



## The efficacy and safety of topical 2% minoxidil solution in longitudinal nail growth

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### Abstract

The nail unit is a dynamic structure that remains mitotically active throughout life. Growth in the normal state occurs in a linear. Some nail diseases can significantly be improved when they accelerated the rate of growth such as onychomycosis (Geyer, Onumah, Uyttendaele & Scher, 2004). Topical minoxidil is one of the drugs that can increase the growth rate of the nail (Aiempakit, Geater, Limtong & Nicoletti, 2017; Suchonwanit, Thammarucha & Leerunyakul, 2019). It may stimulate the length of the nail; however, the main mechanism, preparation, and proper concentration are still unknown. The main objective of this study is to evaluate the nail growth rates of 2% minoxidil at week 4. Twenty participants were randomly divided into 2 groups. In the first group, 2% minoxidil solutions were applied twice daily to all fingernails while the other group has applied the placebo. The nail length was measured at the baseline and 4 weeks after treatment. All fingernails were photographed and checked for side effects by a dermatologist. The result of this study shows that the mean nail growth of 2% minoxidil is longer than the placebo but could not reach statistical significance, except in the right middle finger and right little finger. The mean nail length of the right middle finger and right little finger was  $3.92 \pm 0.60$  mm/month ( $P= 0.015$ ) and  $3.51 \pm 0.54$  mm/month ( $P= 0.013$ ), respectively.

**Keywords:** nail, nail growth, minoxidil, accelerate nail growth

### 1. Introduction

The nail is an organ that covers the distal of the fingers. It has many functions such as protection of the fingertips, tactile sensation, and thermoregulation via the glomus body (Haneke, 2014). Because of its structure and functionality, abnormalities of the nail can affect functional and cosmetic outcomes. It grows continuously non-dependent through life, by which the nail of the middle finger of the dominant hand grows the fastest (Haneke, 2015). Its growth rate is determined by the proliferative capacity of the nail matrix. Many factors are known to influence the speed of nail growth. Some nail diseases can significantly be improved when they accelerated the rate of growth such as onychomycosis. Fungal infection of the nail is a disease of which symptoms are discoloration of the nail, separation of the nail plate from the nail bed, and thickening of the nail. In other words, rapid growth and shedding of the nail plate help to eliminate the colony of fungus that settle in the nail.

In the past, many studies have been conducted to find a drug that can be used to treat various diseases that cause the nails to grow slowly. Minoxidil is a drug that FDA approved for the treatment of androgenetic alopecia (Strazzulla et al., 2018). The mechanism by which minoxidil promotes hair growth is still not completely understood. It is converted to minoxidil sulfate, an active metabolite that opens ATP-sensitive potassium channels localized on the smooth muscle cells of the peripheral artery, leading to a vasodilatory effect (Suchonwanit et al., 2019). The nail organ and hair follicle are related skin appendages and have more in common embryonic structure, and previous research showed that topical minoxidil can stimulate nail growth with increased growth beginning in the first week of application (Aiempakit et al., 2017). Topical minoxidil is one of the drugs that can increase the growth rate of the nail. It may stimulate the length of the nail; however, the main mechanism, preparation, and proper concentration are still unknown. Therefore, the main purpose of the research is to evaluate the efficacy and safety of 2 % topical minoxidil in longitudinal nail growth.



## 2. Objectives

- To evaluate the efficacy of 2 % topical minoxidil in longitudinal nail growth after 4 weeks of treatment
- To identify possible side effects such as systemic reactions, which were a change in blood pressure and pulse rate; cutaneous adverse reactions, including allergic or irritant contact dermatitis; nail color or surface change, and hypertrichosis.

