

Comparative Study of Terbinafine Creams (Lamisil[®] and EU 2000[®]) in the Treatment of Tinea Corporis/cruris

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ABSTRACT:

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Objective: To compare the efficacy of terbinafine creams (Lamisil[®] and EU 2000[®]) in the treatment of tinea corporis/cruris.

Method: The study was designed as a prospective, comparative, randomized, parallel-group and double-blind study. Out-patients of the Dermatology Clinic, Maharaj Nakorn Chiang Mai Hospital, aged between 17-59 years, with a clinical diagnosis of tinea corporis/cruris confirmed by positive microscopy and culture were randomized to receive treatment once daily for 1 week with 1% terbinafine cream, either Lamisil[®] or EU 2000[®]. Patients were assessed at week 0, 1, 2, 4 and 8. At each visit, signs and symptoms of erythema (redness), scaling, papulation, vesiculation and pruritus were scored and skin scrapings were taken for mycological examination.

Results: Thirty patients were included in the study, i.e. 16 treated with Lamisil[®] and 14 with EU 2000[®]. Demographic data showed that patients in the two treatment groups were comparable with regard to previous therapy, age, duration of disease, size and location of lesions. The causative organism was *Trichophyton rubrum* in all patients. More than 50% efficacy in week 2 and the highest efficacy (about 90%) in week 4 were seen in both the Lamisil[®] and EU 2000[®] group. There was no difference in overall efficacy between the two groups ($p>0.05$) at each visit week.

Conclusion: Efficacy of EU 2000[®] cream in 1 week's treatment of tinea corporis/cruris is no different from that of Lamisil[®] cream.

Key words: terbinafine, Lamisil, EU 2000, tinea corporis, tinea cruris

บทคัดย่อ:

สิริ เชี่ยวชาญวิทย์*, สยาม แก้ววิชิต**, วรณดี เต๋อโตติกุล***, นงนุช วัฒนัยธนาคม****. การศึกษาเปรียบเทียบยาครีมเทอร์บินาฟีน (ลามิซิล[®] และ ยู 2000[®]) ในการรักษาโรคกลากที่ลำตัวและซอกพับวารสารโรคผิวหนัง 2545; 18: 92-9.

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วัตถุประสงค์: เพื่อเปรียบเทียบประสิทธิภาพของยาครีมเทอร์บินาฟีน (ลามิซิล[®] และ ยู 2000[®]) ในการรักษาโรคกลากที่ลำตัวและซอกพับ

วิธีการศึกษา: เปรียบเทียบไปข้างหน้า แบบสุ่ม กลุ่มคู่ขนานและปกปิดสองด้าน ทำการศึกษาในผู้ป่วยนอกของคลินิกโรคผิวหนัง โรงพยาบาลมหาราชนครเชียงใหม่ อายุอยู่ในช่วง 17–59 ปี ได้รับการวินิจฉัยว่าเป็นโรคกลากที่ลำตัวหรือซอกพับ โดยยืนยันด้วยผลบวกจากการตรวจภายใต้กล้องจุลทรรศน์และการเพาะเชื้อ สุ่มให้ได้รับการรักษาด้วยยาครีมเทอร์บินาฟีน ขนาดความเข้มข้น 1% ชื่อ ลามิซิล® หรือยู 2000® ทาวันละครั้งเป็นเวลา 1 สัปดาห์ การตรวจติดตามผู้ป่วยสัปดาห์ที่ 0, 1, 2, 4 และ 8 ในแต่ละครั้ง จะบันทึกความรุนแรงของลักษณะอาการแดง สะเก็ด ตุ่มนูน ตุ่มน้ำ และอาการคัน เป็นคะแนน นอกจากนี้ผิวหนังบริเวณที่เป็นโรคกลากจะถูกขูดนำไปตรวจสอบหาเชื้อรา

