LETTER TO THE EDITOR

MICRONEEDLING IMPROVES MINOXIDIL RESPONSE IN ANDROGENETIC ALOPECIA PATIENTS BY UPREGULATING FOLLICULAR SULFOTRANSFERASE ENZYMES

A. SHARMA[1], R. SURVE[1], R. DHURAT[1], R. SINCLAIR[2], Y. TAN[3], Y. ZOU[3], P. MÜLLER RAMOS[4], C. WAMBIER[5], I. VERNER[6], M. KOVACEVIC[7] and A. GOREN[8]

[1]Department of Dermatology, LTM Medical College & Hospital Sion, Mumbai, India; [2]Department of Medicine, University of Melbourne, Parkville. VIC, Australia; [3]Skin & Cosmetic Research Department, Shanghai Skin Disease Hospital, Shanghai, China; [4]Departamento de Dermatologia e Radioterapia, UNESP, Botucatu, SP, Brazil; [5]Department of Dermatology, Brown University, Rhode Island, USA; [6]Verner Clinic for Dermatology and Aesthetics, Tel Aviv, Israel; [7]Department of Dermatovenereology, Sestre Milosrdnice University Hospital Centre, Zagreb, Croatia; [8]Department of Dermatology, Hairmore Hospital Beijing, Beijing, China

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To the Editor,

Microneedling is a minimally invasive procedure of puncturing the skin with small needles. The technique was developed from the attempts of Orentreich and Orentreich in 1995 to treat scars (1). It was further refined by Fernandes in 2006 with the invention of the dermaroller used for collagen induction (1). Since its introduction, microneedling has been used to treat a wide range of dermatological conditions from skin laxity, striae, acne scarring to vitiligo. The proposed mechanism of action in collagen induction is the initiation of the wound repair mechanism following puncturing of the skin. Schmitt et al. (2) characterized the cascade of molecular signaling following microneedling in a human skin model. In their study, five days post-micro needling, tissue remodeling, wound healing, epithelial proliferation and differentiation genes were up-regulated compared to controls. Moreover, microneedling induces the release of growth factors such as vascular endothelial growth factor, fibroblast growth factor, transforming growth factor alpha and beta, platelet-derived growth factor, Wnt3a, β-catenin and Wnt10b (3, 4). Several weeks post-microneedling, additional Type I collagen is deposited in the dermis leading to skin tightening (4).

Previously, our group demonstrated that microneedling in combination with topical minoxidil in the treatment of androgenetic alopecia (AGA) was superior to minoxidil monotherapy. While it is a common belief that the increased efficacy is due to enhanced penetration of topical minoxidil, the rapid absorption of minoxidil into the blood stream is unlikely to account for the sustained benefit seen in patients who combine microneedling and topical minoxidil.

In the study conducted by Dhurat et al. (5), where subjects who underwent microneedling combined with topical minoxidil had superior regrowth compared to minoxidil monotherapy; topical minoxidil was only applied 24 hours after the microneedling procedure.

Minoxidil is a pro-drug converted to its active

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Corresponding Author:
Dr Maja Kovacevic,
Department of Dermatovenerology,
Sestre Milosrdnice University Hospital Centre,
Zagreb, Croatia
Tel.: +385 98 171 5059
e-mail: kovacevic.maja01@gmail.com

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metabolite, minoxidil sulfate, by the sulfotransferase enzymes (SULT1A1) in the outer root sheath of hair follicles (6). Goren et al. (7) demonstrated that a colorimetric assay using plucked human hairs predicts clinical efficacy to minoxidil therapy in androgenetic alopecia; therefore, we hypothesized that the wound repair mechanism induced by microneedling is likely to up-regulate the sulfotransferase enzyme in hair follicles. In fact, Johnson et al. (8) demonstrated that increased sulfotransferase is a marker for keratinocyte differentiation. In the current study, we investigated the effect of microneedling on the follicular sulfotransferase enzyme.

