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Research Article

Clinical efficacy of supramolecular salicylic acid in the treatment of ketoconazole-resistant seborrheic dermatitis of the scalp

Jianghui Li*, Lulu Tang, Shuangshuang Li, Cairong Yan

[1] *Department of Dermatology and Venereology, The Second Affiliated Hospital of Guangxi Medical University, Nanning 530000, Guangxi Zhuang Autonomous Region, China.*

Abstract

Objective: To evaluate the clinical efficacy of supramolecular salicylic acid in the treatment of scalp seborrheic dermatitis that was unresponsive to ketoconazole lotion.

Methods: A retrospective analysis was conducted on 20 patients with scalp seborrheic dermatitis who had previously shown no improvement with ketoconazole lotion. These patients were treated at the Dermatology Clinic of the Second Affiliated Hospital of Guangxi Medical University between December 2024 and May 2025. The clinical efficacy and safety of switching to supramolecular salicylic acid therapy were observed. Results: After 4 weeks of treatment, significant reductions were observed in dandruff score, lesion score, pruritus score, and quality of life score compared to baseline ($P < 0.01$).

Conclusion: Supramolecular salicylic acid effectively improves symptoms in patients with ketoconazole-resistant scalp seborrheic dermatitis, with minimal adverse effects and high patient compliance.

Keywords: Supramolecular salicylic acid, seborrheic dermatitis, ketoconazole lotion, Clinical efficacy

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Scalp seborrheic dermatitis (SSD) is a common chronic, recurrent and inflammatory skin disease with clinical manifestations such as increased dandruff, oily scalp and itching. In particular, large amounts of scalp desquamation can easily cause embarrassment to patients, seriously affecting their daily lives and social life. Ketoconazole has broad-spectrum antifungal, anti-inflammatory and sebum secretion inhibitory effects. Its topical lotion is the first-line drug for the treatment of seborrheic dermatitis, but some patients do not respond well to its use. Salicylic acid is a β-hydroxy acid with anti-inflammatory, broad-spectrum antibacterial, keratinization and sebum regulation effects [1]. With the development of bioindustrial technology, supramolecular salicylic acid has gradually entered the clinical application of dermatology. Due to its high bioavailability and low irritation, it has been widely used in the treatment of scalp seborrheic dermatitis. Among the patients with scalp seborrheic dermatitis who visited our department, some had used ketoconazole lotion for treatment, but the effect was poor, so they switched to supramolecular salicylic acid for treatment. We retrospectively observed its clinical efficacy and safety.

1 Materials and methods

1.1 Cases and materials

This study retrospectively selected 20 patients with scalp seborrheic dermatitis who visited the dermatology clinic of the Second Affiliated Hospital of Guangxi Medical

*Correspondence: Jianghui Li, Department of Dermatology and Venereology, The Second Affiliated Hospital of Guangxi Medical University, Nanning 530000, Guangxi Zhuang Autonomous Region, China. Email: 290797445@qq.com.

University from December 2024 to May 2025 and switched to supramolecular salicylic acid treatment after ineffective treatment with ketoconazole lotion, including 6 males and 14 females. Inclusion criteria: ① Patients aged 18 to 60 years with scalp seborrheic dermatitis, with the main symptoms of erythema, scaling and itching; ② Ketoconazole lotion had been used for more than 4 weeks before treatment, and there was no obvious effect; ③ Completed the entire course of treatment according to the protocol. Exclusion criteria: ① Those who are allergic to the treatment product or have a highly sensitive constitution; ② Patients with other scalp diseases; ③ Taking fluconazole, itraconazole, glucocorticoids, retinoic acid, tetracyclines and other therapeutic drugs that may affect the scalp condition or spironolactone, contraceptives, finasteride and other drugs that affect sex hormones or sex hormone receptors within 4 weeks before treatment. ④ Severe malnutrition, autoimmune diseases, severe mental disorders or other major diseases. ⑤ Pregnant or lactating women or those who plan to become pregnant during treatment. Informed consent was signed before treatment.

