Original Article

Comparison of The Efficacy and Safety of Topical 2% Minoxidil and 5% Minoxidil Solution in Fingernail Growth Rate

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Abstract

Introduction: Nails are one of the organs which have activity throughout human life. Topical 2% minoxidil has been shown to accelerate nail development by being applied topically on the nails. However, the main mechanism to such effect remains unknown. Moreover, the appropriate preparation and concentration of minoxidil still have not yet been identified. It has been postulated that the higher concentration of minoxidil could accelerate the nail growth more than the 2%, lower concentration.

Objectives: To compare the efficacy and safety of fingernail growth rate between topical 5% minoxidil solution and topical 2% minoxidil solution.

Methods: Thirty participants were randomized into 3 groups: 2% minoxidil, 5% minoxidil, and placebo. Each group of participants was instructed to apply the solution twice daily on the 2nd and 4th finger on both hands. Nail lengths were measured at weeks 4 and 8 by using a digital caliper. Possible side effects were assessed by a dermatologist.

Results: The mean nail growth rate of the 2% minoxidil application (3.32 ± 0.63 mm) was greater than the 5% minoxidil application (2.88 ± 0.50 mm) and placebo (2.87 ± 0.08 mm) at week 8 (*p-value* = 0.002). No cutaneous or systemic side effects were observed.

Conclusions: In conclusion, 2% topical minoxidil has shown to stimulate a greater nail growth rate than the 5% topical minoxidil solution. Therefore, 2% topical minoxidil is an adequate concentration for effectively accelerating nail growth rate, without any side effects.

Keywords: Nail, Nail growth, Minoxidil

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Introduction

The nail is a structure that covers the distal part of fingers. It has many functions such as protection of the fingertips, tactile sensation, and thermoregulation via the glomus body (Haneke, 2014). The nail of the middle finger of the dominant hand grows the fastest with the rate of 0.1 mm/day. Whereas, the nail of the little finger grows the slowest. There are many factors that may influence nail growth, such as medications, diseases, and psychological factors. (Geyer, Onumah, Uyttendaele, & Scher, 2004)

In the past, many studies have been conducted to find a drug that can cause the nails to grow faster. However, drugs that affect nail growth in the oral form may have side effects on the body and may interact with drugs that the patient is already taking, so the topical form is used to minimize side effects.

Minoxidil is the medication that has been approved for the treatment of the hair loss.[1] The mechanism for its effect in regrowing hair is not fully understood. It has been postulated that the activated drug affects the ATP-sensitive potassium channels. It opens the potassium channels on the smooth muscle of the arterioles, thus, triggering cell hyperpolarization, which causes vasodilation (Suchonwanit, et al., 2019). In the embryonic stage, the hair follicles and the nail units come from the same origin. Previous research has shown that 2% topical minoxidil can stimulate nail growth (Aiempanakit, et al., 2017). However, it is unknown if increasing the concentration of topical minoxidil would improve the effect of stimulated nail growth. Therefore, in this study, we aimed to evaluate the nail growth rates after applying 2% minoxidil and 5% minoxidil solution.

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 registered at clinicaltrials.in.th. The research was a randomized controlled trial. The protocol was conducted from December 2020 to March 2021 at the Dermatology Clinic, Benjakitti park hospital, Bangkok.

Participants

Thirty participants (4 males and 26 females, aged 18-68 years) were enrolled into the study. The inclusion criteria were participants who have normal nails and age range between 17-70 years old. Participants who were pregnant, lactating, individuals with underlying cutaneous or systemic diseases that can affect nail growth, such as thyroid disease and psoriasis, and participants using medications that can affect nail growth, such as retinoids, chemotherapeutic agents, and Itraconazole were excluded. Participants who had history of allergies to minoxidil were also excluded.

The participants were divided into 3 groups by blocked randomization. Each group of participants was instructed to apply 1 drop (0.05 ml) of the solution (placebo, 2% minoxidil, or 5% minoxidil) to the index and ring finger of both hands on the proximal nail fold. The thumb, middle and little fingernails were not assessed, because they grow at a different rate in comparison with the index and ring fingernails. Solution was applied by using cotton wool and rubbing until the solution was completely absorbed and then, avoiding hand washing for at least 30 minutes afterward. The dosage was approximately 20 milligrams/ml for 2% minoxidil and 50 milligrams/ml for 5% minoxidil. The nail length was measured from the deepest edge of the marked line to the proximal nail fold by using the digital caliper (Mitutoyo, Kawasaki, Japan).

