

Effectiveness of Chuzhi Shengfa Tablets Combined with Ketoconazole Shampoo and Chuzhi Shengfa Tablets Combined with 5% Minoxidil Foam in the Treatment of Male Androgenetic Alopecia

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Abstract: *Objective:* To investigate the clinical efficacy and safety of Chuzhi Shengfa Tablets combined with ketoconazole shampoo and Chuzhi Shengfa Tablets combined with 5% minoxidil foam in the treatment of male androgenetic alopecia. *Methods:* From July 2022 to July 2023, 120 male patients with androgenetic alopecia were selected from our Department of Dermatology and randomly divided into Control Group 1, Control Group 2, Observation Group 1, and Observation Group 2, with 30 patients in each group. Control Group 1 was treated with ketoconazole shampoo, Control Group 2 with 5% minoxidil foam, Observation Group 1 with ketoconazole shampoo combined with Chuzhi Shengfa Tablets, and Observation Group 2 with 5% minoxidil foam combined with Chuzhi Shengfa Tablets. Hair density, hair diameter, scalp oil secretion (using oil secretion scoring), and adverse reactions were compared before and after treatment across the four groups. *Results:* After treatment, hair density and hair diameter significantly increased in all four groups compared to before treatment, while scalp oil secretion scores significantly decreased ($P < 0.05$). The improvements in Observation Groups 1 and 2 were significantly better than those in Control Groups 1 and 2 ($P < 0.05$). No significant differences in the incidence of adverse reactions were observed among the four groups ($P > 0.05$). *Conclusion:* Chuzhi Shengfa Tablets combined with ketoconazole shampoo and Chuzhi Shengfa Tablets combined with 5% minoxidil foam are both effective and safe for treating male androgenetic alopecia. These combinations can significantly improve hair growth and are worthy of clinical promotion.

Keywords: Chuzhi Shengfa Tablets; Ketoconazole shampoo; Minoxidil foam; Male; Androgenetic alopecia

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1. Introduction

Androgenetic alopecia (AGA), also known as seborrheic alopecia, is a common type of hair loss characterized by the progressive miniaturization of hair follicles on the scalp. It predominantly affects young and middle-aged men, severely impacting their quality of life. Hair loss not only affects patients' appearance but also significantly troubles their psychological state and social activities ^[1]. The pathogenesis of AGA is complex and is thought to involve increased sensitivity of hair follicles to androgens and/or elevated expression of the type II 5 α -reductase gene in the affected areas, as well as genetic factors and scalp inflammation ^[2]. Current treatments for AGA include topical minoxidil and oral finasteride, but long-term use of finasteride can have adverse effects, such as gynecomastia, testicular pain, and sexual dysfunction ^[3]. Recently, traditional Chinese medicine (TCM) has garnered increasing attention for the treatment of AGA.

Chuzhi Shengfa Tablets are a Chinese herbal compound made up of 13 ingredients, including *Angelica sinensis*, *Paeonia suffruticosa*, *Ligusticum chuanxiong*, Cortex Dictamni, Periostracum Cicada, *Rehmannia glutinosa*, *Sophora flavescens*, *Kochia scoparia*, *Saposhnikovia divaricata*, processed *Polygonum multiflorum*, *Schizonepeta tenuifolia*, roasted *Bombyx batryticatus*, and Scolopendra. The unique combination of these herbs provides multiple therapeutic effects, including nourishing yin and blood, dispelling wind and activating meridians, relieving itching, and removing excess scalp oil ^[4]. By improving scalp microcirculation and inhibiting scalp inflammation, Chuzhi Shengfa Tablets effectively promote hair growth and optimize the scalp environment, providing comprehensive support for the treatment of AGA.

Ketoconazole shampoo is a broad-spectrum antifungal agent. In addition to its primary antifungal effect, studies have shown that it also has antiandrogenic and anti-inflammatory properties. By inhibiting scalp sebaceous gland secretion, ketoconazole shampoo can alleviate scalp inflammation and effectively improve AGA symptoms. Moreover, ketoconazole shampoo is the most commonly used antifungal medication for treating dandruff and seborrheic dermatitis, and in 2016, it was recommended as the first-line treatment for seborrheic dermatitis by the Asian Consensus on Seborrheic Dermatitis Treatment ^[5]. These characteristics make ketoconazole shampoo highly valuable for clinical applications in improving scalp health.