ผลการศึกษา: ผู้ป่วยจำนวน 30 รายเข้าร่วมในการศึกษานี้ โดยที่ 16 ราย ได้รับการรักษาด้วย ลามิซิล® และอีก 14 รายได้รับการรักษาด้วย ยู 2000® ผู้ป่วยทั้งสองกลุ่มมีประวัติในการรักษา อายุ ช่วงระยะเวลาของการเป็นโรค ขนาดและตำแหน่งของโรคคล้ายคลึงกัน เชื้อที่เป็นสาเหตุของโรคในผู้ป่วยทุกราย คือ *Trichophyton rubrum* พบว่าประสิทธิภาพการรักษาที่สัปดาห์ที่ 2 มากกว่า 50% และประสิทธิภาพสูงสุด (ประมาณ 90%) ที่สัปดาห์ที่ 4 ในทั้งสองกลุ่ม ประสิทธิภาพการรักษาในทั้งสองกลุ่มที่แต่ละสัปดาห์ ไม่แตกต่างกันอย่างมีนัยสำคัญ ($p>0.05$)

สรุปผลการศึกษา: ประสิทธิภาพในการใช้ยาครีม ยู 2000® รักษาโรคกลากที่ลำตัวและซอกพับ วันละครั้งเป็นเวลา 1 สัปดาห์ ไม่แตกต่างจากประสิทธิภาพของการใช้ยาครีมลามิซิล®

คำสำคัญ: เทอร์บินาฟีน, ลามิซิล, ยู 2000, โรคกลากที่ลำตัว, โรคกลากที่ซอกพับ

Introduction

Topical application of antifungal agents is considered the treatment of choice for dermatophytosis. Most of the available drugs are fungistatic, requiring long term treatment to prevent relapses. Terbinafine is a new synthetic allylamine antifungal drug, which provides high cure and low relapse rates after a short period of treatment because of its fungicidal action^{1,2,3}. It is an effective and well tolerated therapy for a wide range of superficial dermatophyte infections, i.e. tinea pedis^{4,5}, tinea corporis^{2,6} and tinea cruris^{2,6}.

EU 2000®, a 1% terbinafine cream, is available in Thailand together with Lamisil®, an innovator

product. In this double-blind study, the EU 2000® used in the treatment of tinea corporis/cruris was compared with Lamisil®. This comparative study was performed to gain information, which will be helpful for physicians, pharmacists, and drug consumers in selecting an appropriate drug. Confidence in therapeutic efficacy will also be enhanced.

Materials and methods

The study was approved by the ethical committee of the Faculty of Pharmacy, Chiang Mai university. Thirty four out-patients of the Dermatology Clinic, Maharaj Nakorn Chiang Mai Hospital, aged between 17–59 years, with a clinical diagnosis of tinea

corporis/cruris confirmed by positive microscopy agreed to join the study. Patients were not included if they had received systemic antifungal drugs in the preceeding 4 weeks or topical antifungal therapy during the previous 2 weeks.

The study was designed as a prospective, comparative, randomized, parallel-group and double-blind study. Patients were randomized to receive treatment once daily for 1 week with 1% terbinafine cream, either Lamisil[®] (Lot No. 828 LO, MFG date 10/2000, Exp. Date 10/2005, Novartis) or EU 2000[®] (Lot No. 020544, MFG date 17/5/2001, Exp date 16/5/2004, Union Drug Labs. Ltd., Thailand). For both drugs, each cream was repacked in the same type and shaped containers in order to ensure that the physician and patients did not know which drugs they were using. Patients were assessed at week 0, 1 (end of treatment), 2, 4 and 8 (follow up visit). At each visit, signs and symptoms of erythema (redness), scaling, papulation, vesiculation and pruritus were scored on scale 0 to 3 (0 = absent, 1 = mild, 2 = moderate, 3 = severe). At each visit, skin scrapings were taken for mycological examination, i.e. KOH preparation microscopy and culture in a Sabouraud's agar, with the results recorded as positive or negative. Clinical efficacy was defined when the total scores of signs and symptoms were ≤ 2 . Mycological efficacy was defined as a negative microscopy finding and negative culture. Overall efficacy was rated as effective if patients showed a

complete cure, i.e. a negative microscopy finding and negative culture with no or minimal residual signs and symptoms (total score ≤ 2).

