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Role of Dutasteride in the Treatment of Androgenetic Alopecia

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Abstract

This study evaluates the role of dutasteride in the treatment of androgenetic alopecia. A prospective, open-labeled interventional study conducted at the Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka from April 2023 to March 2024. Men with Androgenetic alopecia (AGA) who did not show significant improvement when treated with finasteride at a dose of 1 mg/d for at least six months were enrolled. Ninety patients were recruited after taking informed consent. Patients were treated with dutasteride at a dose of 0.5 mg daily for 24 weeks. Clinical assessment was performed by dermatologists and subjective evaluation of overall assessment was done based onchanges in the size of the vertex spot, hair loss on top of the scalp, bitemporal recession, the amount of hair shedding and hair quality on a 3-point rating scale (increased, no change, or decreased). The mean age of study patients was 36.3±12 years and majority of the patients 30(33.3%) belonged to the age group 41- 50 years with followed by 27(30.0%) in the age group 31-40 years. Regarding subjective evaluation of overall assessment, in case of change in size of vertex spot, majority 77(85.6%) showed decreased, in case of hair loss from top of scalp, majority 83(92.2%) reported decreased, in case of bitemporal recession, majority 82(91.1%) showedno change, in case of hair shedding, majority 87(96.7%) showed decreased and in case of hair quality, 85(94.4%) reported increased and no patient reported of decreased. Regarding clinical assessment of investigator that majority of the patients 40(44.5%) was moderately improved (+2), followed by 30(33.3%) was greatly improved (score of +3), 18(20.0%) was slightly improved (+1) and only 2(2.2%) was unchanged (0). Among the ninety patients of androgenetic alopecia, 3(3.3%) showed decreased libido and 2(2.2%) showed erectile dysfunction. The study concluded that dutasteride is effective and safe in the treatment of androgenetic alopecia. This study will provide the therapeutic basis for dutasteride as an alternative treatment option for patients with AGA recalcitrant to finasteride over six months. Therefore, dutasteride will become a treatment of choice for androgenetic alopecia (AGA) in near future.

Keywords: Dutasteride, Androgenetic Alopecia, Efficacy of Dutasteride, Safety of Dutasteride

Introduction

Androgenetic alopecia is a common condition of hair loss, with significant impairment on quality of life often causing psychological distress and characterized by thinning of scalp hair [1, 2]. Hair follicles in persons with androgenetic alopecia (AGA) are genetically susceptible to androgens. The activity of 5-alpha-reductase enzyme converts free testosterone into dihydrotestosterone (DHT). DHT binds to the androgen receptor in the dermal papilla of the hair follicle and the hormone-receptor complex then activates the genes responsible for the gradual hair loss. Peripheral antiandrogens, like the inhibitors of 5-alpha-reductase, have been proven to be effective in stopping this mechanism and to revert hair thinning [3].

Several new therapeutic approaches are emerging for the management of androgenetic alopecia (AGA). Oral finasteride, which inhibits type II enzyme, is a Food and Drug Administration (FDA) approved drug to treat AGA [4]. The finasteride regimen, which has been used for AGA treatment worldwide, has been proved to stimulate new hair growth and produce significant improvement of scalp hair in affected people [5-8]. However, reviewing various studies reported in literature about the efficacy of finasteride in AGA, upto 30-50% of patients failed to show clinical improvement [9]. In a study vertex hair in men with AGA presented improvement in only 48% of patients after 1 year and in only 66% at the end of 2 years when treated with finasteride

1 mg/day [10]. Nevertheless, clinicians usually confront the situation where patients with AGA do not show clinical improvement in hair growth despite the long-term use of finasteride [5, 8]. Even though no more hair loss is the therapeutic effect of finasteride, the patient's expectation from the treatment is not just arrest of the progression of AGA but also its reversal and improvement in their hair density and thickness. This prompts the need for alternate treatment modality [11]. Oral dutasteride a synthetic 4-azasteroid, inhibits both type I and II enzymes, thus decreases serum dihydrotestosterone levels at dose of 0.5 mg/day by more than 90%, while finasteride at a dose of 5 mg/day decreases serum DHT by 70% [20]. Dutasteride is approximately three times more potent than finasteride in inhibiting type I 5AR, and 100 times more potent in inhibiting type II 5AR [12, 13].