Minoxidil can alter the hair follicle growth cycle, promoting hair growth by inducing follicles to transition from the resting phase to the growth phase, extending the growth phase, and shortening the resting phase. Minoxidil is the only topical medication approved by the U.S. Food and Drug Administration (FDA) for the treatment of AGA ^[6]. As interest in AGA treatment grows, 5% minoxidil has gradually become a common topical treatment. However, the liquid form of minoxidil has been found to cause skin irritation. In comparison, the foam formulation does not contain propylene glycol, which reduces the likelihood of skin irritation and allergic reactions, making 5% minoxidil foam more widely recommended internationally for treating AGA ^[7]. This study aims to investigate the clinical efficacy and safety of Chuzhi Shengfa Tablets combined with ketoconazole shampoo and 5% minoxidil foam in the treatment of male androgenetic alopecia, providing a reference for clinical treatment.

2. Materials and methods

2.1. General information

A total of 120 male patients with androgenetic alopecia, admitted to our Department of Dermatology from July 2022 to July 2023, were selected and randomly divided into the observation group and control group,

with 30 cases in each group. Inclusion criteria: (1) Meeting the diagnostic criteria for androgenetic alopecia; (2) Classified as grades II-III on the Hamilton-Norwood scale^[8]; (3) Age between 20 and 45 years; (4) Willing to participate in the study and signing the informed consent form. Exclusion criteria: (1) Suffering from other types of alopecia, such as alopecia areata or telogen effluvium; (2) Suffering from severe diseases of the heart, liver, kidney, or other systems; (3) Currently taking other medications that may affect hair growth; (4) Allergic to the drugs used in this study. There were no statistically significant differences between the two groups in terms of age, disease duration, or the degree of hair loss ($P > 0.05$), making them comparable.

2.2. Methods

- (1) Control Group 1: Patients will be treated with 2% ketoconazole shampoo (Xian Janssen Pharmaceutical Ltd., National Drug Approval No. H20053398). The ketoconazole shampoo will be used twice a week. Patients will apply an appropriate amount of shampoo to the wet scalp during washing, gently massage for 5 minutes, and then rinse thoroughly with water.
- (2) Control Group 2: Patients will use 5% minoxidil foam (Asian Aerosol OAN Pvt. Ltd, Reg ID 695233) for topical treatment. The application will be done twice a day, with 1g applied to the affected area each time, once in the morning and once in the evening. Patients should evenly apply the minoxidil foam to the areas of hair loss and gently massage for 5 minutes to promote absorption and stimulate hair growth.
- (3) Observation Group 1: In addition to using 2% ketoconazole shampoo, patients will also orally take Chuzhi Shengfa Tablets (Dalian Meiluo Pharmaceutical Factory, National Drug Approval No. Z20013214). The dosage for Chuzhi Shengfa Tablets is 6 tablets three times daily, preferably taken after meals.
- (4) Observation Group 2: In addition to using 5% minoxidil foam, patients will orally take Chuzhi Shengfa Tablets. The dosage regimen for Chuzhi Shengfa Tablets is the same as in Observation Group 1.

2.3. Observation indicators

2.3.1. Hair density

A hair imaging analyzer (CK-9000, Japan) was used to measure the hair density (units: hairs/cm²) in the hair loss areas before and after treatment. Each patient was measured three times, and the average value was taken.

2.3.2. Hair diameter

The hair diameter (units: μm) in the hair loss areas before and after treatment was measured using the hair imaging analyzer (CK-9000, Japan). Each patient was measured three times, and the average value was taken.

2.3.3. Scalp oil secretion

The oil secretion scoring method was used to evaluate the scalp oil secretion before and after treatment. The scoring criteria were: (1) 0 points: no oil secretion; (2) 1 point: mild oil secretion, slightly greasy scalp; (3) 2 points: moderate oil secretion, obviously greasy scalp; (4) 3 points: severe oil secretion, very greasy scalp.

2.3.4. Adverse reactions

Adverse reactions during the treatment, such as scalp itching, scalp dryness, and scalp erythema, were recorded,

including the severity and duration of these reactions.

