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# Adverse Effects Encountered during the Therapy of Topical Minoxidil combined with Systemic Finasteride and Topical Minoxidil Alone in Male Androgenetic Alopecia

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**Abstract**

**Background:** Androgenetic alopecia (AGA) is characterized by progressive, patterned hair loss from the scalp. AGA is an extremely common disorder that affects roughly 50% of men by the age of 50 and perhaps as many women older than 40 years. AGA becomes a medical problem only when the hair loss is subjectively seen as excessive, premature, and distressing. **Aim of the study**: To monitor the adverse effects encountered during the therapy of topical minoxidil with systemic finasteride and topical minoxidil alone in male androgenetic alopecia. **Methods:** This randomized clinical trial was carried out for a duration of 6 months, spanning from December 2014 to May 2015. A total of 60 patients with AGA were recruited from Shaheed Monsur Ali Medical College and Hospital and Laser Treat, Dhaka, Bangladesh by purposive sampling. 30 patients (group-A) were treated with finasteride 1 mg daily andminoxidil 2% twice daily and 30 patients (group-B) were treated with minoxidil 2% twice daily. Statistical analysis was performed by using windows based computer software devised with Statistical Packages for Social Sciences (SPSS-22). Prior to the commencement of this study, the research protocol was approved by the ethical committee (Local Ethical committee) of BCPS. **Results:** Patients were clinically assessed for adverse effects, 12 weeks after initiating treatment. In the group given oral finasteride (group A), 8 out of 30 (26.6%) patients reported adverse effects. In the minoxidil only group (group B), 7 out of 30 (23.3%) patients developed adverse effects. The adverse effects disappeared as soon as the treatment was stopped. **Conclusion:** The occurence of adverse effect was almost same in both groups. It can be concluded that addition of oral finasteride to topical minoxidil is as safe as using topical minoxidil alone in treatment of AGA.

**Keywords:** Androgenetic alopecia, Adverse, Topicalminoxidil, Finasteride.

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## INTRODUCTION

Androgenetic alopecia (AGA) is characterized by progressive, patterned hair loss from the scalp. It is also known as male pattern hair loss or common baldness in men. AGA is an extremely common disorder that affects roughly 50% of men by the age of 50 and perhaps as many women older than 40 years. Thinning usually begins between the age of 12 and 40 years. As many as 13% of premenopausal women reportedly have some evidence of androgenetic alopecia. AGA becomes a medical problem only when the hair loss is subjectively seen as excessive, premature, and distressing. Complications of Androgenetic alopecia are psychological trauma, anxiety and depression.

It follows a chronic course with remission and relapses for several years. Pathogenesis of Androgenetic alopecia is multifactorial. The pattern of inheritance is polygenic.[2] Male pattern hair loss results from a combination of hereditary and acquired factors and hormones.[3] The goal of therapy is to increase coverage of the scalp and to retard further hair thinning. Topical minoxidil and oral finasteride have been extensively studied for the treatment of androgenetic alopecia in men. Both drugs have demonstrated efficacy and high tolerability in placebo-controlled randomized trials, supporting their status as first-line agents. These medications, which differ in mechanism of action and route of administration, are given as monotherapy or as combination therapy. Finasteride, a synthetic 4-azasteroid compound, is a specific inhibitor of type II, 5-α reductase isoenzyme responsible for converting testosterone to dihydrotestosterone (DTH), the putative hormonal modulator of AGA in males and females. Finasteride reduces serum and scalp DHT concentrations by approximately 60% to 70%.[12] It may inhibit or reverse miniaturization of hair follicles. Early studies show that 1mg/day is effective in male pattern hair loss.[1] Finasteride is usually well tolerated. However, there is a small risk of transient impotence as an adverse effect, which is fully reversible upon treatment cessation.[16]Adverse effects could be further reduced if finasteride was applied topically to the affected scalp. Minoxidil, a pyrimidine derivative (2,4-diamino- 6-piperidinopyrimidine-3-oxide), was the first drug to become available for treating scalp hair loss. It was formerly synthesised for oral use, as an antihypertensive agent. Minoxidil was surprisingly found to induce hair growth in patients. This unexpected side effect led to the development of a topical minoxidil-containing lotion for alopecia treatment. The product is currently available as solutions containing 2% or 5% minoxidil, in formulations composed of 60% ethanol, 20% propylene glycol and 20% water.[17] The mechanism by which minoxidil promotes hair growth is still not well known, and mixed pathways may be involved. One theory proposes

