

Comparative Study of Topical 1% Terbinafine Cream Versus 1% Clotrimazole Cream in The Treatment of Tinea pedis

Araz Hasan Mohammed(FICMS)¹, Gulikhan Ahmed Omer (MBChB, HD)²

¹ College of Medicine , Hawler Medical University, Erbil, Iraq

² Ministry of Health, Erbil, Iraq

Abstract

Background: Tinea pedis (athletic foot) is the most common dermatophytic fungal infection of the body. It may last for a short or long time and may recur after treatment.

Objective: To assessed and compared the effectiveness and safety of 1% terbinafine cream and 1% clotrimazole cream for the treatment of tinea pedis.

Patients and Methods: Randomized control trial was done in the outpatient clinic of dermatology department in Rizgary Teaching Hospital in Erbil. From March, 2019 to January, 2020. Sixty patients with tinea pedis diag-nosed clinically were included in this study. Thirty patients applied 1% terbinafine cream topically twice daily for one week and thirty patients applied 1% clotrimazole cream topically twice daily for four weeks. Scraping for fungi was performed before and after therapy. Efficacy was assessed by clinical cure and mycological cure. Clinical and mycological cure measured at weeks one, four and six.

Results: Mycological cure rates were 86.7% for terbinafine and 80% for clotrimazole at 4 weeks, 86.7% for terbinafine and 90% for clotrimazole at 6 weeks. At 4 weeks, terbinafine had an 83.3 percent clinical treatment rate and clotrimazole had a 76.67 percent clinical treatment rate; at 6 weeks, terbinafine had an 83.3 percent clinical treatment rate and clotrimazole had an 83.3 percent clinical treatment rate.

Conclusion: The study showed that one week terbinafine two times a day is as effective as four weeks clotrimazole two times a day as well as in terms of mycological treatments and efficient therapies.

Keywords: Terbinafine, clotrimazole, tinea pedis

OPEN ACCESS

Correspondence Address: Araz Hasan Mohammed
College of Medicine, Hawler Medical University, Erbil, Iraq

Email: aras.sherwany@yahoo.com

Copyright: ©Authors, 2023, College of Medicine, University of Diyala. This is an open access article under the CC BY 4.0 license

(<http://creativecommons.org/licenses/by/4.0/>)

Website:

<https://djm.uodiyala.edu.iq/index.php/djm>

Received: 24 August 2022

Accepted: 27 September 2022

Published: 5 April 2023

Introduction

Athlete's foot (tinea pedis) is a dermatophyte infection of the bottoms and interdigital web regions of the feet [1,2]. Among all fungal infections, tinea pedis is the most common [3]. *T. rubrum* causes the majority of infections [4]. Poor cleanliness,

excessive perspiration, occlusion of the foot, and perhaps reduced peripheral circulation all contribute to the spread of infection. Infectious agents may be spread via the use of public swimming pools, showers, and saunas [5]. Factors affecting transmission of

dermatophyte infection are based on where the illness came from, which is usually either human, animal or soil [6]. The prevalence rate of fungal infections is varied widely in the world and not confined to developing countries [7]. There are three clinical types of tinea pedis: Interdigital type, present as interdigital scaling, maceration, fissuring and erythema of the web spaces between the toes [8,9]. Patient often complains of itching and burning sensation [2]. It is the most common presentation of tinea pedis and infection of web spaces [10]. Moccasin type is the second and vesiculobullous type is the third most common type [8,9]. In most cases of superficial dermatophytosis, the infection occur initially on the foot and in time, spreads to other sites [11]. The detection of tinea pedis is usually clinical and demonstration of the fungus by microscopic examination taken from the involved site will confirm the diagnosis [12].

One of the most important goals of antifungal therapy is the elimination of the fungus from the body while causing as little harm as possible [13]. Tinea pedis is a common cutaneous dermatophyte infection that may be treated with topical antifungal medications [1].

Clotrimazole, miconazole, sulconazole, oxiconazole, ciclopirox, econazole, ketoconazole, naftifine, terbinafine, flutrimazole, bifonazole, and butenafine are effective topical antifungal agents [12].

For localized form of tinea pedis topical preparation is recommended. While topical terbinafine may be used for 1–7 days, azole formulations are often effective for up to 30 days [14].

Patients and Methods

Study design

Randomized control trial, comparing between two drugs in the treatment of tinea pedis.

Place of the study

Outpatient clinic of Dermatology Department in Rizgary Teaching Hospital in Erbil city.

