Treatment of Eyebrow Hypotrichosis with 1% Minoxidil Lotion: A Prospective, Randomized, Double-Blind, Placebo-Controlled Trial

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Background: Although there is no standard treatment of eyebrow hypotrichosis, many physicians have been prescribing minoxidil lotion. We demonstrated in the previous study that 2% minoxidil lotion was a safe and effective treatment for eyebrow hypotrichosis.

Objective: The aim of the present study is to determine the efficacy and safety of 1% minoxidil lotion compared to placebo for eyebrow enhancement.

Material and Method: A total of 42 subjects (18-60 years old) were randomized to apply 1% minoxidil on one side of eyebrow and placebo on the other side. Efficacy and side effects were evaluated every 4 weeks for 16 weeks.

Results: Forty subjects (95%) completed this 16-week study. At week 16, 1% minoxidil was significantly superior to placebo for global photographic assessment, eyebrow diameter, eyebrow hair count, and patient’s satisfaction. There was no difference in side effects between two groups.

Conclusion: Our study showed that 1% minoxidil was a well-tolerated and effective treatment for eyebrow hypotrichosis.

Keywords: eyebrow, hypotrichosis, minoxidil, placebos, therapy

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Eyebrow hair serves many important biologic function including sensory transmission and prevention from the element(1). It also has social and aesthetic functions. US FDA (Food and Drug Administration) approved 2-5% minoxidil for the treatment of androgenetic alopecia (AGA) in men and women. The 1% minoxidil solution was demonstrated to be effective and well tolerated in the treatment of AGA among Japanese women(2). We showed in the previous study that 2% minoxidil lotion was superior to placebo in eyebrow enhancement(3). In the present study, we compared the efficacy and safety of 1% minoxidil to placebo for eyebrow hypotrichosis.

Material and Method
The present study was approved by the Ethics Committee of Mae Fah Luang University (ClinicalTrial.gov identifier: NCT01924000). Men and women aged 18-60 years with eyebrow hypotrichosis who were otherwise in good health were enrolled. Subjects were excluded if they had severe seborrheic dermatitis, diseases of scalp or eyebrow, previous treatments of hair or eyebrow during the past 6 months and serious medical conditions.

Study design
Forty-two subjects were randomized to apply 1% minoxidil lotion on one eyebrow and placebo on the other side two times daily for 16 weeks. The primary end point for efficacy assessment was the change in global photographic scores from baseline. The secondary endpoints were the changes in eyebrow diameter, hair number, and subject’s satisfaction. Side effects were also monitored. Subjects had follow-up visit every 4 weeks.

Efficacy evaluation
Global photographic assessment was performed by taking photographs (Visia; Canfield Scientific, NJ) at baseline and during each visit. Three physicians who were blinded to the treatment...
conducted clinical assessment using a 7-point scale: significantly worse (-3), moderately worse (-2), minimally worse (-1), no change(0), minimally improved (+1), moderately improved (+2), and significantly improved (+3)⁴⁹.

Hair count and diameter were measured within 1-cm diameter circular areas using Folliscope (LeadM Corp, Seoul, South Korea). The landmark for measurement was the vertical line drawn up from the mid-pupil. Eyebrow diameter was evaluated by measuring every eyebrow hair and the calculating for mean diameter. Eyebrow count was done by counting every hair.

Subject’s satisfaction was evaluated by providing photographs at baseline and week 16. They evaluated the photos using 7-point scale as global photographic scores.

Safety evaluation
Subjects were assessed for any symptom or sign of dermatitis-rated as mild, moderate, or severe.

**Statistical analysis**
Comparison of the change in global photographic scores between two groups was calculated by Wilcoxon matched-pairs signed ranks test. Paired t-test was used to compare diameter and number of eyebrow between baseline and post-treatment of each drug. Changes from baseline of minoxidil and placebo groups were compared using paired t-test. Subject’s satisfaction between two groups was also compared using Wilcoxon matched-pairs signed ranks test. In term of adverse events, the number of patients were analyzed by using McNemar test for significant change. Determination of P value less than 0.05 indicated significant differences.

