# A Clinical Study of the Effects of Finasteride on Androgenetic Alopecia

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***Background*** **: The 5$\alpha$-reductase inhibitor finasteride blocks the conversion of testosterone to dihydrotestosterone(DHT), the androgen responsible for androgen- etic alopecia in genetically predisposed men.**

***Objective*** **: The purpose of this study was to determine the efficacy of finaster- ide treatment according to the type of androgenetic alopecia in Korea.**

***Methods*** **: 196 patients with finasteride(1.25mg/day) were registered in this study and 68 patients were followed over 8 months. Efficacy was evaluated by global photographs, investigator assessment of clinical change, and patients' self assessment via self administered hair growth questionnaire.**

***Results*** **: Patients' self-assessment demonstrated that finasteride treatment slowed hair loss, increased hair growth, and improved appearance of hair. These improvements were corroborated by objective assessments after 4 months of treatment. Adverse effects such as sexual dysfunction were minimal.**

***Conclusion*** **: Oral finasteride 1.25mg/day slowed the progression of hair loss and increased hair growth in clinical trials of men with androgenetic alopecia over 8 months. With its generally good tolerability profile, finasteride is a new approach to the management of this condition, for which treatment options are few. (Ann Dermatol 12(4) 264~270, 2000).**

*Key Words* : Androgenetic alopecia, Finasteride

Androgenetic alopecia is the most common type of hair loss found in both men and women after puberty. The occurrence of androgenetic alopecia has been increasing recently and due to high concerns about the cosmetic appearance in modern society and better economy, the interest in treatment of this condition is in strong demand. However, there are no satisfactory preventions or treatment methods yet. Non-surgical treatment of androgenetic alopecia includes topical treatment using corticosteroids, or scalp massage, and various kinds of local hair treatments conducted in many private hair clinics[1,2]. These methods have not been very effective in treating the condition. Only topical application of minoxidil has been the mainstay of therapy. However, the disadvantage of topical minoxidil is that it needs to be continuously applied two or three times daily and furthermore, on discontinuing minoxidil, the regained hair starts to shed off.

Androgenetic alopecia is characterized by a gradual decrease in hair follicle and obvious hair loss caused by androgen and genetic predisposition[4-6]. When androgen secretes in a person with family history of hair loss, androgenetic alopecia initiates and its progress is closely related to age. Hair loss is not observed when 5$\alpha$-reductase(5$\alpha$R) which converts testosterone to dihydrotestosterone(DHT), is genetically absent[7]. This suggests that DHT is the primary cause of hair loss among men with androgenetic alopecia. There are type I and II 5$\alpha$R isoenzyme[8-10], and type I tends to distribute in skin, and Type II in hair follicle and prostatic gland. It has been

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reported that as a selective inhibitor of type II 5$\alpha$-reductase, finasteride can reduce the level of DHT in serum[11], prostatic gland[12], and scalp[13,14], thus has been used for treatment of benign prostatic hyperplasia. Recently, it has been used as a new treatment material for androgenetic alopecia[14,15].

Treatment results and side effects of finasteride used for androgenetic alopecia for Caucasians have been reported previously[16], but there were no reports on Koreans. In order to evaluate effectiveness of finasteride among Koreans, we have treated 196 patients at 'Kangbuk Samsung Hospital' who were distributed between Norwood classification model type III and VII. In this research, therapeutic effects and adverse effects of finasteride for androgenetic alopecia were investigated in order to provide basic statistical data on finasteride as an effective treatment material for androgenetic alopecia.

## PATIENTS AND METHODS

196 patients who visited 'Sungkyunkwan University Kangbuk Samsung Hospital' from January 1998 to September 1999, with Norwood classification type III to VII hair loss were treated with finasteride(Proscar®) 1.25mg daily, regardless of patients weight. The exclusions were such as topical minoxidil use, receiving alopecia treatment at private clinic, and patient with antiandrogenic drug within 6 months. Follow up observations of more than 8 months were possible for 68 patients and others were followed less than 7 month. In order to collect data for distribution of clinical pattern, response to the treatment, and long term follow up observation, the following items were compared and analyzed. (1) Clinical pattern and frequency of androgenetic alopecia: male pattern hair loss classified according to Norwood classification[16]; (2) Age when symptom discovered and age at the time of visit; (3) Family history: hereditary presence of androgenetic alopecia were examined by history taking about first degree relatives; (4) Associated diseases; (5) Routine laboratory examination: blood cell count, liver function test, serum iron level, and testosterone level; (6) Serum testosterone level measured using radioisotope method; (7) Results of treatment: evaluation of treatment was conducted by 2 methods; (7-1) Patients' self assessment(Table 1); (7-2) Investigator assessment: Each patient's scalp was divided into regions. Apex point where coronal plane passing through the external auditory canal and median sagittal plane meeting points was assigned, and two different parietal, bitemporofrontal regions were designated. The regions were observed regularly by more than 2 panel dermatologists and growth conditions of scalp hair was evaluated by following categories; Excellent: Appearance and growth of terminal hair(lengths longer than 1cm); Good: Appearance of vellus hair(lengths less than 1cm); Fair: Decrease of hair loss; Poor: No apparent change compared to pretreatment condition; Worse: Worse than pretreatment. This comparison was done by reference to photographs (NIKON F-801 camera) we had taken every two months. (8) Adverse effects; (9) Assessment of drop out group during treatment: During the course of treatment, patients who did not visit for more than 3 months were surveyed about their reason for termination of treatment by phone.

