Efficacy and Safety of 3% Minoxidil versus Combined 3% Minoxidil / 0.1% Finasteride in Male Pattern Hair Loss: A Randomized, Double-Blind, Comparative Study

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Background: *Topical minoxidil and oral finasteride have been used to treat men with androgenetic alopecia (AGA). There are concerns about side effects of oral finasteride especially erectile dysfunction.*
Objective: *To compare the efficacy and safety of the 24 weeks application of 3% minoxidil lotion (MNX) versus combined 3% minoxidil and 0.1% finasteride lotion (MFX) in men with AGA.*
Material and Method: *Forty men with AGA were randomized treated with MNX or MFX. Efficacy was evaluated by hair counts and global photographic assessment. Safety assessment was performed by history and physical examination.*
Results: *At week 24, hair counts were increased from baseline in both groups. However, paired t-test revealed statistical difference only in MFX group (p = 0.044). Unpaired t-test revealed no statistical difference between two groups with respect to change of hair counts at 24 weeks from baseline (p = 0.503). MFX showed significantly higher efficacy than MNX by global photographic assessment (p = 0.003). There was no significant difference in side effects between both groups.*
Conclusion: *Although change of hair counts was not statistically different between two groups, global photographic assessment showed significantly greater improvement in the MFX group than the MNX group. There was no sexual side effect. MFX may be a safe and effective treatment option.*

Keywords: *Topical finasteride, Topical minoxidil, Androgenetic alopecia, Male pattern hair loss*

J Med Assoc Thai 2012; 95 (10): 1312-6
Full text. e-Journal: *http://jmat.mat.or.th*

Androgenetic alopecia (AGA) is the common baldness in men. Currently, only oral finasteride and topical minoxidil are FDA-approved for the treatment of AGA in men[1]. The side effects of oral finasteride include erectile dysfunction, gynecomastia, and loss of libido[2]. Persistent sexual side effects were also reported[3]. Topical finasteride has shown some benefits for AGA especially in Asian men[4-7]. In Thailand, many doctors use the combination of minoxidil and finasteride lotion. The author performed the present study to compare minoxidil lotion versus combined minoxidil and finasteride lotion.

Material and Method

Patient population

Forty men with mild to moderate androgenetic alopecia (III vertex, IV, V modified Norwood-Hamilton classification) were enrolled in the present study. None of them used any systemic or topical drugs for hair loss within six months.

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Study design

The present study was approved by the Ethics Committee of Mae Fah Luang University. Patients were randomly assigned treatment with 3% minoxidil lotion (MNX) or combined 3% minoxidil and 0.1% finasteride lotion (MFX). Lotions were applied twice daily. Follow-up visits were scheduled every four weeks.

Efficacy assessment

The primary endpoint was the change in hair counts at the end of 24 weeks from baseline. The secondary endpoint was the score judged from global photographs by three doctors blinded to the treatment.

Hair count

Hairs were measured within 1-cm diameter circular areas by videodermoscopy. In order to analyze hair count, a clipped area of vertex was selected. A line was drawn from left pinna, passing through the vertex,

to the right pinna. Then, the author cut a 1-cm diameter circular hole at the end of the rectangular plastic template with the fixed length from a midpoint between eyebrows to the vertex. The individual template was created at the first visit. At each subsequent visit (every 4 weeks), the same area was identified and hairs were clipped. In the present study, tattoos were not used to mark the target area. The author measured hair counts twice and used the mean to evaluate the efficacy.

Global photographic assessment

Global photographs were taken using a digital camera. A panel of three doctors who were blinded to the treatment conducted clinical assessments using 7-point scale, greatly decreased (-3), moderately decreased (-2), slightly decreased (-1), no change (0), slightly increased (+1), moderately increased (+2) and greatly increased (+3).

Statistical analysis

The significances of changes in hair density from baseline were performed using the paired t-test. The significances of changes between MNX and MFX were performed using the unpaired t-test. Differences of global photographic assessment were analyzed by the unpaired t-test.

P-values of less than 0.05 were considered statistically significant.

Results

Among 40 enrolled patients, 20 patients in each group, 33 (82.5%) patients completed the present study. Seven patients (4 = MNX, 3 = MFX) dropped out due to the flood disaster in Bangkok in 2011.

Demography

Subject demographics are summarized in Table 1. Differences in baseline characteristics of both groups were not statistically significant.