Recently, several studies have reported the efficacy of dutasteride in patients with AGA. When one of the 17 pairs of identical twins with AGA received dutasteride 0.5 mg/d for 12 months while the other received placebo, dutasteride significantly accelerated hair growth in investigator assessment and patient self-assessment questionnaires [14]. Also, dutasteride increased hair growth significantly in patients with AGA in a dose-dependent manner in a phase II, double-blinded, placebo-controlled, 24-week study [15]. One study showed that the treatment with dutasteride at a dose of 0.5 mg/d was effective in improving the appearance of scalp hair by increasing hair density and thickness in Korean men who had previously shown clinically no improvement in hair growth to the conventional finasteride treatment. After six months of dutasteride treatment, 77.4% of the patients showed significant improvement in global photographic assessment. Compared with the post-finasteride treatment, hair density and thickness significantly increased by 10.3% and 18.9%, respectively, in phototrichogram assessment [5-7]. A randomized, double-blinded, placebo-controlled phase III study compared the efficacy, safety, and tolerability of a daily dose of 0.5 mg of dutasteride for six months vs. Placebo in patients with AGA, dutasteride was found to be significantly more effective than placebo in the aspects of hair count and self-assessment [16].

Though dutasteride was well tolerated in many studies, dutasteride-related sexual dysfunctions have been reported as well [17-19]. Three percent of the patients receiving dutasteride at a dose of 0.5 mg/d for 24 weeks complained of decreased libido and ejaculation disorder [15]. One study reported the incidence of dutasteride-related sexual dysfunction, including impotence, decreased libido and ejaculation disorder, decreased consequently at 11.7, 2.1, 2.4, and 0.5% after 1, 2, 3, and 4 years, respectively [17]. Similarly, another one study also reported dutasteride-related sexual dysfunction in 11.5, 2.8, 2.1, and 0.6% of the patients receiving dutasteride at a dose of 0.5 mg/d after 1, 2, 3, and 4 years [18]. The systemic use of both (dutasteride and finasteride) drugs have been attributed to side effects including sexual impotence, ejaculation disorders, and decrease of libido. Although clinical trials have not demonstrated a clear correlation between the use of these drugs and those side effects, they represent a primary concern for patients considering treatment [3].

Methods and Materials

A prospective, interventional study, conducted at the Department of Dermatology and Venereology, Bangabandhu Sheikh Mujib Medical University (BSMMU), Dhaka. Thestudy wascarried out with patients of androgenetic alopecia, men with aged 18-40 years and who did not show improvement when treated with finasteride at a dose of 1 mg/d for at least six months. Patients using minoxidil, anti-androgenic medications or drugs causing hypertrichosis (phenytoin, acetazolamide, cyclosporine, diazoxide, psoralens, penicillamine, streptomycin and cortisone) or hypotrichosis (anti-coagulants, retinoids, lithium and beta blockers) within the past 6 months; patients with known systemic illnesses, smokers, or tobacco chewers; history of any systemic drugs other than finasteride within the past six months; significant abnormality in a physical and laboratory evaluation including complete blood count, liver function, and renal function test at the screening; history of prostate cancer and first degree relative with prostate cancer before the age of 50 years will be excluded. The study was approved by the Institutional Review Board in our University and informed consents were obtained from all of the patients before initiating dutasteride treatment.A semi-structured data collection sheet was used as research instruments and statistical analysis was performed using SPSS version 22.