Time and duration of the study

From beginning of January 2019 to the end of January 2020. The study took one year to be accomplished.

Research subjects

Any patient diagnosed clinically as having tinea pedis who attended the Dermatology Department in Rizgary Teaching Hospital was selected.

Inclusion criteria

- Patients with localized tinea pedis diagnosed clinically.
- Patients from all age groups of both genders.
- Pregnant and lactating ladies.
- Diabetic patients.

Exclusion criteria

- Affected patients who had systemic antifungal treatment during the last six weeks or topical antifungal treatment within the previous week.
- Moccasin type and concomitant onychomycosis were excluded because These types of dermatophytosis must be controlled with systemic antifungal therapy.
- Peoples who suffering immunosuppressive diseases and those on immunosuppressant therapy.

Sample size

Sixty patients were included in the study.

Methods of sample collection

Randomized sampling method was used for data collection.

The procedure

Sixty patients with tinea pedis diagnosed clinically participants were included in this investigation. Patients were randomized arbitrarily into two equal groups:-

Group A: Thirty patients were administered 1% terbinafine cream orally twice daily for one week.

Group B: For four weeks, 30 patients administered 1% clotrimazole cream twice daily to the affected area. Potassium hydroxide examination was performed before and after therapy, which is direct microscopical examination for detection of fungi by dissolving the scales in 10% potassium hydroxide solution. Efficacy was assessed by clinical cure (no or minimal signs and symptoms) and mycological cure (negative outcomes from a microscope analysis). Clinical and mycological cure was measured at each visit (weeks one, four and six).

Statistical Analysis

The statistical package for social science (SPSS, version 25) was applied to analyze the data, and the Chi-square test of

association was used to compare proportions. When the expected frequency (value) was less than 5 or more than 20% of the cells in the table, Fisher’s exact test was used. To compare the mean of the two samples, student’s t-test of two independent samples was used. A p-value of ≤ 0.05 was regarded as statistically significant.

Results

The study included a total of 60 patients; 27(45%) females and 33(55%) males, ratio of female to male is 1:1.2. Among them thirty patients (18 male and 12 female), their age was ranging from 20-67 years, with mean \pm standard deviation of 41.53 ± 11.35 with mycologically proven tinea pedis received one week of terbinafine 1% cream, and thirty patients (17 male and 13 female), age range was 18-70 years with mean \pm standard deviation of 42.8 ± 11.64 years treated by clotrimazole 1% cream for four weeks. Mycological cure (negative microscopy) and effective medication (mycological cure with no or minimal signs and symptoms) were evaluated 1, 4 and 6 weeks after starting treatment as seen in the Tables (1,2).

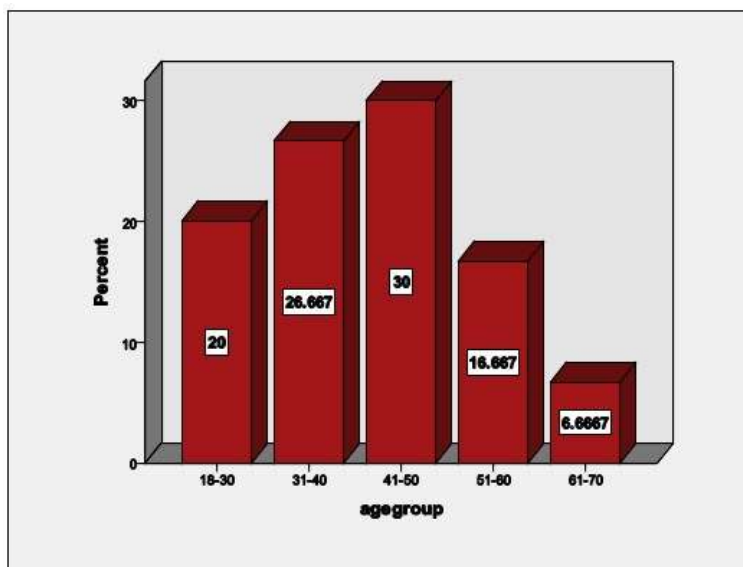


Figure (1): Age groups of participants

Mycological cure rates were 86.7% for terbinafine and 80% for clotrimazole ($p = 0.488$) at 4 weeks, and 90% for terbinafine and 90% for clotrimazole ($p = 0.999$) at 6 weeks as seen in Table (1). Therapy rates that are effective at 4 weeks were 83.3% for terbinafine and 73.33% for clotrimazole ($p=0.354$), and 83.3% for terbinafine and 80 % for clotrimazole ($p=0.743$) at 6 weeks

as seen in Table (2). Adverse effect (skin rash) is seen in 1 patient (3.34%) in terbinafine group and 2 patients (6.67%) in clotrimazole group ($p=0.554$) as seen in Table (3). The findings indicate that one week of twice-daily terbinafine was as beneficial as four weeks of twice-daily clotrimazole in terms of mycological cure and treatment efficacy.