MATERIALS AND METHODS

Six male subjects were recruited from a dermatology department of LTM Hospital Sion, Mumbai. The average age of the subjects was 28 years. All subjects were diagnosed with androgenetic alopecia and had not undergone minoxidil or microneedling treatment during the twelve months prior to the study. A target area (thinning region) on the top of the scalp was used for microneedling which was performed with a roller (ZGTS 192 needles) once a week at the hospital for a total of 3 sessions. The depth of the needle was 1.5 mm. The microneedling drum device was rolled over the affected areas of the scalp in longitudinal, vertical, and diagonal directions until mild erythema was noted, which was considered as the end point of the procedure. All patients were instructed not to apply minoxidil or change their medical regimes for the duration of the study. No other treatments were applied to the scalp. At baseline, 10 hairs were plucked from the target area and analyzed by the Minoxidil Response Test (Applied Biology, Inc. Irvine, CA, USA) which averages the sulfotransferase activity of the 10 collected hair samples. At the end of the study (day 21), 10 additional hairs were plucked from the target area and analyzed by the Minoxidil Response Test.

Table I. *Sulfotransferase enzyme activity following microneedling treatment.*

Subject Nr.	Day 0 (OD)	Day 21 (OD)	% Change
001	0.021	0.128	525.610%
002	0.298	0.261	-12.269%
003	0.368	0.386	4.752%
004	0.205	0.349	70.244%
005	0.379	0.229	-39.670%
006	0.259	0.596	130.242%

RESULTS

All six subjects completed the study. At baseline the average sulfotransferase enzyme activity for the group was 0.2550±0.1321 (OD units). Following three weekly sessions (21 days) of microneedling, the average sulfotransferase enzyme activity for the group increased to 0.3248±0.1612 (OD units). The median increase in sulfotransferase enzyme activity was 37.5% (range: 525.61% to -39.67%), 66% (4/6) subjects had an increase in sulfotransferase enzyme activity compared to baseline, and 16% (1/6) of the subjects predicted at baseline to be non-responders to topical minoxidil became responders following 21 days of microneedling. The raw data is presented in Table I.

DISCUSSION

The use of microneedling in combination with topical minoxidil in the treatment of AGA demonstrated superior regrowth compared to minoxidil monotherapy. In this pilot study, following 3 weekly sessions of microneedling, 66% of subjects presented an increased follicular sulfotransferase enzymatic activity. Despite the small sample size, the large increase in sulfotransferase enzymatic activity post-microneedling strongly suggests the enhanced efficacy associated with microneedling is due to upregulation of sulfotransferase. To our knowledge, this is the first study to elucidate the synergistic mechanism of action of microneedling in combination with topical minoxidil in the treatment of AGA. Future studies with a larger number of volunteers, and comparing levels of microneedling injury, and a group without microneedling would be necessary to verify the data presented in this pilot study.

REFERENCES

1. Singh A, Yadav S. Microneedling: Advances and widening horizons. Indian Dermatol Online J 2016; 7:244-54.
2. Schmitt L, Marquardt Y, Amann P, et al. Comprehensive molecular characterization of microneedling therapy in a human three-dimensional skin model. PLoS One 2018; 13:e0204318.
3. Kim YS, Jeong KH, Kim JE, Woo YJ, Kim BJ, Kang H. Repeated microneedle stimulation induces enhanced hair growth in a murine model. Ann Dermatol 2016; 28:586-92.
4. Aust MC, Reimers K, Gohritz A, Jahn S, et al. Percutaneous collagen induction. Scarless skin rejuvenation: fact or fiction? Clin Exp Dermatol 2010; 35:437-39.
5. Dhurat R, Sukesh MS, Ganesh A, et al. A randomized evaluator blinded study of effect of microneedling in androgenetic alopecia: a pilot study. Int J Trichology 2013; 5:6-11.
6. Buhl AE, Waldon DJ, Baker CA, Johnson GA. Minoxidil sulfate is the active metabolite that stimulates hair follicles. J Invest Dermatol 1990; 95(5):553-37.
7. Goren A, Castano JA, McCoy J, Bermudez F, Lotti T. Novel enzymatic assay predicts minoxidil response in the treatment of androgenetic alopecia. Dermatol Ther 2014; 27(3):171-73.
8. Johnson GA, Baker CA, Knight KA. Minoxidil sulfotransferase, a marker of human keratinocyte differentiation. J Invest Dermatol 1992; 98(5):730-33.