1.2 Methods

1.2.1 Main materials 30% supramolecular salicylic acid (manufacturer: Broda, Broda Technologies Co., Ltd.). 30% supramolecular salicylic acid was used to treat the patient's scalp at 0, 2, and 4 weeks, for a total of 3 times. Treatment method: The dermatologist evenly applied 30% supramolecular salicylic acid to the patient's scalp and gently massaged for 15 to 20 minutes. When frosting or erythema or whitening reaction appeared in the treatment area, the treatment was stopped and immediately rinsed with water.

1.2.2 Follow-up and evaluation The patient was asked to return to the hospital for follow-up at week 6. The follow-up scale evaluation was completed by the researcher and the subject. Among them, the dandruff, erythema, and papule scores of each subject were independently performed by 2 dermatologists. If the two doctors do not reach a consensus, a third doctor will be required to re-evaluate.

1.2.2.1 Dandruff score The 10-point adherent scalp flflaking score (ASFS) was used to assess the severity of scalp dandruff on the entire scalp [2]: the subject's scalp was divided into 8 areas (frontal, top, temporal and occipital regions on both sides), and each area was scored from 0 to 10 according to the severity of scalp dandruff: 0 means no dandruff (none), 1 to 2 means small pieces of powdery grayish-white rough scales (a small amount), 3 to 4 means small to medium-sized scales (mild), 5 to 6 means large and thin scales loosely connected to the scalp (moderate), 7 to 8 means large adherent scales (obvious), and 9 to 10 means thick white to yellow scales tightly attached to the scalp (severe). The ASFS scoring record was used for each score, and the scores of each area were added together to obtain a total score (0 to 80 points).

1.2.2.2 Lesion score[3] The clinical scale for seborrheic dermatitis scalp lesions (4-level scoring method) was used to evaluate the improvement of patients' lesion symptoms before and after treatment: 0 points for no erythema, 1 point for mild (a few light red or yellow-red macules, erythema area <20% of the scalp area, papules ≤5), 2 points for moderate (multiple yellow-red macules with a few isolated papules, erythema area accounting for 20%-40% of the scalp area, papules 6-10), 3 points for severe (multiple infiltrated erythema with a large number of red papules, erythema area ≥40% of the scalp area, maculopapular lesions >10).

1.2.2.3 Pruritus score[3] The pruritus score scale (4-level scoring method) was used to evaluate the improvement of the pruritus symptoms of the subjects before and after treatment: 0 was no pruritus, 1 was mild (slightly aware, no need to scratch, easy to tolerate), 2 was moderate (obviously aware, sometimes scratching, but tolerable, not affecting daily life and sleep), and 3 was severe (often able to feel itch, often scratching, unbearable, affecting daily life and sleep).

1.2.2.4 Quality of life score[4] The dermatology life quality index (DLQI) score was referred to, and the subjects completed the DLQI score to understand the impact of the degree of seborrheic dermatitis on their quality of life.

2 Results

2.1 Clinical symptoms and quality of life

This study used the ASFS score, skin lesion score and pruritus score to evaluate the efficacy of supramolecular salicylic acid in improving the three main symptoms of seborrheic dermatitis: dandruff, erythema and pruritus. After 4 weeks of treatment, the scalp scales of 20 patients were significantly improved, and the ASFS score decreased significantly, which was statistically significant compared with before treatment ($P < 0.01$). The skin lesions such as erythema and papules on the affected scalp were significantly improved, and the scores decreased significantly, which was statistically significant compared with before treatment ($P < 0.01$). The degree of scalp itching was significantly improved, and the score decreased significantly, which was statistically significant compared with before treatment ($P < 0.01$). With the improvement of the above symptoms after treatment, the average DLQI score of the 20 patients after treatment was lower than that before treatment, and the difference before and after treatment was statistically significant ($P < 0.01$) (see the table below).

Table: The improvement of symptoms and quality of life of 20 patients before and after treatment（ $\bar{X}$±s）

Item	Before Treatment	After Treatment	P-value
ASFS Score	7.850±5.537	2.250±1.888	<0.01
Skin Lesion Score	1.350±0.671	0.400±0.503	<0.01
Pruritus Score	1.800±0.768	0.550±0.510	<0.01
DLQI Score	11.85±6.184	3.450±2.235	<0.01

2.2 Adverse reactions

The adverse reactions of this treatment are mild. Each patient only experienced mild burning or itching during the treatment, which was tolerable and gradually eased after about 3 to 5 minutes. After the treatment was completed, there were no obvious subjective symptoms after rinsing with clean water.