## RESULTS

### Clinical pattern of androgenetic alopecia

196 patients with androgenetic alopecia at Sungkyunkwan University Kangbuk Samsung Hospital were analyzed according to Norwood classification from January of 1998 to September

Table 1. Patients' self assessment

| Question | Answer |
|---|---|
| #1: Whether region of hair loss was decreased | |
| #2: Appearance of new hair | excellent |
| #3: Growth of new hair | good |
| #4: Slowing of hair loss | fair |
| #5: Degree of satisfaction regarding frontal hair line | poor |
| #6: Degree of satisfaction regarding hair on top | worse |
| #7: Overall satisfaction | |

of 1999. Among the 196 patients observed, type IIIv was highest with 110(56.1%) patients. Type VII was the least frequent type with 1(1.0%) patient(Table 2). For 68 patients, 8 month follow up observation was possible.

### Age

Patients age distribution ranged from 21 to 64 and average was 34.4 years old. Most of the patients were under the age of 40(71.4 %)(Table 3). Age distribution on the basis of initial hair loss by patients' recall were 17 to 51 with average of 28.9 years old.

### Family History

The survey taken from first-degree relatives, showed that 36.7% of paternal side and 2.4% of maternal side had history of male pattern baldness. 1.2% of 196 patients studied had history from both sides of the family.

### Associated diseases

Among 196 patients, associated diseases were observed in 89(45.5%) of them. Seborrheic dermatitis(34.7%) was highest and acne, atopic dermatitis, disease of thyroid gland, depression, and GI disease were observed in decreasing order(Table 4).

**Table 2.** Distribution of patients by the Norwood type

| Norwood type | No. of patients(%) |
|---|---|
| III | 31/196 (15.8%) |
| IIIa | 7/196 (3.6%) |
| IIIv | 110/196(56.1%) |
| IV | 16/196 (8.2%) |
| IVa | 5/196 (2.6%) |
| V | 14/196 (7.1%) |
| Va | 2/196 (1.0%) |
| VI | 10/196 (5.1%) |
| VII | 1/196 (0.5%) |
| Total | 196/196(100%) |

**Table 3.** Age distribution of the 196 cases of androgenetic alopecia

| Age | No. of patients(%) |
|---|---|
| 21-25 | 20/196 (10.2%) |
| 26-30 | 52/196 (26.5%) |
| 31-35 | 34/196 (17.3%) |
| 36-40 | 34/196 (17.3%) |
| 41-45 | 22/196 (11.2%) |
| 46-50 | 19/196 (9.7%) |
| 51-50 | 15/196 (7.7%) |

### Serum testosterone level

Serum testosterone levels were in the range of 0.7-13.0ng/ml(normal range: 3-10ng/ml) and average was 7.1ng/ml. Only 5(2.6%) of 193 patients examined, showed a high serum testosterone level.

### Result of treatment

(1) Patients' self-assessment: Among 7 questions, 48 of 88(54.5%) patients answered slowing of hair loss. Most participants showed positive results as time progressed(Table 5); (2) Investigator assessment: Appearance of new terminal hair and decrease of hair loss region were observed by 2 or more panel dermatologists comparing with the previous photographs. Thereby, after 4 month and 8 month periods, 34.1% and 83.8% showed an appearance of vellus hair or terminal hair(Fig. 1)(Table 6); (3) Comprehensive evaluation was obtained from patients' self-assessment and investigator's objective observations according to clinical pattern of androgenetic alopecia. Follow up observations were conducted at 2 month intervals. The treatment of finasteride showed best results in type IIIv(86.8%) and also the follow up observation rate was the highest(55.9%). After the appearance of terminal hair, continuous growth was observed(Table 7).

