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Efficacy of combination of ozonated water with oil for treatment of tinea pedis

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ABSTRACT

Objective: To evaluate efficacy of combined therapy with ozonated water and oil on patients with tinea pedis.

Methods: A total of 60 patients with tinea pedis were divided into 2 groups in a randomized and blinded test. Patients in a control group were treated with naftifine hydrochloride and ketoconazole cream once a day. Patients in an ozone group were treated with ozonated water bath and then ozonated oil topical application once a day. Patients in the 2 groups were treated for 4 weeks. Clinical and laboratory data were collected for both groups at the end of the 1st week, the 2nd week, and the 4th week. The Pearson chi-square was performed to compare scores of the clinical signs and symptoms (CSS) and the mycological result between the 2 groups. Independent samples *T*-test was performed to compare the curative effect between the 2 groups.

Results: After 4 weeks' treatment, 6 patients were positive in the control group determined by mycological examination while 1 patient was positive in the ozone group, with no significant difference between the 2 groups ($P>0.05$). Changes in CSS at the end of the 1st week, 2nd week, and 4th week were obtained and showed no significant difference between the 2 groups at the 3 different time points ($P>0.05$). No side effects were observed.

Conclusion: Combination of ozonated water with oil is effective on treatment of tinea pedis and it shows no side effects.

KEY WORDS

tinea pedis; ozonated water; ozonated oil; naftifine hydrochloride and ketoconazole cream

臭氧水联合臭氧油治疗足癣的疗效

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[摘要] 目的: 观察臭氧水联合臭氧油治疗足癣的临床疗效和不良反应。方法: 60例确诊为足癣的患者随机被分为对照组和臭氧组。对照组患者足癣用自来水清洗后用萘替芬酮康唑软膏外涂, 每日1次; 臭氧组患者足癣用臭氧水清洗后外涂臭氧油, 每日1次; 均治疗4周。在治疗第1, 2和4周结束时, 分别采集临床评分数据评价患者病情的改善情况; 并在治疗前、治疗第4周末进行真菌镜检, 评估真菌感染的情况。结果: 治疗4周后, 真菌镜检结果显示臭氧组1例阳性, 对照组6例阳性, 两组间真菌镜检阳性率比较差异无统计学意义($P>0.05$)。第1, 2, 4周的临床评分比较显示不同时间点两组治疗效果差异无统计学意义($P>0.05$)。结论: 臭氧水联合臭氧油外用治疗足癣有效, 且无不良反应。

[关键词] 足癣; 臭氧水; 臭氧油; 萘替芬酮康唑软膏

Tinea pedis, the most common dermatological disease, is a superficial fungal infection of the plantar surface and it can provide a portal of entry for secondary bacterial infection, resulting in profound complications and morbidity. The prevalence of tinea pedis has increased over the last several decades due to an increase in urbanization and the use of sports and fitness facilities. Both the incidence rate and recurrence rate are over 50% in south of China due to the humidity and local living habit—wearing occlusive footwear^[1]. One investigation^[2] in Chinese urban region showed that patients with tinea pedis can relapse 4 times within a year, and it can significantly impact on patients' quality of life and emotional well-being.

Classical therapies for tinea pedis are local application, system agents and combination of medication. Ninety percent patients in China prefer to topical application to tinea pedis^[2]. Conventional drugs like naftifine hydrochloride and ketoconazole cream are common used for topical treatment, but they are usually having side effect of antibiotic, cannot cure secondary bacterial infection, need complex combination of different drugs, or difficult to accommodate all types of tinea pedis^[3-6]. Therefore, it is urgent to pursue a new high-efficiency and safety therapy for tinea pedis.

Ozone is the natural existence of a strong oxidizing bactericide that can quickly remove or killing bacterium, fungi, virus, with wide clinical use^[7]. Ozone can be employed as a bactericidal agent under various forms, such as ozonized water^[8], ozonized oil, ozone associated with other substances, and more frequently the gaseous O_3/O_2 mixture. Ozonated water and oil can kill *Staphylococcus* and *Candida* quickly, to accelerate the anti-inflammatory and antipruritic effect^[9-11]. Ozonated sunflower oil has been tested to treat tinea pedis in clinical trials^[12]. Ozonated water soaking was high-efficient in treating tinea pedis patients in Guangdong Province, south of China^[13]. Besides, at the young age mouse model, ozone can

accelerate wound healing, since ozone can increase TGF- β expression which is crucial for tissue remodeling^[14]. From above, ozone treatment seems to be a ideal solution for tinea pedis. So, in this study, we designed a clinical trial to evaluate the efficacy of the combination of ozonated water and oil in treating tinea pedis.

