hair growth or regrowth has not been properly investigated. The use of certain frequency and current values in a specified treatment regimen may meet the need for an effective, new form of treatment of a troublesome cosmetic condition, androgenic alopecia, to which increased attention has been paid in recent years.4 The terminology "electrotrichogenesis" (ETG) aptly and conventionally describes the phenomenon.

Materials and Methods

Seventy-three white men exhibiting male pattern baldness of severity classification III vertex and IV on the Hamilton scale were enrolled in the study. Other participation requirements were dark hair coloring, age range 19-49 years, and apparent good health. Each participant was subject to a physical examination and the taking of a medical history including information on current treatment and prescription drugs. Previous involvement in other hair studies or use of any hair growth agent within the last 6 months disqualified the subject. A total of 17 subjects (8 treatment and 9 nontreatment control) dropped out of the study largely for reasons of time constraints caused by the lengthy follow-up period. Data for 56 subjects, 30 treatment and 26

control, were collected over a period of 36 weeks for each individual, April 1988 to June 1989. Subjects were randomly assigned to either group A (treatment) or group B (control) using a table of random numbers. The device operator made appropriate device assignments according to the randomization series. All subjects and the investigators were blinded as to group assignments.

The procedure for both groups A and B was identical and required each subject to visit the investigator's medical office. He would be seated in a chair and place his head under a semispherical hood, similar to a salon type hair dryer (Fig. 1). Treatments were given once weekly throughout the 36-week period, except for weeks 1 and 2, 17 and 18, and 33 and 34 when treatments were twice weekly. All treatments were of 12 minutes duration. This schedule was chosen empirically on the basis of experimentation and observation in previous open trials.

A total of four apparently identical devices were used. Two devices were fully operational and used for group A subjects. Two other devices had their output circuitry severed such that no electrical energy reached the hood and were used by group B (control) participants. Performance characteristics of both operational and control devices were monitored throughout the trial. No wires, electrodes, plates, or paddles touched the scalp. The specially designed electrode plates were wholly contained within the structure of the hood and caused the scalp to be passively "bathed" with the emitted electrical field energy. Electrical output at the hood was monitored and measured regularly to ensure adherence to proprietary specifications.

Treatments were not discernible and subjects experienced no sensation whatsoever. The only indication of the machine on or off status was by the pilot light, which blinked during the operating ON mode. In the control machines the pilot light blinked in the same manner.

All subjects were instructed to report any side effects noticed and to maintain their normal lifestyles and habits. They were requested to shampoo daily with a mild commercially available shampoo provided. Medical follow-up enquiries were made by the investigators 4 weeks after commencement and again at the conclusion of the trial regarding the occurrence of side effects.

Electrical characteristics of each treatment are given in Table 1, indicating the selection of polarity and intensity of the electrical field output. Pulse width, frequency, and waveform are constants and fixed inherently in the device circuitry. They are held as proprietary by the owner.

TABLE 1. Treatment Schedule

Week	No. of Treatments	Polarity	Current Value
1	2	+	F
2	2	+	F
3-16	1	-	F
17	2	+	H
18	2	+	F
19-32	1	-	Odd weeks H Even weeks F
33	2	+	H
34	2	+	F
35	1	-	H

36	1	-	F
F = full intensity; H = half intensity.			

Measurement
Terminal hairs in a designated 1 inch (in.) circular area of the scalp were counted on four occasions during the trial; first, prior to the initiation of treatment and again at the end of weeks 12, 24, and 36 of the subject's therapy. Adapting the technique used by investigators of the trichogenetic effects of the drug minoxidil,[5,6] a 1 in. diameter round aperture was cut in a sheet of clear celluloid plastic (8.5 in. x 11 in.) to be used as a template. The template was placed on the scalp with the aperture over the approximate center of the vertex balding area. Measurements were taken from the edge of the template to the tips of the nose and both ears and recorded so that the template could be placed over the same spot in subsequent counts. Each subject was assigned his own template, appropriately identified with his initials, which was maintained in his file.

Following proper placement of the template, an eyebrow pencil was used to describe the edges of the circular area of scalp under the aperture. The template was then removed, and aided by a lighted magnifying glass (x3 power) on a stand, a wooden swab stick was used to count the terminal hairs in the outlined area. At the end of the counting procedure, the scalp markings were gently removed with an alcohol swab.

Results

Pretreatment Comparability of Groups
Table 2 gives the two groups' means (±SD) for each of the selected patient and disease variables mentioned. Also shown for each covariate is the corresponding p value from a two-sample t-test comparing the means of group A with group B. Group A (treatment) and group B (control) did not differ significantly with respect to their mean values of initial hair count or with respect to their mean values for any of the noted covariates.