The Mann-Whitney U test was used to compare the total scores of signs and symptoms between the two groups at each visit week. The Chi-square or Fisher exact test was used for testing the null hypothesis that EU 2000[®] has the same overall efficacy as Lamisil[®].

Results

Thirty four out-patients were enrolled in the study. However, 4 patients (1 in the Lamisil[®] and 3 in the EU 2000[®] group) were excluded from the study after treatment was started because the culture for dermatophytes, which requires 2 weeks of observation, proved to be negative (delayed exclusion). Therefore, 30 patients remained in the study, i.e. 16 treated with Lamisil[®] and 14 with EU 2000[®].

Demographic data showed that patients in the two treatment groups were comparable with regard to previous therapy, age, duration of disease, size and location of lesions. The causative organism was *Trichophyton rubrum* in all patients for both the Lamisil[®] and EU 2000[®] group. Fourteen patients (10 in the Lamisil[®] and 4 in the EU 2000[®] group) had received previous therapy. Most of the therapy was topical antifungal treatment. The mean age of the patients was 28.9 ± 11.9 years in the Lamisil[®] and 34.6 ± 12.7 years in the EU 2000[®] group. The

duration of disease for both groups was not different (t-test, $p > 0.05$), i.e. 5.4 ± 6.7 months for the Lamisil[®] group and 6.6 ± 6.6 months for the EU 2000[®] group. However, there was only 1 female in 16 patients of the Lamisil[®] group, while there were 6 females in 14 patients of the EU 2000[®] group.

Before treatment, the most common signs and symptoms were pruritus (100%), erythema (100%), scaling (100%) and vesiculation (16.7%). The average signs and symptoms, measured by the sum of scores for these factors, were similar in both groups, i.e. 7.9 ± 1.2 for the Lamisil[®] group and 8.1 ± 0.9 for the EU2000[®] group ($p > 0.05$).

Table 1 Average total scores of signs and symptoms ($\pm$ SD)

Week	Lamisil [®] group	EU 2000 [®] group
0	7.88 ± 1.20	8.07 ± 0.92
1	2.50 ± 1.21	2.00 ± 0.88
2	0.69 ± 0.79	0.70 ± 0.80
4	0.44 ± 0.73	0.44 ± 1.09
8	1.00 ± 0.64	1.55 ± 1.01

Note:-There was no significant difference between the two groups at each visit week ($p > 0.05$).