2.4. Statistical analysis

Data were analyzed using SPSS 22.0 statistical software. Measurement data were expressed as mean \pm standard deviation (SD), and comparisons between groups were made using the *t*-test, while intra-group comparisons were performed using the paired *t*-test. Count data were expressed as percentages (%), and group comparisons were made using the χ^2 test. A *P*-value of < 0.05 was considered statistically significant.

3. Results

3.1. Comparison of hair density, hair diameter, and scalp oil secretion scores before and after treatment in the four groups

After three months of treatment, hair density and hair diameter in all four groups significantly increased compared to before treatment, while scalp oil secretion scores significantly decreased ($P < 0.05$). The improvements in Observation Groups 1 and 2 were significantly better than in Control Groups 1 and 2 ($P < 0.05$). See **Table 1**.

Table 1. Comparison of hair density, hair diameter, and scalp oil secretion scores before and after treatment in the four groups (mean \pm SD)

Groups	Hair density (cm ²)		Hair diameter (μ m)		Scalp oil secretion score (points)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Control Group 1 (<i>n</i> = 30)	73.51 \pm 9.48	80.62 \pm 9.81	74.05 \pm 10.91	80.04 \pm 8.10	4.78 \pm 1.39	3.32 \pm 1.22
Control Group 2 (<i>n</i> = 30)	74.26 \pm 9.44	84.36 \pm 9.87	74.56 \pm 10.24	85.67 \pm 8.72	4.65 \pm 1.42	3.11 \pm 1.20
Observation Group 1 (<i>n</i> = 30)	75.04 \pm 9.12	95.67 \pm 10.24 ^{†‡}	75.01 \pm 8.63	92.31 \pm 9.77 ^{†‡}	4.78 \pm 1.35	2.25 \pm 0.93 ^{†‡}
Observation Group 2 (<i>n</i> = 30)	76.69 \pm 10.21	94.81 \pm 9.88 ^{†‡}	76.24 \pm 8.86	90.84 \pm 9.76 ^{†‡}	4.61 \pm 1.23	2.33 \pm 0.97 ^{†‡}

Note: [†] indicates $P < 0.05$ compared with Control Group 1; [‡] indicates $P < 0.05$ compared with Control Group 2.

3.2. Comparison of adverse reactions in the four groups

During the treatment, mild scalp itching occurred in 2 cases (6.67%) in both Observation Groups 1 and 2, which was alleviated after symptomatic treatment. In Control Groups 1 and 2, 3 (10.00%) and 4 (13.33%) cases of mild scalp dryness and scalp itching occurred, respectively, and were relieved after symptomatic treatment. There was no statistically significant difference in the incidence of adverse reactions between the two groups ($P > 0.05$).

4. Discussion

Chuzhi Shengfa Tablets are a classic traditional Chinese medicine composed of 13 herbal ingredients, including *Angelica sinensis*, *Paeonia suffruticosa*, *Ligusticum chuanxiong*, Cortex Dictamni, Periostracum Cicada,

Rehmannia glutinosa, *Sophora flavescens*, *Kochia scoparia*, *Saposhnikovia divaricata*, processed *Polygonum multiflorum*, *Schizonepeta tenuifolia*, roasted *Bombyx batryticatus*, and *Scolopendra*. These herbs are carefully prepared through processes such as fine grinding and decoction^[9]. The medicinal effects include nourishing yin and blood, dispelling wind and relieving itching, promoting blood circulation, and reducing oil secretion. Thus, the medicine is widely used to treat seborrheic alopecia, scalp itching, dandruff, and excessive oil secretion^[10,11]. By regulating and improving the scalp environment, this medicine provides an effective solution, replenishing the liver and kidneys, nourishing the essence and blood, promoting hair growth, and improving scalp health. It fundamentally regulates the constitution and alleviates hair loss symptoms by promoting smooth blood flow and delivering more nutrients to the hair.

Ketoconazole shampoo is a broad-spectrum antifungal drug. Its primary mechanism of action is inhibiting the synthesis of ergosterol in the fungal cell membrane, which destroys the membrane's integrity and eventually leads to the death of fungal cells. Therefore, ketoconazole shampoo has shown remarkable effects in treating various fungal infections. However, its efficacy extends beyond antifungal properties, as it also exhibits anti-inflammatory and anti-androgenic effects. Studies have shown that this shampoo can effectively inhibit sebaceous gland secretion in the scalp, reducing oil content and alleviating scalp inflammation caused by excess oil^[12].