A blinded dermatologist measured the nail length twice and then computed the average. The participants' fingernails were photographed and marked at the baseline. Moreover, examination of blood pressure, pulse rate and cutaneous side effects were recorded. Figure 1 shows the research protocol.

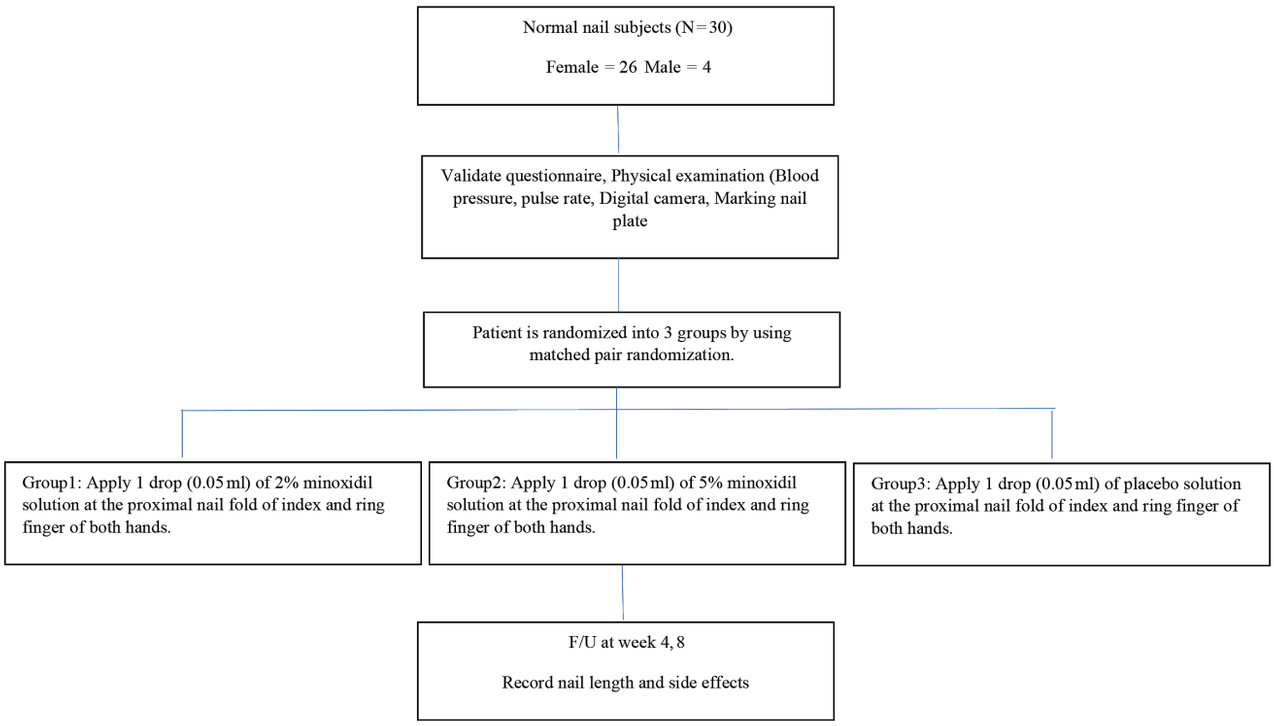

Figure 1 shows the research protocol

Outcomes

The primary outcome was to compare the rate of nail growth between 2% and 5% concentrations of minoxidil for 8 weeks. The secondary outcome was to observe for possible adverse reactions.

Statistical analysis

Statistical analyses were calculated by 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. Quantitative variables were explained by using the mean and standard deviation for continuous variables and number and percentage for categorical variables. Comparison of the mean nail growth rate between the 2% minoxidil, 5% minoxidil, and placebo were performed by using one-way ANOVA, Kruskal-Wallis independent T-test, and Mann-Whitney U test. A *P-value* < 0.05 was defined as statistically significant. Moreover, the paired t-tests were used to compare other continuous variables before and after treatment.

Results

Participants

A total of 30 participants were enrolled into the study. Twenty-six participants (86%) were female. Eighty-two percent of participants were right-hand dominant. The mean age was 41 years. The underlying diseases of the participant were hypertension, dyslipidemia, and gout. Four participants in the placebo group used calcium, vitamin D, and vitamin C. The demographic data in the 2 different groups were not statistically significant. The demographic data is shown in Table 1.