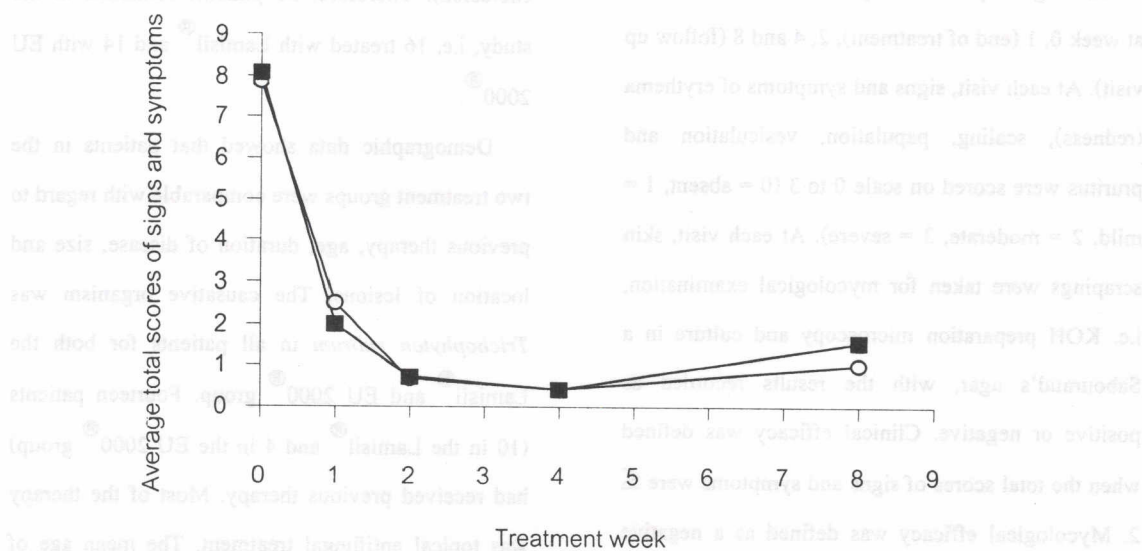


Figure 1 Average total scores of signs and symptoms at each visit week. (○) Lamisil[®] group, (■) EU 2000[®] group

Clinical efficacy

A rapid decrease in signs and symptoms was shown at week 2 and 4 (1 and 3 weeks after treatment) for both the Lamisil[®] and EU 2000[®] group (Table 1, Figure 1). The decrease of signs and

symptoms in the EU 2000[®] group at each visit week showed no significant difference from that in the Lamisil[®] group ($p > 0.05$).

Table 2 Mycological efficacy

Week	Lamisil [®] group (%)	EU 2000 [®] group (%)
0	0/16 (0)	0/14 (0)
1	6/16 (37.5)	6/14 (42.9)
2	11/16 (68.8)	7/14 (50.0)
4	14/16 (87.5)	13/14 (92.9)
8	10/16 (62.5)	12/14 (85.7)

Note:-There was no significant difference between the two groups at each visit week ($p > 0.05$).

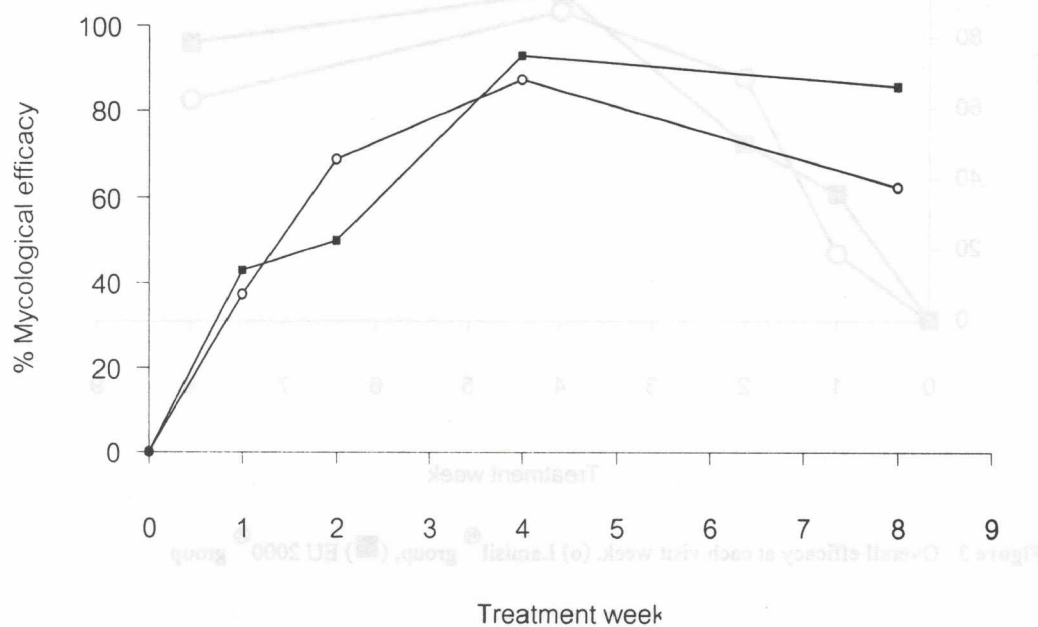


Figure 2 Mycological efficacy at each visit week. (o) Lamisil[®] group, (■) EU 2000[®] group

Mycological efficacy

Mycological efficacy, were measured at each visit week (Table 2, Figure 2). About ninety percent of mycologic clearing at week 4 of both the

Lamisil[®] and EU 2000[®] group was demonstrated.

