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Clinical Efficacy of Lemon Grass Oil Cream in the Treatment of Ring Worm

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Abstract : A randomized controlled trial was conducted to determine the efficacy of lemon grass (*Cymbopogon citratus*, DC) oil cream in the treatment of dermatophytosis at any site of the body except nail and scalp infections in Thai adult patients. Eighty-one patients were enrolled in the study in which 38 cases were allocated to receive lemon grass oil cream and 43 cases to receive clotrimazole cream in an identical package for local application at the skin lesions twice a day for 4 weeks. The outcome was measured clinically and microbiologically by KOH preparation and culture before treatment and 2 and 4 weeks during treatment. Twenty-five cases (30.9%) were lost to follow up. Fifty-six cases completed the course of treatment, 30 cases in the clotrimazole group with a 53.3% cure rate and 26 cases in lemon grass oil group with a 26.9% cure rate. Although clinical signs and symptoms improved in the latter group, they still showed a positive KOH-preparation and / or positive culture. Contact dermatitis from the lemon grass oil cream was found in 1 case but no serious adverse effect was found. The hot climate of Thailand might reduce the concentration of volatile oil "citral" in lemon grass oil cream which could influence the clinical outcome and lead it to be less effective than in a previous *in vitro* study.

เรื่องย่อ : การศึกษาประสิทธิภาพของครีมน้ำมันตะไคร้ในการรักษาโรคกลาก
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คณะผู้วิจัยได้ศึกษาประสิทธิภาพของครีมน้ำมันตะไคร้ (lemon grass oil cream) ในการรักษาโรคกลากที่ผิวหนังบริเวณกลางที่เล็บและหนังศีรษะ ในผู้ป่วยจำนวน 81 ราย โดยแบ่งผู้ป่วยออกเป็น 2 กลุ่มแบบสุ่ม ผู้ป่วยจำนวน 43 รายได้รับ clotrimazole cream และ 38 รายได้รับครีมน้ำมันตะไคร้ในความเข้มข้นร้อยละ 2.5 ทาวันละ 2 ครั้ง (เช้า-เย็น) ติดต่อกันนาน 4 สัปดาห์ ผู้ป่วยทุกคนจะได้รับการตรวจและบันทึกการรอยโรค ขูดขุยเพื่อตรวจหาเชื้อราโดยวิธี KOH preparation และเพาะเชื้อก่อนรักษาและหลังรักษา 2 และ 4 สัปดาห์ ตามลำดับ มีผู้ป่วยจำนวน 25 ราย คิดเป็นร้อยละ 30.9 ที่ได้รับการรักษาไม่ครบถ้วนเนื่องจาก 24 รายไม่มาติดต่อดำเนินการ และผู้ป่วยในกลุ่มครีม น้ำมันตะไคร้ 1 รายต้องหยุดการรักษาเนื่องจากเกิด contact dermatitis ในบริเวณที่ทายา จึงเหลือผู้ป่วยที่สามารถประเมินผลการรักษาได้เพียง 56 ราย เป็นกลุ่มที่ได้รับ clotrimazole 30 ราย รักษาหายร้อยละ 53.3 และกลุ่มที่ได้รับ ครีมน้ำมันตะไคร้ 26 ราย รักษาหายร้อยละ 26.9 แต่ผู้ป่วยทุกรายในกลุ่มหลังนี้มีอาการทางคลินิกทุเลาแม้ว่าจะยังตรวจพบเชื้อด้วยวิธี KOH และ/หรือวิธีการเพาะเชื้อ ไม่พบพิษและผลข้างเคียงที่ร้ายแรงจากการรักษา เนื่องจาก citral ซึ่งเป็นสารออกฤทธิ์ต่อเชื้อกลาก เป็นส่วนประกอบที่สำคัญของน้ำมันหอมระเหยที่สกัดจากใบตะไคร้ ดังนั้น อุณหภูมิอากาศที่สูงของประเทศไทยอาจมีส่วนทำให้ความเข้มข้นของสารนี้ลดลงเมื่อนำมาใช้ทาในการรักษา กลาก ทำให้ประสิทธิภาพในการรักษาไม่ดีเท่าเมื่อทำการศึกษาในห้องทดลอง ซึ่งจำเป็นต้องทำการศึกษาต่อไป

INTRODUCTION

Dermatophytosis or ring worm is one of the most common superficial fungal infections in tropical countries. The recommended treatment is an imidazole compound for topical use which is an imported product and is quite expensive in Thailand. Many herbal medicines have been tried for treatment of dermatophytosis. It has been demonstrated that the volatile oil extracted from lemon grass (one of Thai herbal plants) has fungicidal activity against dermatophytes.¹⁻¹¹ Lemon grass (*Cymbopogon citratus*, DC) is widely distributed in Thailand and is easy to cultivate. Lemon grass oil cream has been developed by the Pharmaceutical and Natural products Department, The Institute of Scientific and Technological Research, Bangkok, Thailand for use as an antifungal cream from local raw material in our country.

In the present study, we have examined the clinical efficacy of lemon grass oil cream and clotrimazole cream in the treatment of ring worm at any site of the body except nails and scalps in Thai adult patients.

MATERIALS AND METHODS

Patients were screened for ring worm by clinical examination and potassium hydroxide (KOH) preparation from skin lesions at the Skin Clinic, Out-patient Department, Siriraj Hospital, Bangkok, Thailand.