## 3. Materials and Methods

### Study design

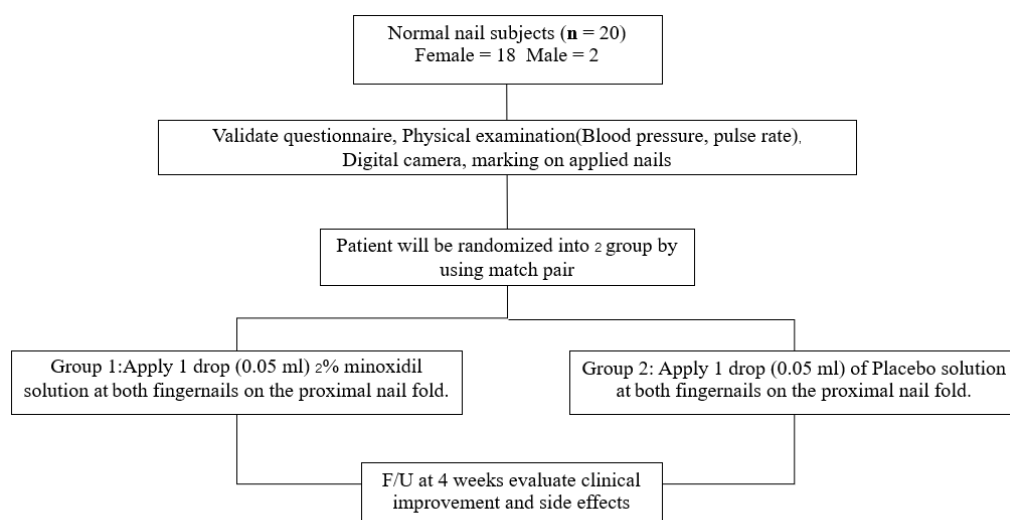
The study was approved by The Human Research Ethics Committee of Thammasat University in accordance with the Declaration of Helsinki, The Belmont Report, CIOMS Guidelines, and the International Practice (ICH-GCP) and was registered at [clinicaltrials.in.th](http://clinicaltrials.in.th). The research was a randomized controlled trial. The protocol was conducted from December 2020 to January 2021 at the Dermatology Clinic, Benjakitti Park Hospital, Bangkok, Thailand.

### Participants

Twenty participants (2 males and 18 females, aged between 16-48 years) were enrolled in the study. The inclusion criteria were healthy participants. The participants who were pregnant, lactating, or had allergies to alcohol or minoxidil were excluded.

### Intervention

The participants were divided into 2 groups by blocked randomization. Each group of participants was instructed to apply 1 drop (0.05 ml) of placebo and 2% minoxidil to both fingernails on the proximal nail fold. The placebo solution was compound with propylene glycol and 60% ethyl alcohol. Using cotton wool rubbed until the solution was absorbed and leave it for at least 2 hours. The dosage was approximately 20 mg/ml for 2% minoxidil. The nail plates were marked by using the nail file at the baseline. The nail length was measured from the deepest edge of a marked line to the proximal nail fold using a digital caliper (Digital Caliper, Mitutoyo, Kawasaki, Japan). The nail length was measured and observed for side effects at week 4 by a single, blinded investigator. Moreover, blood pressure, pulse, and cutaneous side effect were recorded as well. **Figure 1** showed a research procedure.



**Figure 1** Research procedure

[53]



### Outcomes

The primary outcome is to compare the nail growth rates between the 2% minoxidil and placebo at week 4. The secondary outcome is to evaluate the possible adverse cutaneous and systemic side effects.

### Statistical analysis

Statistical analyses were calculated using Stata version 14.0 (College Station, TX, USA). The sample size was calculated using a sample size for a two-sample means test formula. Comparisons of the mean nail growth between the placebo and 2% minoxidil group nails were performed using Independent t-test and Mann-Whitney U test. The P-value < 0.05 was defined as statistically significant.

## 4. Results and Discussion

### 4.1 Participant

Twenty participants were enrolled in the experiment. Eighty-five percent of the participants were right-hand dominant. The remained participants were left-handed. The mean age of the participant was 45 years. The mean age of the 2% minoxidil group was  $47.80 \pm 17.15$  whereas  $42.10 \pm 15.87$  for the placebo group. The age range was between 17 to 69 years old. The underlying diseases of the participant were hypertension, dyslipidemia, and gout. Besides, some participants were taking other supplements. Four participants in the placebo group and two participants in the 2% minoxidil group used calcium, vitamin D, and vitamin C as supplements. Concerning the demographic data, there was also no statistically significant difference between the 2 groups (**Table 1**).

**Table 1** Demographic data

|                          | Placebo     | 2%minoxidil | P-value |
|--------------------------|-------------|-------------|---------|
| <b>Age</b>               | 42.10±15.87 | 47.80±17.15 | 0.450   |
| <b>Sex</b>               |             |             |         |
| <b>Male</b>              | 0 (0.00)    | 2 (20.00)   | 0.474   |
| <b>Female</b>            | 10 (100.00) | 8 (80.00)   |         |
| <b>Hypertension</b>      |             |             | 1.000   |
| <b>Yes</b>               | 0 (0.00)    | 1 (10.00)   |         |
| <b>No</b>                | 10 (100.00) | 9 (90.00)   |         |
| <b>Dyslipidemia</b>      |             |             | 1.000   |
| <b>Yes</b>               | 0 (0.00)    | 1 (10.00)   |         |
| <b>No</b>                | 10 (100.00) | 9 (90.00)   |         |
| <b>Diabetes Mellitus</b> |             |             | 1.000   |
| <b>Yes</b>               | 0 (0.00)    | 0 (0.00)    |         |
| <b>No</b>                | 10 (100.00) | 10 (100.00) |         |
| <b>Other: gout</b>       |             |             | 1.000   |
| <b>Yes</b>               | 0 (0.00)    | 1 (10.00)   |         |
| <b>No</b>                | 10 (100.00) | 9 (90.00)   |         |
| <b>Allergy Drugs</b>     |             |             | 1.000   |
| <b>Yes</b>               | 0 (0.00)    | 1 (10.00)   |         |
| <b>No</b>                | 10 (100.00) | 9 (90.00)   |         |
| <b>Drug/Supplement</b>   |             |             | 0.628   |
| <b>Yes</b>               | 4 (40.00)   | 2 (20.00)   |         |
| <b>No</b>                | 6 (60.00)   | 8 (80.00)   |         |
| <b>Handedness</b>        |             |             | 1.000   |
| <b>Right</b>             | 9 (90.00)   | 8 (80.00)   |         |
| <b>Left</b>              | 1 (10.00)   | 2 (20.00)   |         |