### Adverse effects

10 among 196 patients showed some side effects. 6 patients(3.1%) showed sexual dysfunction. In detail, all 6 complained lack of libido, 5 were accompanied

**Table 4.** Associated diseases in patients with androgenetic alopecia

| Disease | No. of patients(%) |
|---|---|
| Seborrheic dermatitis | 68/196 (34.7%) |
| Acne vulgaris | 6/196 (3.1%) |
| Atopic dermatitis | 5/196 (2.6%) |
| Thyroid disease | 2/196 (1.0%) |
| Depression | 2/196 (1.0%) |
| G.I disease | 2/196 (1.0%) |
| Psoriasis, back pain, hypertension | 4/196 (2.1%) |
| Total | 89/196 (45.4%) |

Table 5. Treatment efficacy of finasteride by the patients

| | No. of patients who have effective* result/ No. of patients who followed up | | | |
|---|---|---|---|---|
| | 2 month | 4 month | 6 month | 8 month |
| Size of bald spot | 3/127(2.4%) | 26/88(29.5%) | 33/73(45.2%) | 38/68(55.9%) |
| Appearance of vellus hair | 8/127(6.3%) | 37/88(42.0%) | 51/73(69.9%) | 53/68(77.9%) |
| Growth of terminal hair | 6/127(4.7%) | 34/88(38.6%) | 48/73(65.8%) | 51/68(75.0%) |
| Slowing hair loss | 29/127(22.8%) | 48/88(54.5%) | 53/73(72.6%) | 61/68(89.7%) |
| Satisfaction with frontal hairline | 4/127(3.1%) | 18/88(20.5%) | 22/73(30.1%) | 22/68(32.4%) |
| Satisfaction with hair on top | 5/127(3.9%) | 34/88(38.6%) | 43/73(58.9%) | 50/68(73.5%) |
| Satisfaction with hair overall | 5/127(3.9%) | 32/88(36.4%) | 40/73(54.8%) | 46/68(67.6%) |

*Efficacy No. of patients with satisfaction include an excellent or good result.

Table 6. Treatment efficacy of finasteride by investigator.

| No. of patients effective*/ No. of patients who followed up | | | |
|---|---|---|---|
| 2mo. | 4mo. | 6mo. | 8mo. |
| 3/127 (0.02%) | 30/88 (34.1%) | 49/73 (67.1%) | 57/68 (83.8%) |

*No. indicates patients with excellent & good results.

Table 7. Treatment efficacy and followed patient in each type of androgenetic alopecia

| | Subjective No*/objective No** (No. of patients followed) | | | |
|---|---|---|---|---|
| | 2mo. | 4mo. | 6mo. | 8mo. |
| III | 1/0(22) | 5/7(16) | 6/8(15) | 7/10(13) |
| IIIA | 0/0(4) | 0/1(2) | 1/1(2) | 1/2(2) |
| IIIV | 3/2(72) | 24/20(52) | 28/35(47) | 33/38(45) |
| IV | 1/1(11) | 2/2(8) | 3/3(5) | 3/4(4) |
| IVA | 0/0(3) | 0/0(2) | 1/1(2) | 1/2(2) |
| V | 0/0(7) | 1/0(5) | 1/1(2) | 1/1(2) |
| VA | 0/0(2) | 0/0(1) | 0/0(0) | 0/0(0) |
| VI | 0/0(5) | 0/0(2) | 0/0(0) | 0/0(0) |
| VII | 0/0(1) | 0/0(0) | 0/0(0) | 0/0(0) |
| Total | 127 | 88 | 73 | 68 |

*No. of patients satisfied overall by their self assessment.

**No. of patients with vellus or terminal hair by investigator.

by impotence. Others complained fatigue, GI trouble, and insomnia(Table 8).

Table 8. Adverse event after oral finasteride

| Adverse event | No. of patients(%) |
|---|---|
| Sexual function (libido decreased, erectile dysfunction) | 6/196 (3.1%) |
| Others (GI trouble, fatigue, insomnia) | 4/196 (2.0%) |
| Total | 10/196 (5.1%) |

Table 9. The causes of discontinuing finasteride therapy

| Cause | No. of patients(%) |
|---|---|
| personal reasons | 31/66 (47.0%) |
| no effect | 19/66 (28.8%) |
| long medication period | 6/66 (9.1%) |
| too expensive | 4/66 (6.1%) |
| private purchase | 3/66 (4.5%) |
| adverse effects | 3/66 (4.5%) |
| Total | 66 (100%) |

**Analysis of drop out group**

Follow up observation was possible on 134 patients from January of 1998 to February of 1999. Complete follow up observation for more than 8 months was conducted on 68 patients(50.7%) and 66(49.3%) failed to complete the observation. Drop out group corresponds to patients who did not visit for more than 3 months. The reasons of drop outs were surveyed over the phone and the reasons were listed at table 9.

