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Original Research Article

SULT1A1 enzyme booster to amplify topical minoxidil response in androgenic alopecia: a single-center prospective study

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ABSTRACT

Background: Androgenetic alopecia (AGA) is a common hair loss disorder affecting individuals across all demographics. Minoxidil, the most widely used treatment for AGA, has limited efficacy, benefiting only 30-40% of users. Previous studies have linked minoxidil's effectiveness to the sulfotransferase enzyme (SULT1A1) in hair follicles, suggesting that boosting this enzyme's activity may improve treatment outcomes in non-responders.
Methods: This study aimed to evaluate the effect of a SULT1A1 enzyme booster in enhancing minoxidil response among AGA patients with limited prior improvement. The study enrolled 101 AGA patients who were non-responders to 5% topical minoxidil. Participants were treated with a combination of SULT1A1 adjuvant solution and 5% topical minoxidil for 90 days. Treatment response was evaluated using clinical assessment and statistical analysis to determine the impact of gender and age on outcomes.
Results: After 90 days of treatment, 65% of the patients exhibited a positive response to the combination therapy. Gender analysis showed a significantly higher positive response in females compared to males ($p<0.05$). However, age did not significantly influence treatment outcomes.
Conclusion: The combination of SULT1A1 enzyme booster and minoxidil demonstrated a promising increase in response among AGA patients who previously showed limited improvement with minoxidil alone. This study contributes to the limited literature on minoxidil booster responses in AGA, offering hope for improved treatment regimens for affected individuals.

Keywords: Androgenetic alopecia, Minoxidil booster, SULT1A1, Sulfotransferase, Topical minoxidil

INTRODUCTION

Androgenetic alopecia (AGA) is a prevalent hair loss disorder influenced by hormones, genetics, and environmental factors, affecting individuals of all ages, genders, and races. The occurrence rate of AGA in the Indian population is 58% among males aged 30-50 years.[1] It is characterized by the progressive diminishment of hair follicles leading to the transformation of terminal hairs to vellus hairs. Its prevalence is less affected in African Americans, Chinese and Japanese individuals than Caucasians.[2] Topical minoxidil is the most popular and Food and Drug Administration (FDA)- approved drug for the treatment of AGA. It promotes hair regrowth through vasodilatation and reduces hair fall.

Despite its good safety profile, topical minoxidil effectiveness is limited to 30-40%. Longer treatment duration is the key obstacle to minoxidil success.[3] Furthermore, studies show minoxidil bioactivity is linked to sulfotransferase enzyme activity in hair follicles,

predicting minoxidil response in AGA patients.[4,5] Minoxidil, a pro-drug, is bio-transformed into active minoxidil sulfate by the sulfotransferase (SULT1A1) enzyme in the outer root sheet of the hair follicles. Insufficient sulfotransferase activity can hinder the effectiveness of minoxidil treatment. However, enhancing SULT1A1 activity through novel formulation has been linked with improved hair growth in AGA patients. Intracellular pH-modulating agents like sodium metabisulphite have been shown to increase the SULT1A1 enzyme booster activity in hair follicles.[11]

Studies suggest adding SULT1A1 enzyme booster into daily minoxidil treatment can trigger hair regrowth in AGA patients.[4,6] To further validate these findings a prospective study is necessary to evaluate the novel SULT1A1 activity booster, which could become a valuable tool for dermatologists in optimizing AGA treatments.[5] In this context, our study aimed to validate the clinical effect of SULT1A1 enzyme booster in enhancing minoxidil response in individuals who had shown limited improvement or no response to standard treatments.

METHODS

Study type

This is a prospective, single-centre study.

Study duration

The study was carried out from July 2023 to January 2024.

Study place

The study was conducted at Cutis hospital, Bangalore, Karnataka, India.

Inclusion criteria

This involved South Indian patients with AGA over 18 years old who had limited or no response to topical minoxidil.

Exclusion criteria

Subjects with scalp conditions like seborrheic dermatitis or drugs like low-dose aspirin or topical tretinoin interfering with the treatment response were excluded from the study.