Table (1): Mycological response to treatment by type of treatment

Mycological response	Treatment group		p-value
	Terbinafine N = 30	Clotrimazole N = 30	
	No. (%)	No. (%)	
Responding at 1 week	8 (26.7%)	6 (20%)	0.544
Responding at 4 week	26 (86.7%)	24 (80%)	0.488
Responding at 6 week	27 (90%)	27 (90%)	0.999

Table (2): Clinical response to treatment by type of treatment

Clinical response	Treatment group		p-value
	Terbinafine N = 30	Clotrimazole N = 30	
	No. (%)	No. (%)	
Responding at 1 week	5 (16.7%)	2 (6.7%)	0.225
Responding at 4 week	25 (83.3%)	22 (73.3%)	0.354
Responding at 6 week	25 (83.3%)	24 (80%)	0.743

Table (3): Association between adverse effect and treatment groups

Treatment group	Side effects		p-value
	Negative	Positive	
Terbinafine	29	1	0.554
Clotrimazole	28	2	

Discussion

Treatment of tinea pedis are either systemic or topical treatment [5,6]. In the past, side-effect profiles have restricted the use of oral medicines. Traditionally, superficial caused by fungi were administered topical antifungal drugs with favorable safety profiles [15,16].

Treatment duration was a significant determinant of patients' compliance in dermatomycosis medical care; consequently, we conducted a randomized controlled trial to compare the effectiveness and tolerability of once-daily treatment with 1% terbinafine cream for one week versus four weeks of treatment with clotrimazole in an effort to

identify a more efficient, rapid treatment with fewer side effects .

Terbinafine allylamine which is fungicidal. It cures dermatophyte infections more quickly [2, 5, 13].

Clotrimazole is topical imidazole preparation used as local treatment for tinea pedis which needs longer duration usually 4 weeks, it is fungistatic [2,12,13].

In our study mycological cure rates were 86.7% for terbinafine and 80% for clotrimazole at 4 weeks, and 90% for terbinafine and 90% for clotrimazole at 6 weeks. Effective treatment rates at 4 weeks were 83.3% for terbinafine and 73.33% for clotrimazole, and 83.3% for terbinafine and 80 % for clotrimazole at 6 weeks, in all instance there is no significant difference between terbinafine 1 week topical treatment and and clotrimazole 4 weeks treatment. Short-term treatment with powerful fungicides, such as terbinafine, may prevent treatment failure due to noncompliance with clotrimazole, which needs four weeks of medication. Also particularly successful for treating interdigital tinea pedis is allylamine administered twice daily for one week [2,17]. In a study of one week topical application of terbinafine was as effective as clotrimazole 4 weeks topical application with same rate of side effect[18] which comparable with our study. In two other studies; terbinafine was more effective than clotrimazole [19,20]. One week treatment of terbinafine showed mycological cure 91.4% after 7 weeks in a study[17], and 88% in another study after 5 week follow up[21]. In another study; after 4 week the response was 94% after 8 weeks[22]. These results were comparable to results obtained in our study.

Overall, the great effectiveness of topical terbinafine in treating tinea pedis after such short-duration treatment is unquestionably attributable to its fungicidal mechanism of action[23].

In another study; clotrimazole was therapeutically effective, as confirmed by mycological cure and clinical improvement which has been done on 64 patients having tinea pedis positive mycological response were seen in 91% and clinical cure in 72% with positive adverse effect in 2 patients only(15(

Regarding the side effect; in a study that has been done, positive side effect was 4% for terbinafine 1 week treatment and 5 % for 4 weeks clotrimazole treatment[17]. Comparable with our study results, side effect was seen in 1 patient (3.34%) in terbinafine group and 2 patients (6.67%) in clotrimazole group.

In our study terbinafine treatment response is higher than that of clotrimazole with no significant difference, which may be due to small sample size and limitation of time, although there is no significant difference between both groups but 1 week terbinafine is shorter duration therapy may provide better patient compliance, more economic and suitable compared to 4 weeks clotrimazole topical application.