No significant difference in mycologic clearing was seen between the Lamisil[®] and EU 2000[®] group at each visit week ($p > 0.05$).

Table 3 Overall efficacy

Week	Lamisil [®] group (%)	EU 2000 [®] group (%)
0	0/16 (0)	0/14 (0)
1	3/16 (37.5)	5/14 (42.9)
2	11/16 (68.8)	7/14 (50.0)
4	14/16 (87.5)	13/14 (92.9)
8	10/16 (62.5)	11/14 (85.7)

Note:-There was no significant difference between the two groups at each visit week ($p > 0.05$).

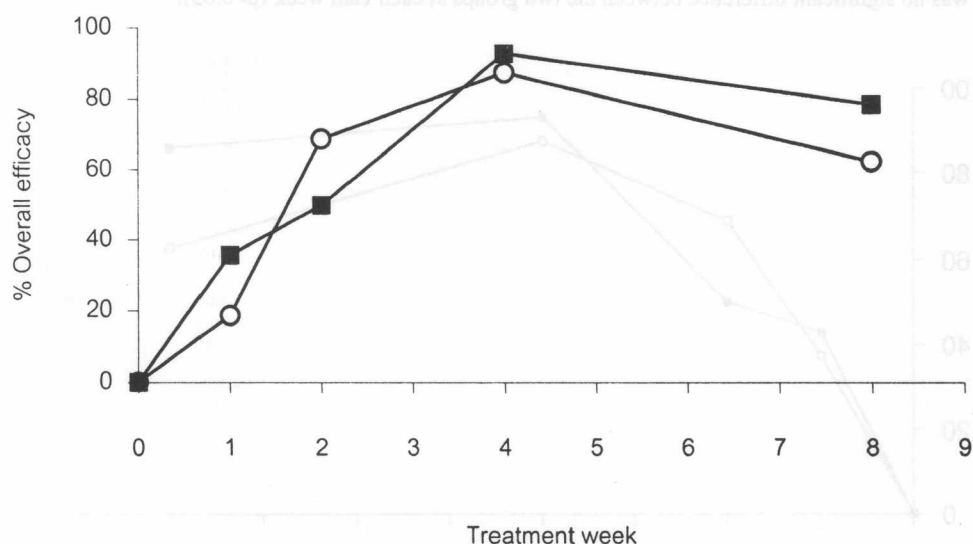


Figure 3 Overall efficacy at each visit week. (o) Lamisil[®] group, (■) EU 2000[®] group

Overall efficacy

The overall effectiveness were similar to the mycological efficacy (Table 3, Figure 3). More than 50% efficacy in week 2 and the highest efficacy (about 90%) in week 4 were seen for both the Lamisil[®] and EU 2000[®] group. There was no difference in the overall efficacy between the two groups at each visit week ($p>0.05$). Recurrence was noticed at follow up week 8, i.e. 25.0 % in the Lamisil[®] group and 14.3 % in the EU 2000[®] group.

Discussion

As in previous reports, terbinafine can be detected for more than 7 days after cessation of topical application^{2,4-6}. This may be because of accumulation of terbinafine in the stratum corneum^{1,3}. The signs and symptoms were clearly relieved at week 2 (1 week after treatment) and the highest efficacy was found at week 4 (3 weeks after treatment). No side effects were found during the therapy.

The decrease of signs and symptoms, and the mycological and overall efficacy in the EU 2000[®] group at each visit week were not different from that

in the Lamisil[®] group ($p>0.05$). Therefore, it may be concluded that, in this study, there was no difference between the use of Lamisil[®] and EU 2000[®] in the treatment of tinea corporis/cruris. However, the recurrence rate at week 8 was still high in both groups. A repeated course of therapy at week 4 may be beneficial in both groups.

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