The inclusion criteria were adult patients, aged from 15-60 years, with dermatophyte skin infections in which the involvement did not exceed 5% of the body surface area and showed positive fungal elements on a KOH preparation.

The exclusion criteria included any patient with a history of allergic reaction to the azoles and pregnant or lactating women.

The proposal was approved by the Committee on Human Rights Related to Research Involving Humans, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand. All patients gave written informed consent after the nature of the study had been explained to them. The patients were assigned by stratified randomization according to sex and the site of lesion to receive lemon grass oil cream or clotrimazole cream. The treatment was

applied topically to the affected sites twice daily for 4 weeks.

Outcome measurement

The primary measure of efficacy was the mycologic cure rate (negative KOH preparation and culture) of the skin lesions. The secondary outcome measure was the clinical response which included reduction or complete disappearance of itching, redness and scaling of the lesion by scoring each parameter from 0 to 4. Each of the outcome measurements was carried out at the start of therapy, 2 weeks and 4 weeks of treatment.

RESULTS

A total of 81 patients were enrolled in the study. There were 39 males and 42 females, with the ages ranged from 18 to 60 years (mean 36.4 yr.). The affected sites and culture results at the first visit be-

fore treatment are shown in Table 1 and 2. Fifty-six patients (69.1% of all cases) were completely treated and followed up, 30 cases were treated with clotrimazole and 26 cases were treated with lemon grass oil cream. The baseline characteristics of age, sex, site of involvement, and causative organisms were similar between these 2 groups. Twenty-five patients (30.9% of all cases) were not completely treated due to loss to follow up in 24 cases, 13 cases in the clotrimazole group and 11 cases in lemon grass oil group, and in 1 case treated with lemon grass oil the treatment was discontinued because of contact dermatitis. The mycologic cure rate of each species of dermatophyte at fourth week of treatment are shown in Table 3. The total mycologic cure rate at second week of treatment were 36.7% in clotrimazole group and 15.4% in lemon grass oil group. The clinical improvements were observed in both groups at second week of treatment although the mycologic cure was not achieved.

Table 1. Involved sites of dermatophytoses.

Site	Number
Face	5
Trunk	22
Groin	32
Hand	9
Foot	13
Total	81

Table 2. Isolated fungal species from infected lesions.

Fungal species	Number (%)
<i>Trichophyton rubrum</i>	56 (69.1)
<i>Trichophyton mentagrophyte</i>	11 (13.6)
<i>Epidermophyton floccosum</i>	5 (6.2)
<i>Microsporum gypseum</i>	4 (4.9)
<i>Candida tropicalis</i>	2 (2.5)
<i>Candida albicans</i>	1 (1.2)
Non-sporulated septate hyaline hyphae	2 (2.5)
Total	81

Table 3. Treatment outcome in both groups*.

Organisms	Clotrimazole (30)		Lemon grass oil (26)	
	cure (%)	not cure (%)	cure (%)	not cure (%)
<i>Trichophyton rubrum</i>	9	13	6	10
<i>Trichophyton mentagrophyte</i>	4	1	1	4
<i>Microsporum gypseum</i>	0	0	0	3
<i>Epidermophyton floccosum</i>	3	0	0	0
Non-sporulated septate hyaline hyphae**	0	0	0	2
Total	16 (53.3)	14 (46.7)	7 (26.9)	19 (73.1)

*cure = mycologic cure at 4th week of treatment which means negative both KOH preparation and culture result, either positive result from KOH preparation or culture means not cure.

**unidentified species.

DISCUSSION

Citral, one of the main components of the volatile oil extracted from lemon grass leaves, has been demonstrated of fungicidal activity against 4 species of dermatophytes, *Trichophyton rubrum*, *Trichophyton mentagrophyte*, *Microsporum gypseum*, and *Epidermophyton floccosum*, in a previous study.¹² These species are commonly found as the causative organisms causing dermatophytoses worldwide and have also been found in our study. The minimum inhibitory concentration (MIC) and minimum lethal concentration (MLC) of lemon grass oil and citral was highest for *M. gypseum*, followed by *T. rubrum*, *T. mentagrophyte* and *E. floccosum* respectively.¹² The most resistant and the most sensitive strains were less commonly found in our study in contrast to the 2 moderately sensitive strains which were the main causative organisms but the treatment outcome was not comparable to the *in vitro* results. Unfortunately, *M. gypseum* which is the most resistant strain was found only in lemon grass oil group. Many factors may influence the clinical response such as the site of the lesions, compliance with the treatment and environmental factors. High temperature may reduce the concentration of volatile oil in lemon grass oil cream. The antifungal activity of lemon grass oil is dose-dependent and 2.5% concentration of lemon

grass oil cream used in this study was the minimum concentration which exhibited better efficacy than those commercial azole creams in the previous study.¹² The drop out rate in this study was quite high and was probably caused by the benign nature of the disease in that the patients did not see the need for follow up. The ones who were not cured might have more symptoms that needed treatment. The patients who did not come back to follow up might be cured although this review could not evaluate. Although the mycologic cure rate of lemon grass oil cream was low, clinical improvement and patient satisfaction were quite high.

In conclusion, lemon grass oil cream showed some efficacy in the treatment of ring worm but the concentration of the active ingredient should be considered as a factor for its effectiveness.

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