

A Pilot Study of the Efficacy in Treatment of Female Pattern Hair Loss using 5% Minoxidil Solution Combined with Oral Chelated Zinc Supplement

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Abstract

Background: Zinc supplement is popular trace element gave to female pattern hair loss (FPHL). But the type of patient, efficacy and side effect in detail of Zinc supplement are not well characterized.

Objective: To determine efficacy and side effect of chelated Zinc in women with FPHL which using 5% minoxidil solution.

Materials and methods: 18 Thai women with FPHL applied 5% topical minoxidil solution twice daily combined with 15 mg oral chelated Zinc for 24 weeks. Then measure growth of hair by global photograph, hair density and hair shaft diameter during 24 weeks of treatment.

Results: All 18 female patients were attached to the study at 24-week follow up visit. The mean age was 47.5 ± 9.7 years (range, 26-61 years). Percentage of increasing in hair density and hair shaft diameter at 24-week follow-up visit after receiving 5% minoxidil solution combined with oral chelated Zinc supplement was 12.2% and 5.5%, respectively. There were statistically significant differences improvement in both hair density and hair shaft diameter ($p < 0.001$ and $p < 0.001$). Furthermore, The assessment of Global Photographic Review (GPR) by two dermatologists showed 11.1% of patients had moderately improved, 61.1% had minimally improved and 27.8% no change. There were no statistically significant differences between serum Zinc and Ferritin. Furthermore, no side effect of oral chelated Zinc was reported.

Conclusions: Using chelated Zinc as additional trace supplements in FPHL has an efficacy to improve hair density and hair shaft diameter with no side effect.

Keywords: Chelated zinc supplement; Minoxidil solution; Female pattern hair loss

Introduction

Female pattern hair loss or androgenetic alopecia is the most common type of hair loss affecting women with reduced hair density [1] and can has a significant negative psychological impact due to the uncertain relationship between androgens and this entity [2]. Currently, the only clinically validated medication for increasing hair density in women with FPHL is topical minoxidil solution with FDA-approved in 2% product form but also increase to 5% in several countries [3]. They have a study comparing the efficacy of the two concentrations show a significant advantage of 5% topical minoxidil solution [4]. The previous studies show that oral administration of Zinc compounds improved hair growth [5] but they still have a few studies about the efficacy and side effects. The common form of Zinc that use for hair loss treatment is chelated Zinc [6]. Consequently, the molecules are attached to the amino acid methionine which enhance more bioavailable and more readily absorbed than inorganic forms [7]. The aim of this study was to determine efficacy and adverse effect of 5%minoxidil solution combined with chelated Zinc in FPHL.

Materials and Methods

This is a pilot-experimental study and was approved by Siriraj IRB. There are 20 patients, all female, with age of 18 or above who were having FPHL and all of them had never been received any topical or systemic treatment for at least 3 months before the enrollment. All participants were treated with 5% topical minoxidil solution twice daily combined with oral chelated Zinc 15 milligram per day for 24 weeks.

Examination of Hair Density and Hair Shaft Diameter using a Digital Microscope and Image Analysis

In the first visit, the patients were tattooed with sterilized ink to

represent 1 cm² target evaluation area in the vertex area. We access the improvements by measure the hair density and hair shaft diameter by using the handheld digital microscope (Dino-Lite™ Polarized microscope) to evaluate target area hair count. The electronic outside micrometer (IP54, EPI micrometer) was used to measure hair diameter. By taking 10 hairs of each patient to be measured and calculated the average diameter for every 4 weeks until 24-week of treatment. Furthermore, Global Photographic Review, serum Zinc and serum ferritin were evaluated before and after 24-week treatment.

Statistical Analysis

The data were shown as means, standard deviation and median. Statistical analysis using Paired t-test and Wilcoxon Signed Rank test to show significant increases of hair density and hair shaft diameter. The difference was considered significant when P value is less than 0.05.