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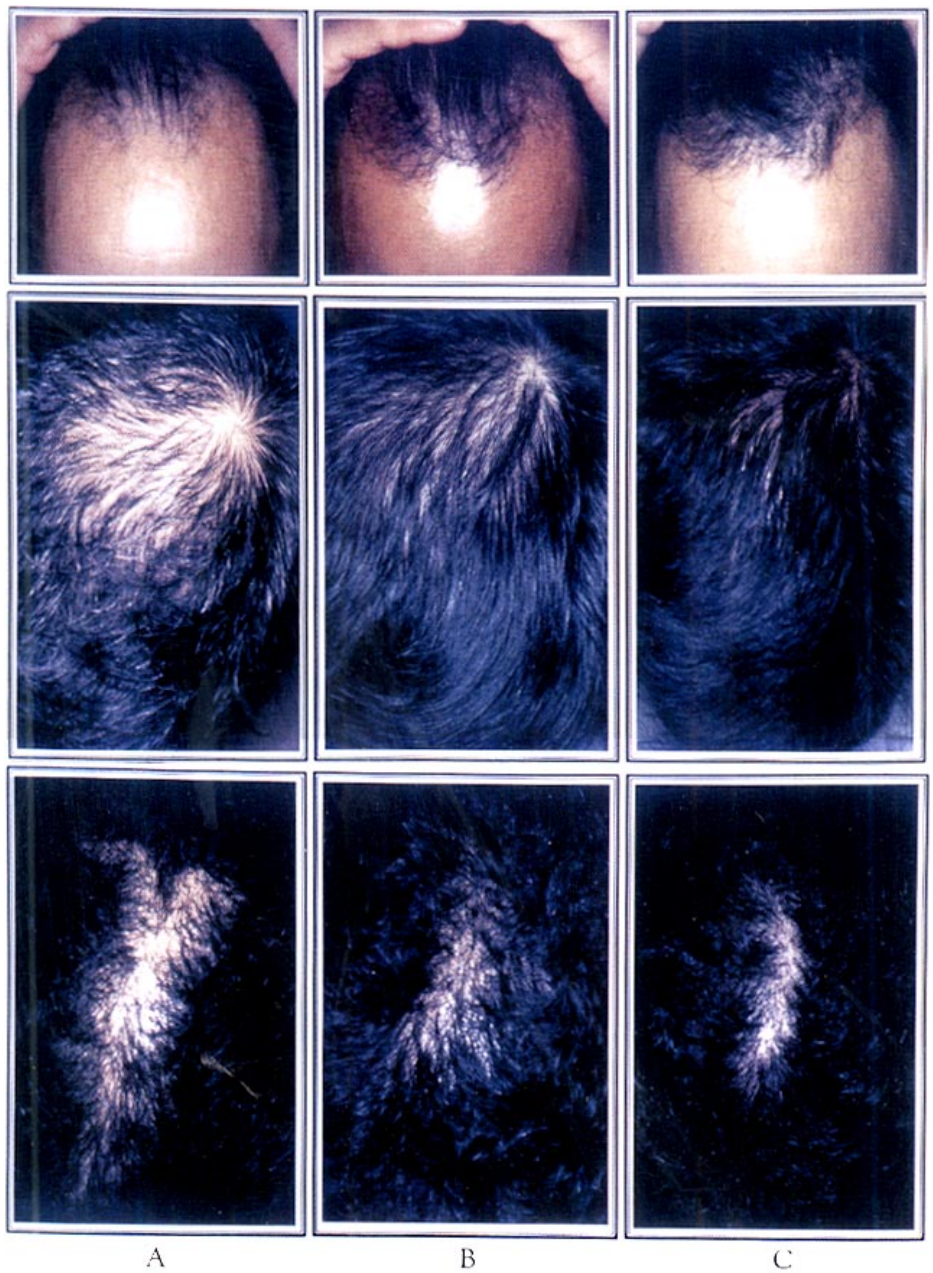


Fig. 1. A. Baseline, B. Month 4 : Slightly increased hair growth, C. Month 8 : Moderately increased hair growth.