**Results**

**Baseline characteristics**
Patient demographic features at baseline were shown in Table1.

**Global photographic scores**
The change of the score from baseline at week 16 showed that results in the 1% minoxidil group (1.12

<table>
<thead>
<tr>
<th>Baseline</th>
<th>Week 16</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="1% Minoxidil" /></td>
<td><img src="image2" alt="Week 16" /></td>
</tr>
<tr>
<td><img src="image3" alt="Placebo" /></td>
<td><img src="image4" alt="Placebo" /></td>
</tr>
</tbody>
</table>

Fig. 1 Eyebrow pictures comparing between baseline and 16 weeks after treated by both solutions (same subject).
Hair diameter and numbers

At week 16, the changes from baseline of eyebrow hair diameter reached statistically significance in both 1% minoxidil group (5.17±6.22 μm, \( p<0.001 \)) and placebo group (2.55±5.87 μm, \( p = 0.009 \)). Likewise, the changes from baseline of eyebrow hair count also reached statistically significance in both 1% minoxidil group (10.45±14.97, \( p<0.001 \)) and placebo group (8.08±10.59, \( p<0.001 \)). Comparing the two groups at week 16, the enhancement of eyebrow hair diameter and number in 1% topical minoxidil group from baseline was statistically significantly superior to the placebo group (2.23±4.80 μm, \( p = 0.006 \) for diameter and 4.18±12.87, \( p = 0.047 \) for number). Figure 2 showed changes of eyebrow hair count.

Patient satisfaction

The minoxidil group score (1.93±1.07) is significantly higher than the placebo group (1.05±0.86, \( p<0.001 \)).

Side effects

Main adverse reactions were skin symptoms including temporarily mild itching and burning in the treatment areas. The incidence of adverse events was 22.5% (9/40) in 1% minoxidil group and 15% (6/40) in placebo group. Statistically significant difference was not reached between two groups (McNemar test for significant change; \( p = 0.250 \)). Six subjects developed adverse reaction on both sides of treatment areas due to vehicles. Three subjects developed side effects from only 1% topical minoxidil-treated side.

Discussion

Patients with eyebrow hypotrichosis should be screened for underlying conditions. Idiopathic eyebrow loss can be treated with topical minoxidil or bimatoprost\(^{3,5,6}\). We demonstrated in the previous study that 2% minoxidil achieved significantly better results in all measured outcomes compared to placebo\(^3\). The significant difference began at week 8 and throughout the rest of the study. In this present

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### Table 1. Subject characteristics of patients at baseline (Total, \( n = 40 \))

<table>
<thead>
<tr>
<th>Subject characteristics</th>
<th>Number (Percentage)</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td>Number (Percentage)</td>
<td>( p )</td>
</tr>
<tr>
<td>Female</td>
<td>27 (67.50)</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>13 (32.50)</td>
<td></td>
</tr>
<tr>
<td>Age (mean±SD)</td>
<td>30.73±7.65 years</td>
<td></td>
</tr>
<tr>
<td>Mean and SD of eyebrow hair diameter (μm)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1% Minoxidil</td>
<td>71.78±7.57</td>
<td>0.617</td>
</tr>
<tr>
<td>Placebo</td>
<td>72.18±8.57</td>
<td></td>
</tr>
<tr>
<td>Mean and SD of eyebrow number (hair)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1% Minoxidil</td>
<td>67.10±17.03</td>
<td>0.369</td>
</tr>
<tr>
<td>Placebo</td>
<td>65.30±16.12</td>
<td></td>
</tr>
</tbody>
</table>

SD, standard deviation
study, the significant changes of all parameters (global photographic scores, eyebrow diameter and number) began at week 16. These results indicated an earlier response to treatment with 2% minoxidil. It is possible that increasing concentration of minoxidil yields earlier remarkable result. Interestingly, the significant changes from baseline in all parameters were also noted in placebo group. This might reflect the natural hair cycle of eyebrows. Another possible explanation was that applying lotion can massage hair and stimulate hair growth. More studies are needed to test these hypothesis. This findings show that it is important to include placebo group in clinical trials.