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that minoxidil, metabolised to minoxidilsulfate in the hair follicles, acts as a potassium channel agonist to reduce the cytoplasmic free $Ca^{2+}$ concentration. Minoxidil appears to increase the duration of the anagen phase, and its angiogenic effects reverse miniaturization of hair follicles. This prevents epidermal growth factor from inhibiting hair formation. Thus, hair growth is promoted.[17,9]Generally, minoxidil is well tolerated with long-term daily use. Adverse events are primarily dermatologic and include irritant contact dermatitis and, less often, allergic contact dermatitis.[18]

## MATERIALS AND METHODS

This randomized clinical trial was conducted in the Department of Dermatology and Venereology at Shaheed Monsur Ali Medical College and Hospital and Laser Treat, Dhaka, Bangladesh. Duration of study was 6 months, starting from December 2014 to May 2015. A total of 60 patients with AGA were selected by purposive sampling. 30 patients (group-A) were treated with finasteride 1 mg daily with minoxidil 2% twice daily and 30 patients (group-B) were treated with minoxidil 2% twice daily. Patients were clinically assessed at baseline and at weeks 4, 8 and 12. Complete history, general physical and dermatological examination were done for all enrolled patients. History and physical findings were recorded in a structured questionnaire. Data was collected using a preformed data collection sheet. Statistical analysis was performed using windows-based computer software, Statistical Packages for Social Sciences (SPSS-22). Prior to the commencement of this study, the research protocol was approved by the ethical committee (Local Ethical committee) of BCPS.

**Inclusion Criteria**

- Patients clinically diagnosed with any grade of AGA
- Male sex
- Age ≥ 16 years
- Patients willing to take part in the study

**Exclusion Criteria**

- Patients not willing to participate in the study
- Female sex
- Individuals taking any form of topical or oral medication for at least three months prior to the study.
- Patients suffering from any concomitant systemic illness- eg. Diabetes mellitus, Hypertension.

## RESULTS

**Table 1: Distribution of patients according to age**

| Age (years) | Group | | p value |
|---|---|---|---|
| | Group A | Group B | |
| 21 - 30 | 7 (23.3) | 19 (63.3) | 0.006 |
| 31 - 40 | 19 (63.3) | 10 (33.3) | |
| >40 | 4 (13.3) | 1 (3.3) | |
| Total | 30 (100.0) | 30 (100.0) | |
| Mean ± SD | 35.0 ± 5.1 | 28.9 ± 5.2 | <0.001 |
| Min - Max | 25 - 46 | 21 - 41 | |

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**Table 2: Distribution of patients according to occupation**

| Occupation | Group | | p value |
|---|---|---|---|
| | Group A | Group B | |
| Service holder | 11 (36.7) | 18 (60.0) | 0.001 |
| Student | 0 (0.0) | 8 (26.7) | |
| Businessman | 6 (20.0) | 1 (3.3) | |
| Doctor | 8 (26.7) | 3 (10.0) | |
| Engineer | 5 (16.7) | 0 (0.0) | |
| Total | 30 (100.0) | 30 (100.0) | |

**Table 3: Distribution of patients according to hair pull test**

| Hair pull test | Group | | p value |
|---|---|---|---|
| | Group A | Group B | |
| Positive | 28 (93.3) | 6 (20.0) | 0.001 |
| Negative | 2 (6.7) | 24 (80.0) | |
| Total | 30 (100.0) | 30 (100.0) | |

**Table 4: Distribution of patients according to grading**

| Grading | Group | | p value |
|---|---|---|---|
| | Group A | Group B | |
| Grade I | 0 (0.0) | 15 (50.0) | 0.001 |
| Grade II | 10 (33.4) | 13 (43.3) | |
| Grade III | 13 (43.3) | 1 (3.3) | |
| Grade IV | 7 (23.3) | 1 (3.3) | |
| Total | 30 (100.0) | 30 (100.0) | |