Conclusions

One week topical terbinafine was preferred because of short duration of therapy and fungicidal activity that enhance patient compliance and better treatment outcomes.

Recommendations

We recommend to use the topical terbinafine for the treatment of tinea pedis rather than the topical clotri-mazole

application. Topical terbinafine causes less side effects and its use for lesser time duration makes it a better option for the treatment. The researchers recommend further studies and research in this field to explore more and gain better knowledge and information upon larger sample size of subjects.

Source of funding: The current study was funded by our charges with no any other funding sources elsewhere.

Ethical clearance: The College of Medicine Research Ethics Committee of Hawler Medical University has approved this study for publication. Before being included in the trial, each patient gave their verbal agreement after being fully informed.

Conflict of interest: Nil

References

- [1] Sobera JO, Elewski B E. Fungal Disease. In: Bologna JL, Jorizzo JL, Rapini RP. *Dermatology*, 3rd ed, volume 1. New York: Mosby, 2012; 161-68.
- [2] HabifTP. *Clinical Dermatology*, 5th ed. China: Elsevier Mosby, 2010; 491-540.
- [3] Verma S, Heffernan, MP. Superficial fungal infection. In: Wolff K, Goldsmith LA, Katz SI, Gilchrist B A, Paller A S, Leffel DJ. *Fitzpatrick's Dermatology in General Medicine*, 7thed, Volume 2. New York: McGraw Hill, 2008; 1807-21.
- [4] Robbin C M, Elston D M. Tinea Pedis [Internet]. 2015 [Updated: Nov 19, 2015; cited 2016 JULY25]. Available from: <http://emedicine.medscape.com/article/1091684-overview>
- [5] Sterry W, Paus R, Burgdorf W. *Thieme Clinical Companions Dermatology*. 6th ed. Germany: Thieme; 2006; 123-126.
- [6] Hunter J, Savin J, Dahl M, Weller R. *Clinical Dermatology*. 4th ed. UK: blackwell; 2008; 248
- [7] Asadi M A, Dehghani R, Sharif M R. Epidemiologic study of onychomycosis and tinea pedis in Kashan, Iran. *Jundishapur Journal of Microbiology* 2009; 2(2): 61-4.
- [8] Fitzpatrick's JE, Morelli JG. *Dermatology Secrets Plus*. 4thed .China: Elsevier Mosby; 2007, 13; 456-67.
- [9] Szepletowski JC, Reich A, Garlowska E. Factors influencing coexistence of toe nail onychomycosis with tinea pedis and other dermatomycosis. *Arch Dermatol*. 2006; 146: 1279-84.
- [10] Wolff K, Johnson RA, Suurmond D. *Fitzpatrick's Color Atlas and Synopsis of Clinical Dermatology*. 5th ed. New York: McGraw-Hill, 2004; 692.
- [11] Rodgers P, Bassler M. Treating onychomycosis. *Am Fam Physician*. 2001; 63:663-8.
- [12] James W D, Berger T G, Elston D M. *Andrews Disease of the Skin Clinical Dermatology*. 11th ed. China: Saunders Elsevier; 2011; 294.
- [13] Dennis M. Dixon and Thomas J. Walsh. *Medical Microbiology*. 4th ed. USA: Galveston; 1996; 76
- [14] Burns T, Breathnach S, Cox N, Griffiths C. *Rooks Textbook of Dermatology*, 8thed . Singapore: Fabulous Printers Pte Ltd. 2010; 36-48
- [15] Crevits B, Picoto A, Staberg B, Urbanowski S, Silny W. Comparison of efficacy and safety of oral fluconazole and topical clotrimazole in the treatment of tinea corporis, tinea cruris, tinea pedis, and cutaneous candidiasis. *Curr Ther res*. 1998; 59 (7): 503-10