Adverse effects of topical minoxidil are mainly dermatologic(7). In 2012, there was one case report that central serous chorioretinopathy was potentially related to an 8 month topical minoxidil for AGA(6). We have not seen this problem in our studies or practices treating AGA or eyebrow hypotrichosis. Minoxidil lotion is still approved for over-the-counter usage in the USA. However, ophthalmologist should be consulted, if the patient has any eye problems. Twenty two point five percent (9/40) of patients developed side effects in the present study (1% minoxidil) compared to 12.82% (5/30) in the previous study (2% minoxidil). This could be due to different sample batches. However, the percentage of side effect was not significantly different from placebo group. In conclusion, 1% minoxidil is a safe and effective treatment for eyebrow hypotrichosis.

What is already known to this topic?
In the previous study, we demonstrated that 2% minoxidil lotion was a safe and effective treatment for eyebrow hypotrichosis.

What this study adds?
In the present study, we show that 1% minoxidil lotion is a safe and effective treatment for eyebrow hypotrichosis.

Acknowledgment
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Potential conflict of interest
None.

References
การรักษาภาวะคิ้วบางโดยการใช้ไมนอกซิดิลโคลน 1% : การศึกษาแบบสุ่ม ปรากฏ 2 ทางและเทียบกับยาหลอก

นันท์ วรพันธุ์พงศ์, ชูชัย ตั้งเลิศสัมพันธ์

ภูมิหลัง: ปัจจุบันยังไม่มียาที่เป็นมาตรฐานในการรักษาภาวะคิ้วบาง ผู้วิจัยได้เคยทดลองการใช้ยาไมนอกซิดิลโคลน 2% ที่มีผลในการรักษาภาวะคิ้วบางได้ดีกว่ายาหลอก

วัตถุประสงค์: เพื่อเปรียบเทียบประสิทธิผลและความปลอดภัยของ 1% ไมนอกซิดิลโคลนกับยาหลอกในการรักษาภาวะคิ้วบาง

วัสดุและวิธีการ: ผู้เข้าร่วมวิจัยจำนวน 42 ราย (อายุ 18-60 ปี) ได้รับการสุ่มเพื่อรับยาไมนอกซิดิลโคลน 1% ทาข้างหนึ่ง และยาหลอกทางข้างอื่น ผู้วิจัยได้ประเมินผลการรักษาและผลข้างเคียงจากการรักษาทุก 4 สัปดาห์ เป็นเวลา 16 สัปดาห์

ผลการศึกษา: ผู้เข้าร่วมวิจัยจำนวน 40 ราย (95%) เข้าร่วมจนกระทั่งสิ้นสุดงานวิจัย 16 สัปดาห์ ในสัปดาห์ที่ 16 พบว่า คิ้วข้างที่ใช้ยาไมนอกซิดิลโคลน 1% ให้ผลดีกว่าข้างที่ใช้ยาหลอก ตามที่ประเมินผลการเปลี่ยนแปลงของภาพถ่ายโดยรวม, เส้นผ่านศูนย์กลางและจำนวนของขนที่เพิ่มขึ้น และคะแนนความพึงพอใจที่สูงกว่าของข้างที่ใช้ยาไมนอกซิดิลโคลน มีนัยสำคัญทางสถิติ ในข้างหลังซึ่งมีผลสถิติในแต่ละกลุ่ม ไม่แตกต่างกันระหว่าง 2 กลุ่ม

สรุป: ไม นอกจากซิดิลโคลน 1% มีประสิทธิภาพและความปลอดภัยในการรักษาภาวะคิ้วบาง