In group A, 19(63.3%) patients were in age group 31-40 years followed by 7 (23.3%) and 4 (13.3%) were in age group 21 – 30 years and >40 years respectively. In group B, 19(63.3%) patients were in age group 21-30 years followed by 10 (33.3%) and 1 (3.3%) were in age group 31 – 40 years and >40 years respectively. Mean age of the patient in group A was 35.0 ± 5.1 years and group B was 28.9 ± 5.2 years [Table 1]. In both groups maximum patients were in service. In group A, 11 (36.7%) patients were in service followed by 8 (26.7%), 6 (20.0%) and 5 (16.7%) were doctor, businessman and engineer respectively. In group B, 18 (60.0%) patients were in service followed by 8 (26.7%), 3 (10.0%) and 1 (3.3%) were student, doctor and businessman respectively [Table 2]. In group A, 28 (93.3%) cases were positive and in group B, 6 (20.0%) cases were positive in hair pull test [Table 3]. In group A, 13 (43.3%) cases had grade III alopecia followed by 10 (33.4%) cases and 7 (23.3) cases were grade II and grade IV respectively. In group B, 15 (50.0) cases had grade I alopecia followed by 13 (43.3%) cases, 1 (3.3) case and 1 (3.3) case with grade II, grade III and grade IV alopecia respectively [Table 4]. Result of hair pull test was gradually improved in both groups, but improvement rate was better in group A compared to group B [Table 5]. Patients were clinically assessed at 4, 8 and 12 weeks after initiating treatment. Adverse effects reported throughout the study were itching, erythema, hair plucking, breast tenderness, decreased libido, facial hair growth, acne, anorexia and nausea. In the group given oral finasteride (group A), adverse effects were noted in 8 out of 30 (26.6%) patients. Among the 8 patients, 3 (37.5%) suffered from loss of libido, 3 (37.5%) reported breast tenderness, 1 (12.5%) had local erythema and 1 (12.5%) noticed facial hair growth. In the group administered 5% minoxidil (group B), 7 out of 30

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patients encountered adverse effects. Among the 7 patients, 3 (42.9%) noticed increased facial hair growth, 2 (28.6%) had erythema, 1 (14.3%) reported itching and 1 (14.3%) developed tendency of hair plucking. The adverse events disappeared as soon as the treatment was stopped [Table 6].

**Table V: Comparison of hair pull test between two groups at 1st follow up, 2nd follow up and 3rd follow up**

| Hair pull test | 1st follow up | | 2nd follow up | | 3rd follow up | |
|---|---|---|---|---|---|---|
| | Group A | Group B | Group A | Group B | Group A | Group B |
| Positive | 22 (73.3) | 6 (20.0) | 9 (30.0) | 2 (6.7) | 0 (0.0) | 1 (3.3) |
| Negative | 8 (26.7) | 24 (80.0) | 21 (70.0) | 28 (93.3) | 30 (100.0) | 29 (96.7) |
| Total | 30 (100.0) | 30 (100.0) | 30 (100.0) | 30 (100.0) | 30 (100.0) | 30 (100.0) |

**Table VI: Distribution of patients according to adverse effects**

| Adverse effects | 1st follow up | | 2nd follow up | | 3rd follow up | |
|---|---|---|---|---|---|---|
| | Group A | Group B | Group A | Group B | Group A | Group B |
| Itching | 1 (9.1) | 4 (36.4) | 1 (12.5) | 4 (44.4) | 0 (0.0) | 1 (14.3) |
| Erythema | 1 (9.1) | 3 (27.3) | 0 (0.0) | 2 (22.2) | 1 (12.5) | 2 (28.6) |
| Hair plucking | 0 (0.0) | 3 (27.3) | 0 (0.0) | 1 (11.1) | 0 (0.0) | 1 (14.3) |
| Breast tenderness | 3 (27.3) | 0 (0.0) | 3 (37.5) | 0 (0.0) | 3 (37.5) | 0 (0.0) |
| Anorexia | 2 (18.2) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Decreased of libido | 1 (9.1) | 0 (0.0) | 2 (25.0) | 0 (0.0) | 3 (37.5) | 0 (0.0) |
| Nausea | 2 (18.2) | 0 (0.0) | 1 (12.5) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Facial hair growth | 0 (0.0) | 1 (9.1) | 1 (12.5) | 2 (22.2) | 1 (12.5) | 3 (42.9) |
| Acne | 1 (9.1) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) |
| Total | 11 (100.0) | 11 (100.0) | 8 (100.0) | 9 (100.0) | 8 (100.0) | 7 (100.0) |