Treatment

Each subject received 90 days of treatment and was instructed to apply minoxidil booster containing sodium metabisulphite twice daily, 10 minutes before 5% topical minoxidil application. Follow-up appointments were scheduled at 45 and 90 days.

Objective assessment

The physician's global photography assessment was conducted to assess hair growth at baseline and 90 days by an investigator. The treatment response was rated on a scale as follows-2 (moderately worse), -1 (slightly worse), 0 (no change), +1 (slightly improved) and +2 (moderately improved).

Statistical analysis

Statistical analysis was conducted using SPSS software. To check the correlation between gender, age and the treatment response, Pearson chi-square analysis was considered. In further, to check the influence of treatment on age and gender logistic regression analysis was performed.

RESULTS

Demographic details

Demographic details revealed an average age of 29.5 years (range 18 to 54) with 83 males and 18 females (Table 1). Physician's global photography revealed a positive response in 65% of AGA patients who previously did not respond well to minoxidil alone while only 35% were non-responders. Treatment response was rated on a scale from -2 (moderately worse) to +2 (moderately improved), as shown in Figure 1.

Slight response in 41 subjects and a moderate response in 25 subjects was observed (Figure 2). Among those who did not respond to the minoxidil booster, AGA worsened moderately in 2 patients, slightly worsened in 14 patients, and 19 patients showed no change from baseline to the treatment endpoint (after 90 days) (Figure 3). No adverse events were reported.

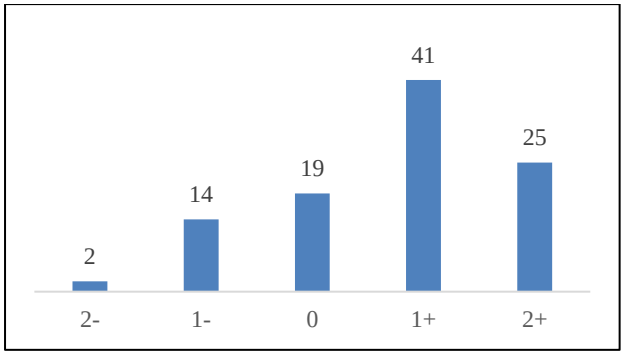
Table 1: Demographic details.

Gender	N
Male	83
Female	18
Age, Average in years (Range)	29.5 (18-54)
Male	28.6 (18-54)
Female	34 (19-50)

Treatment response vs gender

The cross-tabulation of treatment versus gender revealed that 75.8% of males and 24.2% of females responded to the booster treatment while 94.3% of males and 5.7% of females did not respond to the treatment. The chi-square tests indicate a significant association between treatment and gender with p value 0.021. Fisher's exact test also supports this association with a two-sided p-value of 0.027 and a one-sided p value of 0.016. These results

suggest that treatment response varies significantly between genders.



2-(moderately worse), 1-(slightly worse), 0 (no change), +1 (slightly improved), and +2 (moderately improved)

Figure 1: Treatment response to minoxidil booster after 90 days of application where x-axis is the treatment response, y-axis is the patient response in numbers.

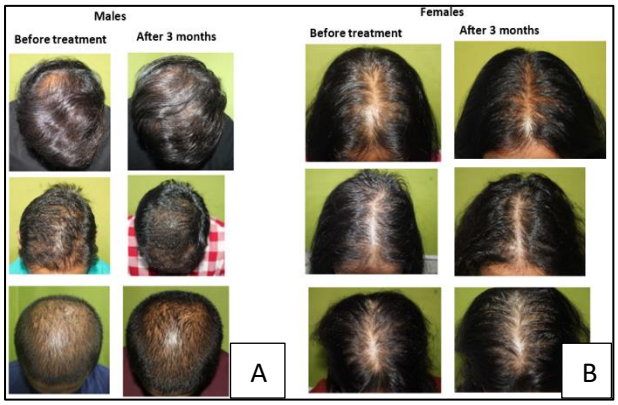


Figure 2 (A and B): Minoxidil booster treatment response seen in both males and females.