Comparison of Terminal Hair Counts
Prior to therapy, subjects in group A had a mean terminal hair count of about 91, whereas group B subjects had a slightly greater terminal hair count mean of about 111. This difference is not significant statistically, but it does affect the analysis of the changes in subjects' counts of terminal hairs. Accordingly, the comparison of changes in terminal hair counts was used as the analytical parameter. At week 36 increased growth count was 66.1% over baseline for group A (150.83 versus 90.83) compared with 25.6% for group B (139.23 versus 110.85).

TABLE 2. Pretreatment Comparability of Groups

	Group A	**Group B**	**Two-sided P Value**
Duration of baldness (yr)	9.93 ± 5.83	12.23 ± 6.13	0.157
Age (yr)	37.23 ± 5.24	37.96 ± 6.76	0.652
Weight (lb)	167.60 ± 16.47	168.62 ± 23.11	0.849
Pulse rate (/min)	67.00 ± 4.69	67.15 ± 6.39	0.918
Alcohol (drinks/wk)	4.77 ± 2.76	5.58 ± 4.88	0.440
Bald spot diameter (in.)	2.92 ± 1.14	2.88 ± 1.11	0.902
Values are mean ± SD.			

Comparison of Changes in Terminal Hair Counts
Table 3 shows the two groups' means (±SD) for changes in terminal hair counts from baseline

to week 36. P values are reported for two-sample t-tests to compare the groups' mean changes at each interval. (The p values obtained from corresponding nonparametric two-sample Mann-Whitney tests are similar to the p values reported in Table 3 for the t-tests.) Considering changes from each subject's baseline data, therefore, group A showed significantly greater change than group B.

TABLE 3. Terminal Hair Count Differences from Baseline

	Group A	Group B	Two-sided P Value	95% Confidence Intervals for the Difference in Mean Change from Baseline
Week 12 - baseline	18.50 ± 34.02	-9.96 ± 44.47	0.0090	28.46 ± 21.06 (7.40, 49.52)
Week 24 - baseline	35.83 ± 43.49	9.76 ± 42.00	0.0298	26.07 ± 23.42 (2.65, 49.49)
Week 36 - baseline	60.00 ± 53.68	28.39 ± 51.89	0.0298	31.62 ± 28.39 (3.23, 60.01)

Unless otherwise indicated, values are mean ± SD.

Table 4 compares group A and group B with respect to the directions of changes for individual subjects as increase (+), no change (0), or decrease (-) in hair counts at the end of weeks 12, 24, and 36. For two of the three contingency tables, a chi-square test (with two degrees of freedom) shows a significant difference between the two groups with respect to the frequencies of positive and negative changes from subjects' baseline counts. In group A at week 36, compared with baseline, 83.3% showed increase (growth) and 96.7% showed growth or no further loss.

TABLE 4. Individual Direction of Change in Hair Count

	Week 12 - Baseline			Week 24 - Baseline			Week 36 - Baseline		
	Group A	Group B	Total	Group A	Group B	Total	Group A	Group B	Total
+	18	8	26	25	14	39	25	16	41
0	6	3	9	2	3	5	4	2	6
-	6	15	21	3	8	11	1	8	9
	30	26	56	30	25*	55*	30	26	56
x^2	8.46			5.16			7.84		
P value	0.0145			0.0756			0.0198		

**One subject value reading was missed at week 24.*

Role of Covariate Factors

Using analysis of covariance procedures, none of the covariates considered in Table 2 was found to be a significant predictor of hair regrowth, except for the bald spot diameter ($p < 0.01$). Table 2 also shows that the two groups are exceptionally well balanced with respect to this covariate.

Side Effects

Notable during the course of the 36-week treatment period was the total lack of side effects. Enquiries made both during and at the conclusion of the study elicited no attributable side effects or untoward reactions from the subjects. Subsequent to the medical examination at the commencement of the study, vital signs were monitored at week 4 and again at the conclusion of the 36-week program. In all cases these were within normal ranges. There were no symptoms of central nervous system (CNS) pathology. No laboratory tests were considered

necessary.

Electrical Parameters

The devices used in this study passed inspection by the Canadian Standards Association, and although they should not be used on persons with wet hair, the low voltages and high output impedence do not constitute a shock hazard even if there were physical contact between the wet hair and the hood plates.

The current densities in the body due to the effects of the electric field have no detrimental effect on the health of persons using the device. Schwan[7] studied the possibility of dangerous current levels due to electrical fields of the type used in these devices and concluded that for there to be dangerous current levels flowing in the subject, electric field densities would have to be 300 million volts per meter (v/m). This is 5 orders of magnitude or roughly 100,000 times the electric field strength levels calculated as existing between the plates of the device.