3 Discussion

Ketoconazole lotion is a first-line drug for the treatment of seborrheic dermatitis. If its efficacy is poor, it may be related to the following factors: ① Resistance formation: The genome duplication of Malassezia can lead to overexpression of ERG4 and ERG11 genes, thereby enhancing the ability to synthesize ergosterol and reducing the sensitivity of ketoconazole [5]; the formation of biofilm is one of the important mechanisms of Malassezia resistance. The drug efflux pumps and matrix components (such as β-1,3-glucan) in the biofilm can limit the penetration of drugs, thereby enhancing drug resistance [6]. ② Drug application factors: Ketoconazole lotion needs to stay on the

scalp for 3 to 5 minutes to penetrate the stratum corneum. Short-term contact cannot effectively kill fungi. The lotion concentration is usually 1% to 2%, which has limited effect on fungi deep in the hair follicles, especially for patients with severe inflammation or thickened stratum corneum. ③ Scalp environmental factors: Long-term use of ketoconazole may destroy the balance of scalp microecology. While inhibiting Malassezia, it can lead to excessive proliferation of bacteria (such as Staphylococcus aureus) or other fungi, aggravating inflammation. Seborrheic dermatitis is often accompanied by acne, atopic dermatitis or psoriasis [7]. Therefore, antifungal treatment alone cannot cover mixed infections and requires combined antibacterial or anti-inflammatory drugs. ④ Host-related factors: Patients with impaired immune function (such as HIV and diabetes) have reduced fungal clearance ability, and the efficacy of ketoconazole alone is limited. In patients with gastric acid deficiency (such as long-term use of acid suppressants), the absorption rate of ketoconazole decreases by more than 50%, affecting the systemic antifungal effect [8]. ⑤ Non-fungal dominant factors: Seborrheic dermatitis is not a purely fungal infection. Immune abnormalities (such as activation of the Th17 pathway), neurogenic inflammation, and genetic factors can all drive the disease.

Salicylic acid (SA) is a β-hydroxy acid with multiple biological activities. Its mechanism for treating seborrheic dermatitis is as follows: ① Keratin regulation: 30% salicylic acid can promote keratin exfoliation and remove abnormal scales. ② Anti-inflammatory: By inhibiting the activity of cyclooxygenase (COX), blocking arachidonic acid metabolism, and reducing prostaglandin E2 synthesis [9]. At the same time, it downregulates the expression of inflammatory factors such as IL-6, IL-1, and TNF-α, and inhibits the activation of NF-κB transcription factors [10]. ③ Antibacterial: It has a direct inhibitory effect on seborrheic dermatitis-related pathogens (such as Malassezia and Staphylococcus epidermidis). ④ Oil control: Salicylic acid can dissolve excess sebum and inhibit excessive proliferation of sebaceous gland cells [11]. Due to the limitation of traditional salicylic acid being soluble in ethanol, it can cause additional irritation to the skin, is unstable in nature, and is prone to crystallization, which reduces the efficacy. However, supramolecular salicylic acid avoids the above disadvantages through supramolecular preparation technology and greatly improves the efficacy. Lei et al. [12] found that supramolecular salicylic acid combined with active zinc and active zinc alone can improve the clinical symptoms and quality of life of SSD patients. The total effective rate of supramolecular salicylic acid combined with active zinc in the treatment of SSD is better than that of active zinc alone; supramolecular salicylic acid combined with active zinc in the treatment of SSD is better than that of active zinc alone in terms of skin lesion regression.

In summary, for patients with ketoconazole lotion that is ineffective in treating scalp seborrheic dermatitis, switching to supramolecular salicylic acid treatment can effectively improve their clinical symptoms of scalp scaling, erythema, papules and itching. After receiving treatment, the quality of life of patients is also significantly improved, and the product is well tolerated without serious adverse reactions.

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None

Conflict of Interests

None

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