Results

All of 20 patients, there have 18 patients, completed treatment at 24-week follow up visit and 2 patients, were dropped out due to

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adverse effects that were pruritus and scaling after receiving 5% topical minoxidil solution. The mean age was 47.5 ± 9.7 years (range, 26-61 years) where as age of onset was 41 years and the duration of hair loss was about 7 months before the study. Percentage of increasing in hair density and hair shaft diameter at 24-week follow-up visit after receiving 5% minoxidil solution combined with 15 mg oral chelated zinc supplement were 12.2% (from 118.4 to 132.9) and 5.5% (57.3 to 60.5 micron), respectively. There were statistically significant differences improvement in both hair density and hair shaft diameter ($p < 0.001$ and $p < 0.001$, respectively). Furthermore, the assessment of Global Photographic Review by two dermatologists showed 11.1% of patients had moderately improved, 61.1% had minimally improved and 27.8% no change. For the patient self-assessment, it showed that 55.5% of patients had significantly improved, 27.7% had moderately improved and 16.7% had minimally improved. Incidentally, there were no statistically significant differences between serum Zinc and serum ferritin and no adverse effect of oral chelated Zinc was reported (Tables 1 and 2).

Discussion

As we know that topical minoxidil solution appears to be effective and safe for the treatment of androgenetic alopecia. 5% minoxidil is approved by the FDA (US) to treat androgenic alopecia (male pattern hair loss) [8] while 2% concentration is most frequently used worldwide for female pattern hair loss [9].

In women, the use of 5% topical minoxidil solution applied twice daily has been demonstrated to be more efficacious than 2% minoxidil; however, there is a higher incidence of side effects with the stronger preparation such as scalp pruritus, local irritation, and unwanted hypertrichosis. In a recent study the use of 5% topical minoxidil foam once daily was shown to be as effective at 2% topical minoxidil solution applied twice daily [3]. Another randomized, placebo controlled trial comparing the efficacy of topical 5% solution with topical 2% and placebo in women demonstrated statistically significant increased hair growth in both the 5% and 2% group over the placebo group, but not necessarily in the 5% over the 2% group [4].

Zinc is the well-known trace element that associated with hair shedding. Zinc deficiency is caused by inadequate intake or absorption, increased zinc excretion, or increased bodily need for zinc. Zinc deficiency symptoms include growth retardation, hair loss, diarrhea, delayed sexual maturation, impotence, eye and skin conditions, and loss of appetite [10]. Intake recommendations for Zinc and other

nutrients are provided in the Dietary Reference Intakes that include Recommended Dietary Allowance, Adequate Intake and Tolerable Upper Intake Level. The current Recommended Dietary Allowance for Zinc taken by mouth is: 11 milligrams for males 19 years old and older; 8 milligrams for females 19 years and older; 11 milligrams for pregnant females 19 years old and older; and 12 milligrams for lactating females 19 years and older. It is safe to take Zinc supplements with an approximate 40 mg-50 mg Zinc content on a daily basis by means of no adverse effects because human body absorbs approximately 20%-40% of the Zinc it digests [11].

Zinc is regarded as relatively safe and generally well tolerated when taken at recommended doses, few studies report side effects. Occasionally, adverse effects such as nausea, vomiting, loss of appetite, stomach cramps, diarrhea, and headaches [11]. Intakes of 150-450 mg of zinc per day have been associated with such chronic effects as altered iron function, low copper status, reduced immune function, and reduced levels of high-density lipoproteins [12]. Supplements contain several forms of Zinc, including Zinc gluconate, Zinc sulfate, and Zinc acetate and chelated Zinc. Despite that, the common form of Zinc that use for hair loss treatment is chelated Zinc because the molecules are attached to the amino acid methionine, which enhance more bioavailable and more readily absorbed than inorganic forms [7].