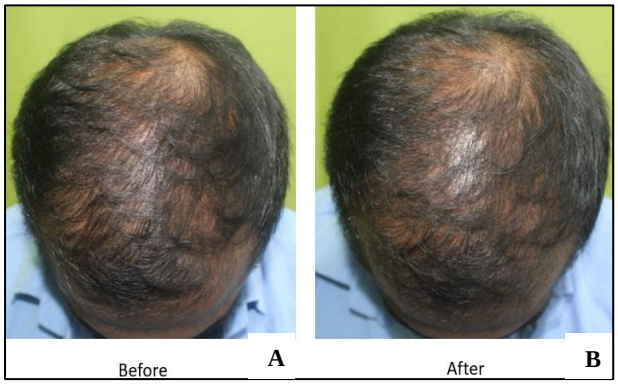


Figure 3 (A and B): Minoxidil booster treatment non responder.

Treatment response vs age

The cross-tabulation for treatment versus age showed no significant association. The chi-square test showed a p-value of 0.84. The result suggests that treatment response significantly does not differ across the varied age groups.

Treatment response prediction with respect to age and gender

The logistic regression showed that females were associated with a significant increase in the odds of minoxidil booster treatment responders with an odds ratio of 4.901 than males and a p value of 0.045. Age, however, is not a significant predictor of treatment response, with an odds ratio of 1.015 and a p value of 0.577. The constant term is not statistically significant (p=0.984). These findings indicate that females had higher odds of a positive treatment response compared to males.

DISCUSSION

The activity of SULT1A1 in hair follicles has been identified as a prognostic marker for predicting the effectiveness of minoxidil treatment in patients with androgenetic alopecia.[4,7,8,13] SULT1A1 is a gene that encodes for the enzyme sulfotransferase which catalyzes the sulfate conjugation of drugs, xenobiotics, neurotransmitters and hormones in humans. This genetically polymorphic enzyme exhibits inheritance and leads to variations in enzyme activity among individuals.[9]

Physiologically, in the hair follicles, sulfation reaction occurs by the transfer of a sulfonyl group, catalyzed by sulfotransferase enzyme. This process utilizes the universal sulfuryl group donor for SULT, 3'-phosphoadenosine-5'-phosphosulfate (PAPS), transferring a sulfonyl group to p-nitrophenol (PNP), under the catalysis of sulfotransferase enzyme.

This reaction yields the sulfated product, p-nitrophenyl sulfate (PNPS), and releases adenosine-3′, 5′-diphosphate (PAP).[10] Sulfotransferase enzyme, with two binding sites for PAPS and PNP, facilitates sulfation by inducing a conformational change that aligns the sulfonyl group of PAPS with the hydroxyl group of PNP, leading to the formation of PNPS and the release of PAP.[11]

$$\text{PAPS} + \text{PNP} \xrightarrow{\text{Sulfotransferase}} \text{PAP} + \text{PNPS}$$

During the differentiation of epithelial keratinocytes, studies have confirmed that the induction of minoxidil sulfotransferase enzyme serves as a key bioindicator.[12,13] The research identifies that supplementing scalp SULT1A1 with naturally occurring minoxidil sulfotransferase enzymes from plants has enhanced minoxidil response in AGA.[6]

It has been hypothesized that intracellular pH modulation upregulates sulfotransferase activity. When sulfotransferase activity is insufficient, the response to minoxidil treatment may be hindered.[4,5,7] In this study, sodium metabisulphite, an alkylating agent present in the

formulation may alter intracellular pH, thereby effectively activating sulfotransferase enzymes and promoting efficient sulfation reactions.[7] As a result, incorporating a minoxidil booster may improve sulfotransferase activation in cases where the enzyme activity is inadequate.

Our study, encompassing both male and female participants (n=101) showed 65% responders and 35% non-responders, echoes Dhurat et al.[4] findings, indicating the promising effectiveness of the minoxidil booster. Statistical analysis revealed no significant relationship between age and treatment (chi-square test p-value 0.84). However, gender significantly influenced treatment response (chi-square test p value 0.021), with females having a higher proportion of positive responses compared to males (p value 0.045) indicating a need for gender-specific considerations in treatment.