I Patients and methods

I.1 Patients

A controlled randomized study was carried out, comparing ozonated water and oil with the recognized antimycotic drug naftifine hydrochloride and ketoconazole. A total of 60 outpatients were clinically (presence of maceration, desquamation, fissures, erythema, vesicles and/or pruritus) and mycologically (positive mycological of skin) diagnosed as tinea pedis. Patients were divided into 2 groups, using a randomized list ($n=30$ for each).

The ozone group: Patients washed their feet with ozonated water for 10 minutes and immersed their feet in a bath tub containing ozonated water for 20 minutes, and then applied ozonated oil, once a day, for 4 weeks.

The control group: Patients applied naftifine hydrochloride and ketoconazole cream after cleaning with water, once a day, for 4 weeks^[15].

Inclusion criteria: 1) Age between 12 and 70 years old, 2) Microscopic fungi were positive, 3) Tinea pedis was diagnosed according to the clinical manifestation, 4) Patient voluntarily joined this study with informed consents.

Exclusion criteria: 1) The local severe bacterial infections or interference treatment for other skin disease, 2) Pyrrole drug allergy, 3) Severe disease, e.g. chronic obstructive pulmonary disease, 4) Long-term use of corticosteroids or within 2 weeks of topical antifungal drug, 5) During the treatment of other antifungal drugs, 6)

Pregnant woman or lactating women.

The age range was from 18 to 60 years, including 12 males and 48 females. No significant difference in age and sex between the ozone group and the control group ($P>0.05$). The participants voluntarily joined this study after signing informed consent forms.

1.2 Materials

Ozonated oil was provided by Hunan Health Care Technology Co. Ltd. Ozonated water was created by Ozone Water Generating Instrument (Hunan Health Care Technology Co. Ltd.) at the Department of Dermatology of the Third Xiangya Hospital.

Naftifine hydrochloride and ketoconazole cream was from Chongqing Hua Bang Pharmaceutical Ltd. Company (Batch number: H20051949).

1.3 Mycological examination

We collected specimens of the skin lesion from the patient and put it on a glass slide. One drop of 10% KOH was added to dissolve the sample, then observed the fungal mycel or spore under microscope. Fungal mycel or spore was considered to be positive sign of fungal infection.

1.4 Comprehensive evaluation of therapeutic efficiency

Clinical signs and symptoms including erythema, papula, vesicle, scale, soak and erosion, pruritus were evaluated by the investigator and recorded at the end of the 1st, 2nd and 4th week according to a 4-point scale (0=absent, 1=mild, 2=moderate, 3=severe)^[12]. Adverse events were collected throughout the study.

1.5 Clinical signs and symptoms score

Each clinical sign or symptom was assessed separately. The investigator evaluated the severity of each sign or symptom over the entire target foot.

Clinical signs and symptoms score (CSS)=(CSS before treatment-CSS after treatment)/CSS before treatment. Cured, change rate of CSS=100%; improved, $60\% \leq$ change rate of CSS<100%; same, $20\% \leq$ change rate of CSS<60%; worse, change rate of CSS<20%.

1.6 Statistical analysis

The data were analyzed with SPSS 19.0 software. Analysis was performed using the Pearson chi-square to compare scores of total clinical signs and symptoms (s/s)

and the mycological result between the 2 groups. Using independent samples *t*-test to compare the curative effect between the 2 groups. $P<0.05$ was considered statistically significant.

2 Results

2.1 Mycological examination result

After 4 weeks' treatment, 6 patients in the control group were positive while 1 patient in the ozone group was positive in mycological examination (Figure 1). There was no significant difference between the 2 groups ($\chi^2=0.35$, $P>0.05$).

2.2 Comparison of CSS change rate between the ozone and control group

Changes of CSS at the end of the 1st, 2nd, and 4th week were obtained (Figure 2), showed no significant difference between the ozone group and the control group at the 3 different time points ($P>0.05$).