#### 4.2 Nail growth

The nail growth rate of the participants has no statistically significant difference between the 2% minoxidil and placebo groups considering the growth rate of the nail plate. The results of the nail growth showed the mean nail growth rate of the participants who used 2% minoxidil was greater than that of the placebo group on the right middle and little fingers with a statistical significance. The mean growth of the 2% minoxidil group in middle nails was  $3.92 \pm 0.60$  mm/month compared with  $3.22 \pm 0.66$  mm/month in the placebo group ( $P = 0.015$ ). The change in the little finger of the right hand was  $3.51 \pm 0.54$  mm/month, greater than  $2.77 \pm 0.80$  mm/month of the placebo group ( $P = 0.013$ ) as shown in Figures 2 and 3. When looking at the nail growth rate of each finger in all groups, the most increased nail length in the 2% minoxidil group was a middle finger on the right hand ( $3.92 \pm 0.60$ ) that more than the average nail growth from the recent literature that the middle nail growth rate was 3.65 mm/month (Yaemsiri, Hou, Slining & He, 2010). When focused on only 2% minoxidil group. The ratio of the dominant hand was 8:2 (right: left). The result showed that the right hand has a greater nail growth rate than the left hand.

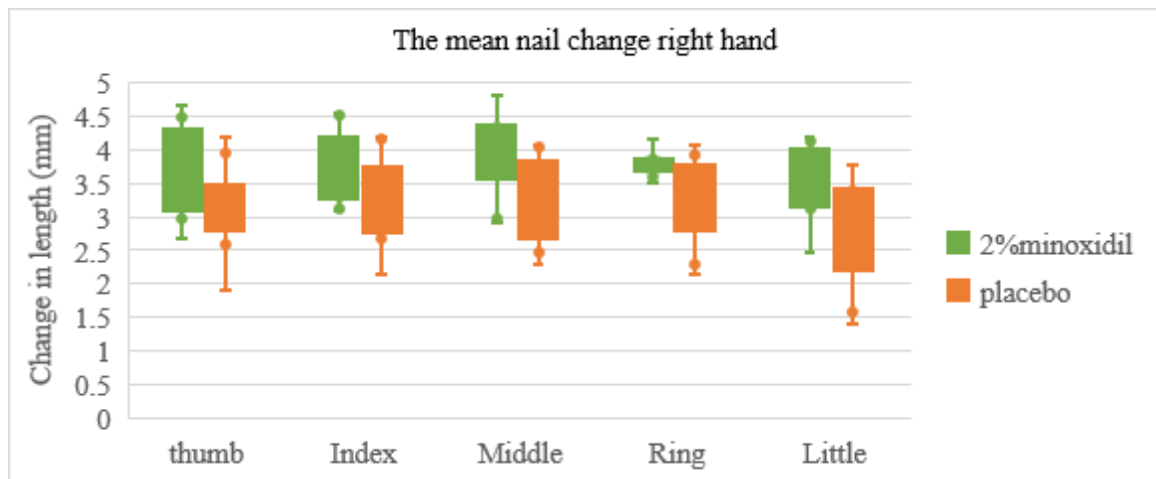


Figure 2 The mean change in length of the nails on the right hand

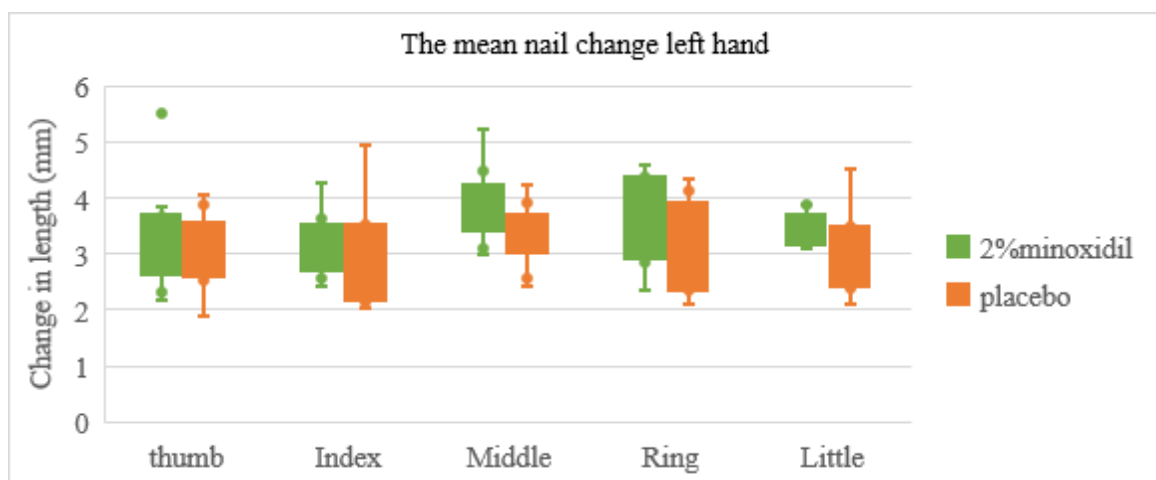


Figure 3 The mean change in length of the nails on the left hand



In the secondary outcome, both groups of the participants showed no change in pulse rate and systolic/diastolic blood pressure in month 1 compared with the baseline. There was no cutaneous side effect for 1 month (**Table 2**).

**Table 2** Systemic change in 2% minoxidil group

|                 | Mean  | diff | [95% Conf. Interval] |          | P-value |
|-----------------|-------|------|----------------------|----------|---------|
| <b>Systolic</b> |       |      |                      |          |         |
| baseline        | 117.8 |      |                      |          |         |
| 1 month         | 117.6 | -0.2 | -11.52933            | 11.92933 | 0.0386  |
| <b>Pulse</b>    |       |      |                      |          |         |
| baseline        | 75.7  |      |                      |          |         |
| 1 month         | 78.6  | 2.9  | -6.47599             | .6759896 | -1.8345 |