Variation in response rates to the booster treatment can be ascribed to the differing activity levels of SULT1A1 in the outer root sheath of hair follicles.[7] Genetic variations, such as SNPs and copy number variations, in SULT1A1 across different ethnic or racial groups can impact minoxidil efficacy in promoting hair growth.[4,14]

The study limitations include its single-center design, a small sample size, short follow-up period, inclusion of a diverse population, an unequal sample size of gender, lack of control group and the inability to compare the efficacy of the booster to that of 5% minoxidil alone.

CONCLUSION

SULT1A1 adjuvant solution alongside 5% topical minoxidil demonstrated both slight and moderate improvement, pointing to its effective intervention for AGA patients with suboptimal responses to minoxidil. This study contributes information to the limited literature on minoxidil boosters and offers hope for better treatment options for individuals with inadequate responses to topical minoxidil.

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Conflict of interest: None declared
Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Shankar DK, Chakravarthi M, Shilpakar R. Male androgenetic alopecia: Population-based study in 1,005 subjects. Int J Trichol. 2009;1:131-3.
2. Mantovani GP, Marra C, De Maria F, Pinto V, De Santis G. Adipose-derived stromal vascular fraction (SVF) for the treatment of androgenic alopecia (AGA): a systematic review. Acta Biomed. 2023;17(5):2023236.
3. Shadi, Z. Compliance to topical minoxidil and reasons for discontinuation among patients with Androgenetic Alopecia. Dermatol Ther (Heidelb). 2023;13:1157-69.
4. Dhurat R, Daruwalla S, Pai S. SULT1A1 (Minoxidil Sulfotransferase) enzyme booster significantly improves response to topical minoxidil for hair regrowth. J Cosmet Dermatol. 2021;4:1–4.
5. Goren A, Castano JA, McCoy J, Bmudez F, Lotti, T. Novel enzymatic assay predicts minoxidil response in the treatment of androgenetic alopecia. Dermatologic Therapy. 2013;27(3):171–3.
6. Mehta N, Huang S, Dhura R. Minoxidil sulfotransferase enzymatical activity in plants: A novel paradigm in increasing minoxidil response in androgenetic alopecia. J Cosmet Dermatol. 2023;10:1-5.
7. Ramos PM, McCoy J, Wambier C, Shapiro J, Vañó-Galvan S, Sinclair R, et al. Novel topical booster enhances follicular sulfotransferase activity in patients with androgenetic alopecia: a new strategy to improve minoxidil response. J Eur Acad Dermatol Venereol. 2020;34(12):799-800.
8. Roberts J, Desai N, McCoy J, Goren A. Sulfotransferase activity in plucked hair follicles predicts response to topical minoxidil in the treatment of female androgenetic alopecia. Dermatol Ther. 2014;27(4):252-4.
9. Hebbring SJ, Adjei AA, Baer JL, Jenkins GD, Zhang J, Cunningham JM, et al. Human SULT1A1 gene: copy number differences and functional implications. Hum Mol Genet. 2007;1;16(5):463-70.
10. Tyapochkin E, Cook PF, Chen G. para-Nitrophenyl sulfate activation of human sulfotransferase 1A1 is consistent with intercepting the middle dot PAP complex and reformation of E middle dot PAPS. J Biol Chem. 2009;23;284(43):29357-64.
11. Paul P, Suwan J, Liu J, Dordick JS, Linhardt RJ. Recent advances in sulfotransferase enzyme activity assays. Anal Bioanal Chem. 2012;403(6):1491-500.
12. Johnson GA, Baker CA, Knight KA. Minoxidil sulfotransferase, a marker of human keratinocyte differentiation. J Invest Dermatol. 1992;98(5):730-3.
13. Pietrauszka K, Bergler-Czop B. Sulfotransferase SULT1A1 activity in hair follicle, a prognostic marker of response to the minoxidil treatment in patients with androgenetic alopecia: a review. Postepy Dermatol Alergol. 2022;39(3):472-478..
14. Daniels J, Kadlubar S. Pharmacogenetics of SULT1A1. Pharmacogenomics. 2014;15(14):1823-38.

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