## DISCUSSION

The cause of androgenetic alopecia, also commonly known as 'male pattern baldness', is not well known. Testosterone in a male with genetic predisposition turns into dihydrotestosterone by 5$\alpha$-reductase enzyme delaying hair follicle cells protein synthesis, thus causing increase in telogen hair follicle rate as one ages[17-20], and thereby causing hair loss. Therefore, male hormone, androgen, along with genetic predisposition and age, is a critical element in the cause of androgenetic alopecia[21,22].

The hair follicle which is sensitive to androgen, converts testosterone to DHT by 5$\alpha$-reductase[23-25]. According to many published papers, there are two different types of isoenzyme present in hair follicles. Type I 5$\alpha$-reductase is distributed in seba-

ceous gland, and type II 5$\alpha$-reductase in hair papilla and outer root sheath of hair follicle. Therefore, type II 5$\alpha$-reductase is the main element in DHT production in hair follicle and men have a higher amount of these enzymes than women, and also bitemporofrontal and parietal regions have a higher amount than that of occipital area[26,27].

Finasteride($C_{23}H_{36}N_2O_2$) which is widely praised as an effective treatment agent for androgenetic alopecia is a 4-azasteroidal derivatives and has molecular weight of 372.55. It dissolves in chloroform and alcohol but is insoluble in water(Fig. 2).

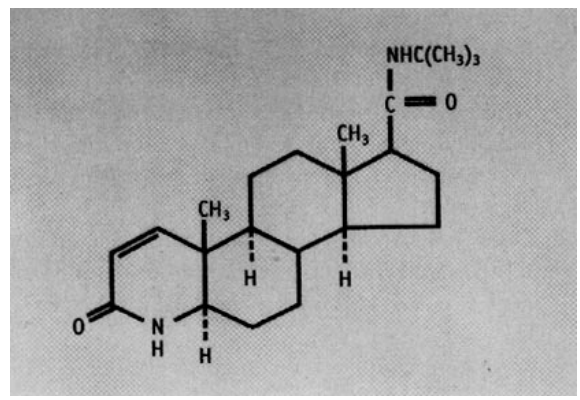


Fig. 2. Molecular structure of finasteride.

In this study, there had been no 1mg finasteride tablet available, so we used a quarter of 5mg finasteride tablet which had been used in treating benign prostatic hyperplasia. Most patients reported their subjective effectiveness of the drug 4 month after the initiation of treatment. Objective observation also showed emergence and continuous growth of hair. Although, bitemporal recess was not analyzed exactly, according to subjective assessment by patients, many noticed improvements with stopped or decreased hair loss. The observation made by two or more specialists on particular region of scalp area, also showed appearance of vellus hair. Continuous observation showed emergence and growth of terminal hair from many patients. Therefore, we believe that a longer period of observation will produce better results.

In our results, hair growth rate was especially high in type IIIv compared to other types. This suggests that the treatment is more effective on vertical region hair loss, which is more common in Koreans compared to Caucasian males[20].

Finasteride with concentration of more than 4 times has been used in treating benign prostatic hyperplasia for years, and many have reported its safety. In our study 3.1% showed symptoms of sexual dysfunction while others complained about fatigue, GI disturbance, and insomnia but recovered fully after termination of treatment. Finasteride is recommended to be used only for men with androgenetic alopecia. If used on pregnant woman, it suppresses the conversion of fetal testosterone to DHT and interferes with masculinizaton of male fetus. It is also reported that finasteride showed no effect on postmenopausal woman with androgenetic alopecia[28].

We have finalized our study only with patients of 8 months of follow-up. Therefore to complete this study and to find accurate finasteride result, continuous work-up with the drop outs(28.8%) are absolutely necessary. Also among the drop out patients who have failed to follow up because of their hope of the dramatic result from finasteride effect did not reach their satisfaction, so we should explain to them to endure at least 4 months of treatment to notice slowing of hair loss, and the appearance of new hair by themselves.

The evaluation of hair re-growth was mainly performed by three different dermatologists by visual inspection using clinical photographs. Therefore, a sophisticated analysis and accurate localization procedures such as using macrophotographs and tattoos were not fully performed. Moreover, our study was not controlled as a placebo group to compare the subjects taking finasteride was not enrolled. Although these biases may leave a room for reliability in our study, most of the patients taking finasteride 1.25mg daily showed remarkable improvement within 4 months of therapy, which suggests that DHT is a critical cause of androgenetic alopecia, and finasteride is an effective new material with few side effects.

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