Minoxidil foam is a topical medication with a unique formulation, notably free of propylene glycol, making it particularly effective in reducing oil secretion, relieving itching, soothing burning sensations, and preventing contact dermatitis. The foam's texture allows it to adhere tightly to the affected area, preventing it from spreading to healthy skin, ensuring a concentrated release of the medication, and enhancing the therapeutic effect. Notably, when combined with AHA exfoliants, it effectively opens hair follicles, significantly promoting the absorption of Minoxidil, allowing the drug to penetrate more easily into the follicles and maximize its effect. Additionally, the glycerin content in Minoxidil foam plays a crucial role in deeply moisturizing and hydrating the scalp, providing protection and reducing dryness and discomfort.

The results of this study indicate that after treatment, the hair density and hair diameter of patients receiving treatment were significantly higher than before. The scalp oil secretion scores in Observation Group 1 (Ketoconazole shampoo + Chuzhi Shengfa Tablets) also significantly decreased, and the improvement was superior to that in Control Groups 1 and 2, with a significant difference ($P < 0.05$), while the difference compared to Observation Group 2 was not significant. These findings suggest that the combination of Chuzhi Shengfa Tablets and Ketoconazole shampoo can effectively improve hair growth in male androgenetic alopecia patients. The significant therapeutic effects may be closely related to the synergistic action of the two drugs. Chuzhi Shengfa Tablets improve the scalp microenvironment through multiple pathways, especially in promoting hair growth. Its ingredients help regulate the physiological state of the scalp and enhance follicle function. Ketoconazole shampoo, on the other hand, improves scalp conditions by inhibiting fungal growth, providing anti-inflammatory effects, and exerting anti-androgenic mechanisms. When used together, the two medications act on multiple levels to achieve better therapeutic outcomes. Notably, the incidence of adverse reactions in Control Group 1 and Observation Group 1 was low, with no statistically significant difference. This suggests that the combination of Chuzhi Shengfa Tablets and Ketoconazole shampoo has good safety in the treatment of male androgenetic alopecia.

Chuzhi Shengfa Tablets regulate endocrine function and improve the scalp environment, reducing oil secretion and providing a good foundation for hair growth. Meanwhile, 5% Minoxidil foam directly stimulates

blood circulation in the hair follicles, prolongs the anagen phase, and shortens the telogen phase, promoting new hair growth ^[7]. This dual action ensures a more significant hair regrowth effect, helping patients increase hair density and regain confidence. The natural ingredients in Chuzhi Shengfa Tablets soothe scalp discomfort, avoiding irritation that may be caused by single medications, while Minoxidil foam is convenient to use, absorbs quickly, and does not leave a greasy feel, making it suitable for people with fast-paced lifestyles. It is worth noting that the incidence of adverse reactions in Control Group 2 and Observation Group 2 was also low, with no statistically significant difference. This indicates the efficacy and safety of the combination of Chuzhi Shengfa Tablets and 5% Minoxidil foam in treating male androgenetic alopecia, providing an important basis for future treatment strategies.

Of course, there are some limitations to this study, such as the small sample size, short observation period, and lack of long-term follow-up data. Future research needs to involve larger sample sizes and longer-term clinical studies to further verify the long-term efficacy and safety of the combination of Chuzhi Shengfa Tablets with Ketoconazole shampoo and 5% Minoxidil foam in treating male androgenetic alopecia.

In conclusion, the combination of Chuzhi Shengfa Tablets with Ketoconazole shampoo and Chuzhi Shengfa Tablets with 5% Minoxidil foam has shown significant efficacy and good safety in treating male androgenetic alopecia. This combined therapy effectively promotes hair growth, improves hair density, and enhances overall hair quality, significantly boosting patients' confidence and quality of life. Given its excellent results and acceptable side effects, the combination of Chuzhi Shengfa Tablets with Ketoconazole shampoo and 5% Minoxidil foam has broad application value in clinical practice.

Disclosure statement

The authors declare no conflict of interest.

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