Knickerbocker et al.[8] exposed 22 male mice to a 60 Hz field of 190,000 v/m for 1,500 hours during the course of 10.5 months. No effect on health, behavior, or reproductive ability of the animals was found. Necropsies done after the exposure to the electric field did not reveal any adverse pathologic effects.[9] The subject devices produce less than 4,000 v/m, about 2% of the levels used in the Knickerbocker et al. study[8] and for a much shorter period of time.

Discussion

The use of exogenous electrical stimulation has been shown to stimulate growth of skeletal tissue in nonunited fractures[1,10,11,12] and to speed up significantly healing in soft tissue wounds including decubitus ulcers.[13] Indeed, the early physiologic processes of osteogenesis, e.g., better collagen organization within early callus,[14] hyaline cartilage production in the vicinity of healing osteotomies,[15] and a more rapid return of medullary circulation.[16] Bassett and Hermann[17] showed that the proliferative and functional capacity of connective tissue cells can be affected *in vitro* by charge separation phenomena similar to those produced piezoelectrically by bone and cartilage *in vivo*. Robinson noted that fibroblast activity can be affected by field strengths even lower than the endogenous fields in animals.[18]

Becker et al. showed that electrical current directly stimulated cell dedifferentiation of red cells and that these then redifferentiated as cartilage cells, which continued on to become bone cells.[10,19] The roles of DNA and RNA were demonstrated as being the instigatory mechanism in the process; this phenomenon was shown also by Bassett and Hermann[17] and Alvarez et al.[13] in soft tissue, the latter noting significant collagen synthesis and wound epithelialization. Nikolaev et al.[20] summarized their experience as improving the microcirculation, reducing the intensity of the inflammatory process, stimulating metabolism in the cells, intensifying proliferation and differentiation of fibroblasts, and aiding fibrillogenesis and proliferation of the epithelium.

Parkinson[21] described a pulsed electrical field in a capacitive system as producing a transient field in the molecules and larger components of the medium between the electrodes of the system. The field is intrinsically neutralized, but changes take place in the cell membrane due to the impulsive force of the field, which could result in a redistribution of membrane protein known to have an effect on the growth and mobility of certain cell types.

Bourguignon and Bourguignon[22] confirmed earlier suggestions by Binder[23] that pulsed electrical stimulation triggered an electrophysiologic effect in cells rather than cause an electrochemical reaction, and that while the mechanism remains unknown, the temperature of the medium, the pH, and the effects of released metal ions from electrodes are not involved. Later, they elucidated two cellular activation events: the influx of calcium ions into the cells and the exposure of additional insulin receptors on the cell surface, as being part of the DNA and protein synthesis process and important to the healing of skin wounds.[24] Biedebach[25] postulated that electrical current causes sufficient membrane depolarization to allow calcium ions from the interstitial fluid to enter through voltage-dependent calcium channels in the cell membrane. The resulting elevation in intracellular calcium level would then stimulate increased ATP production within the mitochondria, activate the protein kinase mechanisms necessary to stimulate transcription and translation mechanisms to produce new cellular protein, and play an essential role in turning on mitotic cell division and migration. Omura et al. have shown it possible to create rapid change in cell membrane capacitance and appropriately open the voltage sensitive calcium channels by the use of a rapidly changing electrostatic field, without direct contact between electrodes and tissue.[26]

It is not illogical to extend the electrically induced activity of fibroblasts and epithelial cells to the hair follicle and its characteristic and cyclical activity. If one presumes that a quiescent follicle is sensitive to specific levels of electrical stimulation, as Becker and Selden suggested is the case in nonunited fractures,10 these follicle cell groups are capable of being regenerated into or prolonged in their anagen phase. The etiology of hair growth is known, if not fully understood, but Montagna and Chase27 and Messenger28 demonstrated the involvement of the dermal papilla in the growth process of hair including differentiation, development, and cycle control. Messenger28 suggested also that the papilla contains "a functionally unique population of fibroblast-like cells." It is proposed that these cellular groups are electrically sensitive and will respond to specific exogenous current levels and wave characteristics in a manner similar to that demonstrated in the healing of soft tissue wounds and fractures. Further studies dealing specifically with hair follicle components are indicated to shed further light on this electrophysiologic process, electrotrichogenesis.

Acknowledgements
The statistical compilation was done by Jonathan Berkowitz, Ph.D., and Ned Glick, Ph.D., of Berkowitz & Associates, Vancouver, British Columbia and the Department of Statistics, University of British Columbia. Sherry Phillips provided technical assistance and administration duties throughout the trial program.

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Supported by the Current Technology Corporation, Vancouver, British Columbia, Canada.

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