Hair count

At initial visits, mean hair counts in MFX and MNX groups were 58.09 ± 13.39 and 62.41 ± 15.49 respectively (Table 2). Both groups demonstrated increased hair counts from baseline during the present study. After 24 weeks, hair count in the MFX group was 62.91 ± 13.43 and was significantly different from baseline (p = 0.044, Table 3). Hair count in the MNX

Table 1. Demographic characteristics at baseline

	MFX		MNX		p-value
	n (n = 17)	%	n (n = 16)	%	
Age (year)	34.18 ± 7.04 (27-49)	-	34.50 ± 5.18 (27-46)	-	0.882+
Onset of disease(year)	7.47 ± 6.04 (1-20)	-	5.06 ± 3.34 (1-11)	-	0.166+
Hair count	58.09 ± 13.39	-	62.41 ± 15.49	-	0.397+
Stage of AGA					0.601*
Total	17	51.52	16	48.48	
3V	14	82.35	15	93.75	
4	3	17.65	1	6.25	
5	-	-	-	-	
Family history of AGA					0.870*
No history	8	47.06	5	31.25	
Father history	4	23.53	5	31.25	
Mother history	1	5.88	-	-	
Brother history	2	11.76	2	12.50	
Father and mother	1	5.88	1	6.25	
Father and brother	1	5.88	3	18.75	
Mother and brother	-	-	-	-	
Past treatment					0.259*
No	10	58.82	13	81.25	
Yes	7	41.18	3	18.75	

+ Unpaired t-test presented by mean ± SD (min-max)

* Fisher's exact test

group was 65.31 ± 18.91 and was not significantly different from baseline (p = 0.114, Table 3). The mean change in hair counts after 24 weeks was not statistically different in the MFX group compared with the MNX group (p = 0.503, Table 2).

Global photographic assessment

Mean scores awarded by three doctors using 7-point scale at six months after treatments were 1.84 ± 0.79 and 1.02 ± 0.69 in MFX and MNX groups respectively (Table 4). There was statistical difference between these groups (p = 0.003).

Safety assessment

Four of 17 subjects (23.53%) in MFX and six of 16 (37.5%) in MNX groups experienced contact dermatitis. There were no statistical differences between these groups by Fisher's exact test. There was no sexual side effect in either group.

Discussion

Minoxidil solution was approved for men by the FDA in 1988. The exact mechanism is still unclear. Adverse effects are mainly dermatologic[1]. Scalp irritation, including dryness, scaling and itching may occur. Oral finasteride has been used for the treatment of male AGA since 1997. It is a potent and highly sensitive selective 5α-reductase type-2 inhibitor[8]. The side effects include decreased libido in 1.8% of the recipients vs. 1.3% in the placebo group, erectile dysfunction in 1.3% of the recipients vs. 0.7% in the placebo group and decreased ejaculation volume in 0.8% of the recipients vs. 0.4% in the placebo group[8,9]. The sexual side effects are usually reversible. However, there were some reports of persistence sexual-related problems[3]. The Medicines and Healthcare Products Regulatory Agency of the United Kingdom and the Swedish Medical Products Agency have both updated their patient information leaflets to include a statement that "persistence of erectile dysfunction after discontinuation of treatment with Propecia has been reported in post-marketing use"[3].

Efficacies of topical finasteride have been reported. In 1997, 0.005% finasteride solution was used to treat male AGA[7]. Charuwichitratana et al demonstrated that 0.1% finasteride solution seemed to have beneficial effects on male AGA[4]. A double-blind, placebo controlled, randomized study in 50 men showed that 0.5% finasteride lotion increased hair count and global photographic assessment at six months[5]. 1% finasteride gel and oral finasteride 1 mg/day were shown to have similar therapeutic effects[6]. The author conducted the randomized, double-blind trial to evaluate minoxidil lotion versus combined minoxidil and finasteride lotion.

In the present study, the author found that change in hair count of MFX was more than that of MNX but was not statistically different. The mean

Table 2. Hair count assessment

	MFX (n = 17)	MNX (n = 16)
Baseline	58.09 ± 13.39	62.41 ± 15.49
Week 12	65.26 ± 14.77	67.59 ± 17.18
Week 24	62.91 ± 13.43	65.31 ± 18.91
Week 24-baseline*	4.82 ± 9.12	2.91 ± 6.93

* Unpaired t-test. There were no significant differences between MFX and MNX groups (p = 0.503)

Table 4. Global photographic assessment score

	Mean ± SD	
	MFX	MNX
Doctor 1	2.06 ± 1.03	1.75 ± 1.13
Doctor 2	1.41 ± 0.87	0.44 ± 0.63
Doctor 3	2.06 ± 1.03	0.88 ± 0.96
Total+	1.84 ± 0.79	1.02 ± 0.69

+ Unpaired t-test, statistically significant difference (p = 0.003)