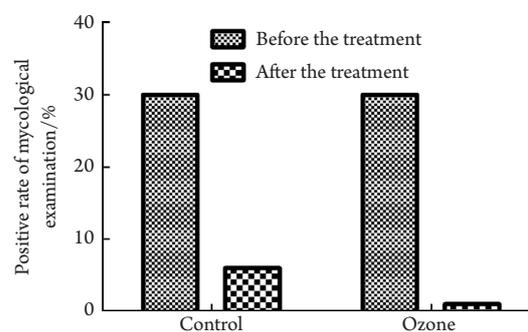


Figure 1 Mycological examination after 4-week treatment

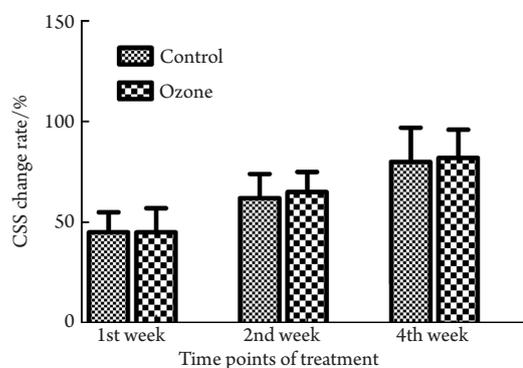


Figure 2 CSS change rate at different treating time points

2.3 Total clinical effect

After the 1st, 2nd, and 4th week, the percentages of

cured, improved, same, and worse patients were calculated, and the significant differences in constituent ratios of

clinical effect were not found between the ozone group and the control group ($P>0.05$, Figure 3).

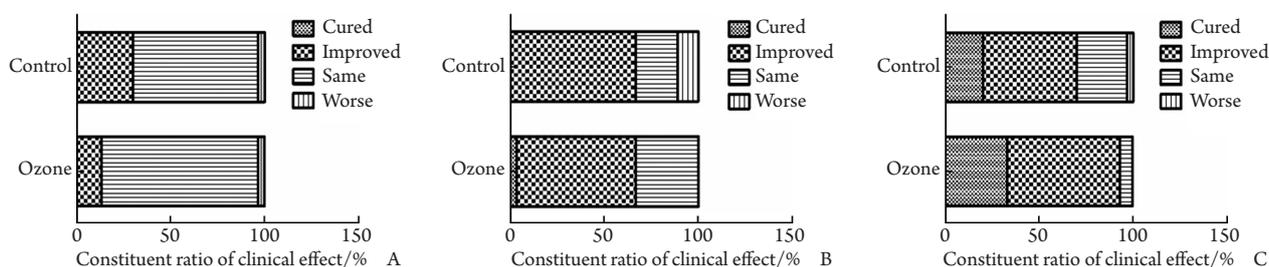


Figure 3 Total composite clinical effect

A: First week; B: Second week; C: Fourth week

3 Discussion

The investigation showed the evaluation of efficacy of ozonated water and oil as germicidal agents against tinea pedis. In this study, 29 patients in the mycological examination were negative and 1 patient was positive in the ozone group, while 24 were negative and 6 were positive in the control group, with no significant differences between the 2 groups. In the whole trail, 1 patient had desquamation of skin after topical application of ozone, and after a few days later, the symptoms disappeared, without affecting the normal use of drugs. No obvious side effects were observed in the ozone group. Topical application of ozone is an effective treatment for tinea pedis when compared with local application of naftifine hydrochloride and ketoconazole cream.

Tinea pedis, a worldwide spread fungus infection disease, with a high morbidity and high recurrence, is used to be treated with antifungal drugs. But most of synthetic antifungal drugs had side effects especially when they were used in a long-term application. One of alternative treatments to conventional treatment is topical ozone therapy. The clinical application of ozone is only a history of a few decades, but it shows the advantages in many ways. Ozone gas has been used to treat trichophytonrubrum and trichophytonmentagrophytes, and it can kill more than 99% of viable fungi presented in various experimental systems^[14]. Gupta et al^[15] identified that ozone gas is effective in sanitizing contaminated footwear. Menéndez et al^[12] comparing topical ozonized sunflower oil and ketoconazole cream in 200 patients, found no significant differences between the 2 groups. No side-effects or

bacterial super-infections were observed. They considered that the ozonated sunflower oil can be an effective alternative and low-cost antimycotic drug.

In our study, we combined ozonated water and oil to treat tinea pedis. The ozonated water has cleanout and convergence effect, while the ozonated oil can moisturize excessive hyperplasia of skin keratosis. The combination of flowing ozonated water and ozonated oil have the incomparable advantages of naftifine hydrochloride and ketoconazole cream, and better than one form application of ozone. The experimental results showed that the ozone treatment for tinea pedis is safe and effective, and is suitable for various types of tinea pedis, worthy of promotion and application in clinic.

Conflict of interest: The authors declare that they have no conflicts of interest to disclose.

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