Procedure of data collection

About ninety patientswith AGA were enrolled. All patients were instructed not to use topical minoxidil or any androgenic or anti-androgenic treatment during the course of the study. After the initial screening visit, patients eligible to enter the study were treated with dutasteride at a dose of 0.5 mg daily for 24 weeks. Follow-up visits were scheduled every four weeks. At each visit, a medical examination was done, and adverse effects were recorded. High-resolution digital photographs were taken at every visit. Patients who skipped the medication for more than one week at each visit were withdrawn.

Efficacy assessments: Clinical assessments were performed by dermatologists using clinical photographs with a standardized vertex and frontal view. We independently reviewed the paired slides of scalp at the baseline and at post-dutasteride treatment, using a seven-point scale as follows: Greatly improved (score of +3); moderately improved (+2); slightly improved (+1); unchanged (0); slightly aggravated (−1); moderately aggravated (−2); and greatly aggravated (−3). Patients were asked also to rate changes in the size of the vertex spot, hair loss on top of the scalp, bitemporal recession, the amount of hair shedding and hair quality on a 3-point rating scale (increased, no change, or decreased).

Safety assessments: Safety assessments were performed through physical examination, laboratory evaluations, and reports of sexual function and adverse events every 4 weekly. Complete blood count, Serum ALT, Serum creatinine tests were conducted at baseline, 3 months and at completion of treatment (6 months). Sexual functions were evaluated by asking subjects about the occurrence of decreased libido, erectile dysfunction, and ejaculation disorder.

Ethical consideration

Prior to the commencement of this study, approval from Institutional Review Board (IRB) was taken. Before enrollment of the patients into the study, the objectives of

the study along with its risks and benefits of this study were explained to the patients in easily understandable local language, so that they can make independent decision about their participation. All the participants were elaborately informed about the natural history and the prognosis of their disease. Patients were informed by the primary investigator regarding the side effects of the medications prior to enrollment in the study. The patients were explained that they have the right to refuse or accept to participate in the study in its any stage and it do not hamper their treatment procedure and they will not receive financial benefit from this study. The patients were assured that all information and records will be kept confidential, and the study results will be helpful for both the patients and the physicians in making rational approach of the case management and control of this health issue.

Results

Table 1: Distribution of the study patients by age (n=90)

Age (years)	Number (%)
<30	21(23.3%)
31-40	27(30.0%)
41-50	30(33.3%)
>50	12(13.3%)
Total	90(100.0%)
Mean±SD Range (min-max)	36.3±12.0 18-56

Table 1 showed that mean age of study patients was 36.3±12 years and majority of the patients 30(33.3%) belonged to the age group 41- 50 years, followed by 27(30.0%) in the age group 31-40 years, 21(23.3%) in the age group <30 yearsand 12(13.3%) in the age group <50 years.

Table 2: Distribution of the study patients by subjective evaluation (n=90)

Subjective evaluation of overall Assessment	Decreased	No change	Increased
Change in size of vertex spot	77(85.6%)	11(12.2%)	2(2.2%)
Hair loss from top of scalp	83(92.2%)	7(7.8%)	0
Bitemporal recession	8(8.9%)	82(91.1%)	0
Hair shedding	87(96.7%)	3(3.3%)	0
Hair quality	0	5(5.6%)	85(94.4%)

Table 2 showed that subjective evaluation of overall assessment in case of change in size of vertex spot, 77(85.6%) showed decreased, 11(12.2%) showedno change and 2(2.2%) reportedincreased. In case of hair loss from top of scalp, 83(92.2%) showed decreased, 7(7.8%) showedno change and no patient reported of increased. In case of bitemporal recession, 8(8.9%) showed decreased, 82(91.1%) showedno change and no patient reported of increased. In case of hair shedding, 87(96.7%) showed decreased, 3(3.3%) showedno change and no patient reported of increased and in case of hair quality, 5(5.6%) showedno change, 85(94.4%) increased and no patient reported of decreased.