Table 3. Hair count change between baseline and week 24

	MED	Mean ± SD	Paired dif.	p-value
Week 24-baseline	MFX (n = 17)	62.91 ± 13.43 58.09 ± 13.39	4.82 ± 9.12	0.044*
	MNX (n = 16)	62.41 ± 15.49 65.31 ± 18.91	2.91 ± 6.93	0.114

Paired t-test
MED = medication
* Statistically significant difference

scores for the global photographic assessment by three doctors demonstrated significantly greater efficacy for MFX compared with the MNX group. Therefore, MFX seemed to be more efficacious than MNX. Reduction of hair counts in both groups after three months might be related to a hair life cycle (Table 2). The occurrences of contact dermatitis were similar in both groups. The incidences were high because the author included all clinical manifestation such as pruritus without a rash. These symptoms were minor and did not preclude patients from continuing the present study. The author also noted that reports of absence of family history of AGA in Thai men in the present study (30-50%) were higher than other studies (10-30%)[10,11].

In conclusion, MFX shows good benefits without sexual problems. It is a promising treatment for male AGA. The author recommends further study with higher concentration of finasteride, greater number of patients and longer follow-up periods.

Acknowledgement

The present study was supported by the research fund of Dermatological Society of Thailand. The author wants to thank Professor Somyot Charuwichitratana, MD for his valuable suggestions and Assistant Professor Puwat Charukamnoetkanok, MD for his English review.

Potential conflicts of interest

None.

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การเปรียบเทียบประสิทธิภาพและผลข้างเคียงระหว่างไมนอกซิดิลโลชั่นร้อยละ 3 กับฟินาสเทอไรด์ร้อยละ 0.1 ที่ผสม ไมนอกซิดิลโลชั่นร้อยละ 3: การศึกษาแบบสุ่มและปกปิด 2 ทาง

ชูชัย ตั้งเลิศสัมพันธ์

ภูมิหลัง: *ปัจจุบันมีการใช้ไมนอกซิดิลรูปแบบทาและฟินาสเทอไรด์รูปแบบรับประทานในการรักษาโรคผมบางแบบพันธุกรรม และฮอร์โมนเพศชาย (androgenetic alopecia, AGA) เรื่องผลข้างเคียงของฟินาสเทอไรด์รูปแบบรับประทานบางอย่างยังเป็นปัญหาที่สำคัญโดยเฉพาะเกี่ยวกับเรื่องสมรรถภาพทางเพศ*

วัตถุประสงค์: *เพื่อเปรียบเทียบประสิทธิภาพและผลข้างเคียงระหว่างไมนอกซิดิลโลชั่น (MNX) ร้อยละ 3 กับฟินาสเทอไรด์ร้อยละ 0.1 ที่ผสมไมนอกซิดิลโลชั่น (MFX) ร้อยละ 3 หลังการรักษา AGA ในเพศชายเมื่อครบ 24 สัปดาห์*

วัสดุและวิธีการ: *ใช้วิธีสุ่มเพศชายที่เป็น AGA จำนวน 40 คน ให้ได้รับ MNX หรือ MFX ประเมินผลจากการวัดจำนวนผม และภาพถ่ายโดยรวม ส่วนผลข้างเคียงประเมินจากการซักประวัติและตรวจร่างกาย*

ผลการศึกษา: *ที่ 24 สัปดาห์พบว่าจำนวนเส้นผมเพิ่มขึ้นจากก่อนการรักษาทั้งสองกลุ่ม แต่กลุ่มที่ได้รับ MFX แตกต่างอย่างมีนัยสำคัญทางสถิติ ($p = 0.044$) แต่เมื่อเปรียบเทียบระหว่างสองกลุ่มพบว่าไม่มีความแตกต่างอย่างมีนัยสำคัญทางสถิติ ($p = 0.503$) ในกลุ่ม MFX มีคะแนนภาพถ่ายโดยรวมสูงกว่ากลุ่ม MNX อย่างมีนัยสำคัญทางสถิติ ($p = 0.003$) โดยทั้งสองกลุ่มไม่มีความแตกต่างกันในเรื่องผลข้างเคียง*

สรุป: *ถึงแม้ว่าทั้งสองกลุ่มไม่มีความแตกต่างกันอย่างมีนัยสำคัญทางสถิติในเรื่องจำนวนของเส้นผมที่นับได้ แต่คะแนนที่ได้จากการประเมินภาพถ่ายโดยรวมในกลุ่ม MFX สูงกว่าอย่างมีนัยสำคัญทางสถิติและไม่มีผลข้างเคียงที่เกี่ยวกับเรื่องสมรรถภาพทางเพศ ดังนั้น MFX จึงอาจเป็นอีกทางเลือกหนึ่งที่ดีและปลอดภัยสำหรับ AGA ในเพศชาย*