## DISCUSSION

In this study mean age of the patients in group A was 35.0 ± 5.1 years and group B was 28.9 ± 5.2 years. Most of the patients were in age group 21-40 years in both groups. Kapadia et al,[4] revealed that all of their study subjects were 18-42 years age group. Similarly, all of the study subjects were within range of 18-41 year in Kaufman et al,[5] 18-40 years in Van Neste et al,[6] 23-47 years in Olsen et al[7] in their respective studies. In group A, maximum 11 (36.7%) patients were in service followed by 8 (26.7%), 6 (20.0%) and 5 (16.7%) were doctor, businessman and engineer respectively. In group B, maximum 18 (60.0%) patients were in service followed by 8 (26.7%), 3 (10.0%) and 1(3.3%) were student, doctor and businessman respectively. Regarding hair pull test 28 (93.3%) and 6 (20.0%) cases were positive in group A and group B respectively. In group A, maximum 13 (43.3%) cases were grade III followed by 10 (33.4%) cases and 7 (23.3) cases were grade II and grade IV respectively. In group B, maximum 15

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(50.0) cases were grade I followed by 13 (43.3%) cases, 1 (3.3) case and 1 (3.3) case were grade II, grade III and grade IV respectively. Result of hair pull test was gradually improved in both groups but improvement rate was better in group A comparing group B. Many researchers have investigated the effect of minoxidil on male scalp as a function of treatment time. De Villez[8]reported that hypertrichosis first became observable some 4 months into the therapy when fine, colorlessvellus hairs in the balding area began to lengthen. In this study, adverse effects were noted at the end of 4, 8 and 12 weeks of therapy. At the end of 12 weeks, 26.6% cases in group A and 23.3% cases in group B showed some adverse effects, but these were not age related.[9-11] In the group given oral finasteride (group A) 37.5% suffered from loss of libido, 37.5% reported breast tenderness, 12.5% had local erythema and 12.5% noticed facial hair growth. In the group administered 5% minoxidil (group B) 42.9% noticed increased facial hair growth, 28.6% had erythema, 14.3% reported itching and 14.3% developed tendency of hair plucking. However, there is a small risk of transient impotence as an adverse effect, which is fully reversible upon treatment cessation.[12] Some of the patients who experienced side effects did not drop out of the treatment because of perceived good results. The incidence of adverse events was 5.3% - 8.7% (13/150) who were treated with 1% to 5% minoxidil.[3] In the group given oral finasteride, side effects were noted in 7 patients: 6 patients suffered from loss of libido, and 1 patient had an increase in other body hairs; irritation of the scalp was seen in 1 patient in the group administered 5% minoxidil.[13] There were no serious side effects. Two instances of allergic contact dermatitis and four of pruritus were attributed to use of the drug. Two individuals complained of impotence, which disappeared within a few days of discontinuation of topical minoxidil.[14] In this study there is no such adverse effect with topical minoxidil. The authors concluded that in Japanese men with androgenetic alopecia, long-term use of oral finasteride maintained progressive hair regrowth without recognized adverse effects.[15]

***Limitations of the study:***

This study was carried out at two different centersin Dhaka city using a small sample size. So, it may not be adequate to represent the whole population.

## CONCLUSION

The occurence of adverse effect was almost same in both groups. It can be concluded that addition of oral finasteride to topical minoxidil is as safe as using topical minoxidil alone in treatment of AGA. However, this study may not reflect incidence of adverse effects in a larger population. We recommend carrying out multi-centric studies using larger sample sizes.

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