#### 4.3 Discussion

The result from this study showed that a 2% topical minoxidil solution could stimulate nail growth. It made the nail of the right little finger grow faster than the placebo with a statistical significance in 1 month. However, the statistical result shows no significance. It may be from the lower concentration of the minoxidil solution and the volume per droplet. Moreover, due to the Covid19 pandemic, the government suggested people always wash their hands. So, the hand sanitizer may wash out the solution that the participant applied to the nail fold before its absorbed. Another hypothesis that the 2% minoxidil did not significantly increase the nail growth is due to the limited cell response of stem cells in the proximal nail fold. It means that when the stem cell at proximal nail fold was stimulated by the minoxidil to the maximum level. The growth rate will be constantly stable. We detected an increase in nail growth rate in all fingers by using topical minoxidil. Due to the unknown exactly mechanism of minoxidil for hair growth. It was founded topical minoxidil could upregulate the VEGF (Yano, Brown & Detmar, 2001) or nitric oxide (Yum et al., 2018). It may act by activation of the ATP-sensitive potassium (KATP) channels to relax vascular smooth muscle (Farrokhi, Gashti, Hoormand, Bakhtiarian & Habibi, 2019), decrease blood pressure, and increase blood flow (Gümüş, Ödemiş, Yılmaz & Tuncer, 2012). So, the greater rate of nail growth might be the result of cutaneous blood flow.

When compared the result with the previous literature. Aiempanakit found that 5% minoxidil could stimulate nail growth. The mean growth nails were 4.27 mm (Aiempanakit et al., 2017). So, the growth rate of fingernails depended on the concentration of minoxidil solution. Moreover, the mean nail growth rate for fingernails was 3.47 mm/month, this study was conducted on 22 young adults. From this study, the nail growth rate from the first to the fifth finger were 3.55, 3.54, 3.65, 3.42, and 3.08 mm/month (Yaemsiri et al., 2010), respectively. This study showed the same result that the longest growth of the nails was middle fingernails. Both groups showed that the nail growth rate of the right hand was greater than the other hand. From the previous knowledge that the nail on handedness or dominant hand grows faster than the other side. However, this study observed the nail length at only 4 weeks after treatment. The growth rate might be more significant if the treatment was applied for a longer duration.

#### 5. Conclusion

Application of the 2% topical minoxidil solution to the proximal fold of the right little finger results in increased nail growth. No adverse effects were found from using the minoxidil solution. This study could be useful for patients who have nail diseases. Moreover, this study could explain the limited cell response of stem cells in the proximal nail fold.

Further research with larger samples and prolonged treatment is needed to explore the mechanism of action of minoxidil in accelerated nail growth.



## 6. Acknowledgements

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