Table 1 Demographic data

	Placebo	2% minoxidil	5%minoxidil	P-value
Age	42.10 + 15.87	47.80 + 17.15	35.80 + 16.80	0.288
Sex				
Male	0.(0.00)	2(20.00)	2(20.00)	0.507
Female	10(100)	8(80.00)	8(80.00)	
Drug/Supplement				0.668
Yes	4(40.00)	2(20.00)	2(20.00)	0.507
No	6(100.00)	8(80.00)	8(80.00)	
Handedness				1.00
Right	9(90.00)	8(80.00)	8(80.00)	
Left	1(10.00)	2(20.00)	2(20.00)	

Nail growth

Before starting the protocol, we marked the measure point on 2nd and 4th fingers on both hands. The measurement of nail length was done at baseline, week 4 and week 8.

The rates of nail growth were compared between the three groups: 2% minoxidil, 5% minoxidil, and placebo group. At four weeks, the mean nail growth rate was 3.58 ± 0.66 mm/month, 3.48 ± 0.65 mm/month, 3.15 ± 0.75 mm/month in 2% minoxidil, 5% minoxidil, and placebo, respectively. The length of nail growth in the 2% minoxidil group was higher than the placebo group with statistical significance (P = 0.019). However, there was no difference between 2% minoxidil and 5% minoxidil. Furthermore, at eight weeks, the mean of nail growth rate in 2% minoxidil group was significantly higher than both placebo and 5% minoxidil (P = <0.001). The average nail growth rate at week 8 of the 2% minoxidil group was 3.32 ± 0.63 mm/month, exceeding other groups, 2.88 ± 0.50 mm/month in the 5% minoxidil group, and 2.87 ± 0.54 mm/month in the placebo group. There was no statistically significant difference between the placebo and 5% minoxidil group. As a result, 2% minoxidil solution has shown to be an adequate concentration to effectively stimulate the nail growth after 4 and 8 weeks of topical application. The mean nail growth rates are shown in Table 2.

No adverse reactions observed during the study in all groups.

Table 2 Comparison of the means of nail growth rate between 2% minoxidil, 5% minoxidil and placebo.

	Placebo (N = 40)	2%minoxidil (N = 40)	5%Minoxidil (N = 40)	P-value
The mean nail growth rate at week 4	3.15 + 0.75	3.58 + 0.66	3.48 + 0.65	0.017
The mean nail growth rate at week 8	2.87 + 0.54	3.32 + 0.63	2.88 + 0.50	<0.001

One-way ANOVA, multiple comparison: Scheffe

Discussion

Currently, topical medications that can stimulate nail growth is understudied. This study showed an increase in nail growth rate on all fingernails after applying topical minoxidil. Both concentrations, 2% and 5% topical minoxidil solutions could stimulate nail growth compared to the placebo, with statistical significance at week 4. In contrast, only 2% minoxidil solution could stimulate nail growth with statistically significant difference from the placebo at week 8. There were no local or systemic side effects observed throughout the study.

We compared the result with the previous literature. Aiempanakit found that 5% minoxidil could stimulate nail growth in the first month (Aiempanakit et al., 2017). The same result was obtained from our research, that 5% minoxidil has a higher nail growth rate than the placebo with statistical significance only in the first 4 weeks.

The mechanism of minoxidil in promoting hair growth remains unknown. It was found that topical minoxidil could upregulate VEGF (Yano, Brown, & Detmar, 2001) or nitric oxide (Yum et al., 2018). It could also activate ATP-sensitive potassium (KATP) channels and relax vascular smooth muscle (Farrokhi, Gashti, Hoormand, Bakhtiarian, & Habibi, 2019), decrease blood pressure, and increase blood flow (Gümüş, Ödemiş, Yılmaz, & Tuncer, 2012). It could be possible that topical minoxidil can accelerate nail growth by increasing cutaneous blood flow to the nail.

With regard to the question of why greater growth rates in 5% minoxidil and 2% minoxidil were detected only in the first month, it could possibly be an autoregulation of nail blood flow in response to different concentrations of minoxidil and with higher concentrations there might have been earlier adaptation of the blood circulation in the hand. Another opinion that may support our result is related to prostaglandin (PGE2) from the minoxidil solution. It was discovered that Minoxidil can increase PGE2 by activating prostaglandin endoperoxide synthase-1 enzyme. (30) PGE2 upregulates genes in the β-catenin pathway of dermal papilla cells. The Dermal papilla are found in the nail matrix at the proximal nail fold. Moreover, wnt-β-catenin signaling is also found at the nail stem cell, which is used in nail plate production. This study could explain the limited cell response of stem cells in the proximal nail fold.