Table 3: Distribution of the study patients by clinical assessment of investigator (n=90)

Clinical Assessment of investigator	Dutasteride-no (%)
greatly aggravated (−3)	0
moderately aggravated (−2)	0
slightly aggravated (−1)	0
unchanged (0)	2(2.2%)
slightly improved (+1)	18(20.0%)
moderately improved (+2)	40(44.5%)
greatly improved (score of +3)	30(33.3%)

Table 3 showed regarding clinical assessment of investigator that majority of the patients 40(44.5%) was moderately improved (+2), followed by 30(33.3%) was greatly improved (score of +3), 18(20.0%) was slightly improved (+1) and only 2(2.2%) was unchanged (0).

Table 4: Distribution of the study patients by adverse effects (n=90)

Adverse effects	Number (%)
Decreased libido	3(3.3%)
Erectile dysfunction	2(2.2%)
Dizziness	1(1.1%)
Mood disturbance	1(1.1%)
Total	7(7.7%)

Among the ninety patients of androgenetic alopecia, 3(3.3%) showed decreased libido, 2(2.2%) showed erectile dysfunction, 1(1.1%) showed dizziness and 1(1.1%) mood disturbance.

Discussion

In current study, mean age of study patients was 36.3±12 years and majority of the patients 30(33.3%) belonged to the age group 41- 50 years with followed by 27(30.0%) in the age group 31-40 years.In study of Shanshanwal *et al*, the mean age of patients was 27.6 years in the dutasteride group [20]. In current study, subjective evaluation of overall assessment in case of change in size of vertex spot, majority 77(85.6%) showed decreased, in case of hair loss from top of scalp, majority 83(92.2%) reported decreased, in case of bitemporal recession, majority 82(91.1%) showedno change, in case of hair shedding, majority 87(96.7%) showed decreasedand in case of hair quality, 85(94.4%) reportedincreased and no patient reported of decreased. Regarding clinical assessment of investigator that majority of the patients 40(44.5%) was moderately improved (+2), followed by 30(33.3%) was greatly improved (score of +3), 18(20.0%) was slightly improved (+1) and only 2(2.2%) was unchanged (0). In a 24-week, double-blind, placebo controlled, dose-ranging study by Olsen *et al*., dutasteride increased hair growth in a dose-dependent manner [15]. Dutasteride, 0.5 mg and 2.5 mg significantly improved hair counts after 24 weeks [16]. Other studies have confirmed efficacy of oral dutasteride compared with placebo in men with androgenetic alopecia [5-7]. Jung *et al*. treated 31 Korean men with androgenetic alopecia who had not shown significant improvement when treated with finasteride 1 mg for at least 6 months with dutasteride 0.5 mg. After 6

months, the hair density and thickness increased by 10.3% and 18.9% respectively [10].

Among the ninety patients of androgenetic alopecia, 3(3.3%) showed decreased libido, 2(2.2%) showed erectile dysfunction, 1(1.1%) showed dizziness and 1(1.1%) mood disturbance. In study of Shanshanwal *et al*, Erectile dysfunction and loss of libido was seen in 3 and 4 patients in the dutasteride group [20]. The incidence of sexual side effects in this study in the dutasteride group (15.6%) was similar to that reported by Jung *et al*. (17.1%) [10]. Dutasteride-related sexual dysfunction had been shown to decrease in frequency when treatment was continued for up to 4 years [19, 20]. In this study, dutasteride was relatively well-tolerated with comparable sexual side effects which was consistent with previously reported data [16, 5, 6]. Several large population-based long-term placebo-controlled studies have demonstrated no clear evidence of the negative effect of 5-alpha reductase inhibitor on erectile function [21]. Erectile dysfunction has also been reported to be a placebo effect [8]. Sexual disorders, including decreased libido, ejaculation disorder, and impotence, have psychological factors in their pathophysiology. Therefore, the obsessive idea that they are taking the drug that could possibly influence their sexual dysfunction could increase the incidence of sexual dysfunction [21].

Conclusion

The study concluded that dutasteride is effective and safe in the treatment of androgenetic alopecia. This study will provide the therapeutic basis for dutasteride as an alternative treatment option for patients with androgenetic alopecia (AGA) recalcitrant to finasteride over six months.

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