- [16] Jain s. *Dermatology Illustrated Study Guide and Comprehensive Board Review*. Uk Springer Science+Business Media, 2012; 203.
- [17] Korting H. C, Tietz H.J , Bräutigam M , Mayser P. , Rapatz G , Paul C. One week terbinafine 1% cream (Lamisil®) once daily is effective in the treatment of interdigital tinea pedis: a vehicle controlled study. *Med Mycol* 2001; 39(4): 335-40
- [18] Schopf R, Hettler O, Bräutigam M, Weidinger G, Kaben U, Mayser P , Resl V. Efficacy and tolerability of terbinafine 1% topical solution used for 1 week compared with 4 weeks clotrimazole 1% topical solution in the treatment of interdigital tinea pedis: a randomized, double-blind, multicentre, 8-week clinical trial. *Mycoses* 2002; 42(5): 415–20
- [19] . Evanse G. A comparison of terbinafine (Lamisil®) 1% cream given for one week with clotrimazole (Canesten®) 1% cream given for four weeks in the treatment of tinea pedis. *BJD* 2006;130(43): 12–14
- [20] Dodman B, Williamson D M, Brown GJ, Evans E G V, Bowen R G. Comparison of terbinafine and clotrimazole in treating tinea pedis. *BMJ* 1993; 307: 645-7.
- [21] Berman B, Ellis C, Leydon J, Lowe N, Savin R, Shupack J. efficacy of a 1 week, twice daily regimen of terbinafine 1 % cream in the treatment of interdigital tinea pedis: results of placebo-controlled, double-blind, multicenter trials. *JAAD* 1992; 26(6): 956-60.
- [22] Ledezma E, Marcano K, Jorquera A, De Sousa L, Padilla M. Efficacy of ajoene in the treatment of tinea pedis: A double-blind and comparative study with terbinafine. *JAAD* 2000; 43(5): 829–32
- [23] Evanse G. Tinea pedis: Clinical Experience and Efficacy of Short Treatment [Internet]. *Dermatology*.2009; 3: 194.

دراسة مقارنة لكريم تيربينافين (١٪) مع كريم كلوتريمازول (١٪) في علاج سعفة القدم (القدم الرياضية)

اراز حسن محمد^١، گوليخان احمد عمر^٢

المخلص

خلفية الدراسة: تينيا ببديس (القدم الرياضية) هي العدوى الفطرية الجلدية الأكثر شيوعاً في الجسم. قد يستمر لفترة قصيرة أو طويلة وقد يتكرر بعد العلاج.

اهداف الدراسة: لتقييم ومقارنة الكريمة الفعالة والسلامة بنسبة ١٪ من كريم التربينافين وكريم الكلوتريمازول بنسبة ١٪ لعلاج سعفة القدم (القدم الرياضية).

المرضى والطرائق: تم إجراء تجربة التحكم العشوائي في العيادة الخارجية لقسم الأمراض الجلدية في مستشفى ريزغاري التعليمي في أربيل. من مارس ٢٠١٩ إلى يناير ٢٠٢٠. تم تضمين ستين مريضاً يعانون من قسيده صغيرة من الأنف المنقوع سريريًا في هذه الدراسة. استخدم ثلاثون مريضاً كريم تيربينافين بنسبة ١٪ موضعياً مرتين يوميًا لمدة أسبوع واحد، وقام ثلاثون مريضاً بتطبيق كريم كلوتريمازول بنسبة ١٪ موضعياً مرتين يوميًا لمدة أربعة أسابيع. تم إجراء كشط الفطريات قبل العلاج وبعده. تم تقييم الفعالية من خلال العلاج السريري والعلاج الفطري. تم قياس العلاج السريري والفطري في الأسبوع الأول والرابع والسادس.

النتائج: كانت معدلات العلاج الفطري ٨٦,٧٪ للتربينافين و ٨٠٪ للكلوتريمازول في ٤ أسابيع، و ٨٦,٧٪ للتربينافين و ٩٠٪ للكلوتريمازول في ٦ أسابيع. في ٤ أسابيع، كان معدل العلاج السريري للتربينافين ٨٣,٣ في المائة وكان معدل العلاج السريري للكلوتريمازول ٧٦,٦٧ في المائة؛ في ٦ أسابيع، كان معدل العلاج السريري في تيربينافين ٨٣,٣ في المائة وكان معدل العلاج السريري في كلوتريمازول ٨٣,٣ في المائة.

الاستنتاجات: أظهرت الدراسة أن أسبوع واحد من التربينافين مرتين في اليوم فعال مثل أربعة أسابيع من الكلوتريمازول مرتين في اليوم وكذلك من حيث العلاجات الفطرية والعلاجات الفعالة.

الكلمات المفتاحية: تيربينافين. كلوتريمازول. سعفة القدم
البريد الإلكتروني: aras.sherwany@yahoo.com

تاريخ استلام البحث: ٢٤ آب ٢٠٢٢

تاريخ قبول البحث: ٢٧ ايلول ٢٠٢٢

^١ كلية الطب – جامعة هولير الطبية - اربيل - العراق

^٢ مستشفى رابرين التعليمي- اربيل - العراق