Topical minoxidil is a well-known medication that is commonly used to treat alopecia. Using topical application, instead of oral ingestion, helps to eliminate systemic side effects that could occur such as generalized hair growth. Moreover, the nails and hair follicles similarly share some common structures. Thus, it is possible that minoxidil could possibly increase nail growth just like it increases hair growth. This study has shown that topical minoxidil can effectively stimulate nail growth, even though the effect of minoxidil on nail growth might not be as substantial as stimulating hair growth. This difference in stimulating growth is understandable, as the absorption through the thick keratinized nail is much more difficult than in the scalp or mucosal area. In addition, further studies could be extended to investigate better routes of drug delivery and increased drug absorption. Also, larger patient samples and longer treatment periods could be considered, to identify the mechanism of action of minoxidil in nail growth stimulation. Our study was limited by its small sample size and 2 months application period. Therefore, we recommend larger trials with longer periods of application to see the trend of treatment results.

In conclusion, topical application of both 2% and 5% minoxidil to proximal folds can increase the nail growth. 2% minoxidil can significantly increase the nail growth at both 4 weeks and 8 weeks. Thus, 2% concentration is adequate to stimulate nail growth without inducing any adverse side effects. Hopefully, this study could be useful for patients who have nail disorders and assist them to regain their nails back faster.

References

1. Aiempanakit K, Geater A, Limtong P, Nicoletti K. The use of topical minoxidil to accelerate nail growth: a pilot study. *Int J Dermatol.* 2017;56(7):788-791. doi:10.1111/ijd.13620.
2. Farrokhi M, Gashti MZ, Hoormand M, Bakhtiarian A, Habibi R. Combination therapy profoundly improved skin flap survival by modulating KATP channels and nitric oxide. *Adv Med Sci.* 2019;64(1):117-123. doi:https://doi.org/10.1016/j.advms.2018.08.015.
3. Geyer AS, Onumah N, Uyttendaele H, Scher RK. Modulation of linear nail growth to treat diseases of the nail. *J Am Acad Dermatol.* 2004;50(2):229-234. doi:10.1016/j.jaad.2003.07.011.
4. Gümüş N, Ödemiş Y, Yılmaz S, Tuncer E. Effect of Topically Applied Minoxidil on the Survival of Rat Dorsal Skin Flap. *Aesthetic Plastic Surgery.* 2012;36(6):1382-1386. doi:10.1007/s00266-012-9966-2.
5. Haneke E. Anatomy, biology, physiology and basic pathology of the nail organ. *Hautarzt.* 2014;65(4):282-290. doi:10.1007/s00105-013-2702-2.

6. Haneke E. Anatomy of the nail unit and the nail biopsy. *Semin Cutan Med Surg.* 2015;34(2):95-100. doi:10.12788/j.sder.2015.0143.
7. Strazzulla LC, Wang EHC, Avila L, Lo Sicco K, Brinster N, Christiano AM, Shapiro J. Alopecia areata: An appraisal of new treatment approaches and overview of current therapies. *J Am Acad Dermatol.* 2018;78(1):15-24. doi:10.1016/j.jaad.2017.04.1142.
8. Suchonwanit P, Thammarucha S, Leerunyakul K. Minoxidil and its use in hair disorders: a review. *Drug Des Devel Ther.* 2019;13:2777-2786. doi:10.2147/dddt.S214907.
9. Yaemsiri S, Hou N, Slining MM, He K. Growth rate of human fingernails and toenails in healthy American young adults. *J Eur Acad Dermatol Venereol.* 2010;24(4):420-423. doi:10.1111/j.1468-3083.2009.03426.x.
10. Yano K, Brown LF, Detmar M. Control of hair growth and follicle size by VEGF-mediated angiogenesis. *J Clin Invest.* 2001;107(4): 409-417. doi:10.1172/jci11317.
11. Yum S, Jeong S, Kim D, et al. Minoxidil Induction of VEGF Is Mediated by Inhibition of HIF-Prolyl Hydroxylase. *Int J Mol Sci.* 2018;19(1):53.