Although its mechanisms of action and efficacy are still uncertain, lower zinc levels especially have been linked consistently with different types of alopecia, probably due to its importance in metabolism and hair growth. Zinc is an important cofactor for multiple enzymes, it takes part in vital functional activities in hair follicle and it is a strong inhibitor of hair follicle regression as well as speed up hair follicle recovery [13]. Oral Zinc compounds have been used for decades for treating disorders such as telogen effluvium [14,15] and alopecia areata [16]. The previous studies show that oral administration of Zinc sulphate improved hair growth in alopecia areata [5]. There are several reports stating that the serum Zinc level is low in alopecia areata patients [17,18]. Although the pathogenesis of this reduced serum Zinc level is unknown. Serum Zinc levels has been found to be lower in patients with alopecia areata than in control population. In a study on 15 patients, hair regrowth was observed in 9 patients (67%) after oral Zinc gluconate administration [19]. Another study showed that serum Zinc levels were significantly decreased in alopecia areata patients whose disease was extensive, prolonged, and resistant to treatment [20]. Alhaj et al. demonstrated a 4-year girl with diffuse alopecia due to dietary Zinc deficiency. Her hair loss discontinued in 3 weeks after Zinc supplementation and she had no evidence of alopecia at a 4-month follow-up visit [21]. Slonim et al. showed the improvement in alopecia with oral zinc supplementation in a child with inadequate caloric intake [22]. Nevertheless, they still have a few studies about the efficacy and side effects especially in androgenetic alopecia. However oral zinc supplementation has often been used for the treatment of hair loss, even in the absence of zinc deficiency. Although its mechanisms of action have not been fully defined.

In our clinical experiences, we found that using oral chelated Zinc supplement combined with 5% minoxidil solution have more advantages. The use of 5% topical minoxidil solution applied twice daily have more beneficial result than 2% minoxidil solution. There were minimal side effects with 5% minoxidil, all of which were very well tolerated. This 24-week trial showed an efficacy of using 5% minoxidil solution combined with oral chelated Zinc supplement in the treatment of women with FPHL.

In this study, the serum Zinc were sustained its normal range

	Baseline	24-wks follow up	P-value
Hair count*(hairs)	118.4 ± 5.3	132.9 ± 19.6	<0.001
Hair diameter* (micron)	57.3 ± 5.5	60.5 ± 6.8	<0.001
Terminal/vellus ratio**	3.2 (0.6,17.0)	2.4 (0.8,8.5)	0.076

* Mean±SD, Paired t-test

**Median (min,max), Wilcoxon Signed Rank test

Table 1: The mean changes from baseline in target area hair count in 24 week follow up.

Adverse effects	5% minoxidil solution (N=20)
Erythema	0
Dryness	0
Pruritus	1
Scaling	1
Others	0

Table 2: Two participants developed an allergic contact dermatitis to minoxidil and were dropped out during the study.

except one participants who have lower serum Zinc level but she have increased hair density and hair shaft diameter and her serum Zinc turn to normal range after treatment. Two participants developed an allergic contact dermatitis to minoxidil, but no systemic adverse effects were detected. Therefore these two participants were dropped out during the study. Incidentally no any adverse effects of oral chelated Zinc were reported due to small sample size. The result suggested that all the participants have an improvement in both hair density and hair shaft diameter. Furthermore, the assessment of Global Photographic Review by two dermatologists showed most of the participants had minimally improved. For the patient self-assessment, it showed more than 50% of participants had significantly improved. We conducted the study in 6 months so it could not evaluate treatment efficacy that topical minoxidil reached the maximal result at 1 year of treatment [23].

Furthermore, we can't compare our study with the previous studies due to the difference methods and no studies determined the therapeutic effect of oral Zinc.

From those results, we found that 5% minoxidil solution combined with oral chelated Zinc supplement have an efficacy in treatment of FPHL so this is a pilot study for further subsequent clinical studies with two arms double blind control study and larger number of participants.

Limitation

This paper doesn't show additive effect of oral zinc compare with minoxidil because this study is a pilot study for further subsequent clinical studies with two arms double blind control study and larger number of participants.

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