

# Management of Athlete's foot with topical Zinc Sulphate (15%) Solution versus Clotrimazole (1%) Solution

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### Abstract

**Background:** Athlete's foot (tinea pedis) is by far the commonest fungal infections of the integument in the developed world that usually begins between the toes. Multiple drugs were used for the treatment of athlete's foot and including both; topical and systemic agents.Zinc sulphate has been used as topical antifungal agent.

**Objective:** Comparison the efficacy of 15% zinc sulphate solution topically in the management of tinea pedis with topical clotrimazole solution.

**Patients and Methods:** A therapeutic, single blind, comparative, study of Zinc Sulphate solution (15%) in the management of tinea pedis in comparison with clotrimazole solution (both topically), that conducted in the Unit of Dermatology and Venereology ,Baquba Teaching Hospital, extended from March 2020- July 2021. Fifty patients, 31 males and 19 females with tinea pedis were registered in this study. Divided to 2 groups of patients included in the study:

Group A: Use the topical zinc sulphate solution 15%.

Group B: Use the topical 1% Clotrimazole solution.

A complete history with examination clinically were done for all patients with tinea pedis involving all the relevant points. All patients were used the medicine twice daily for 30 days, and follow there to be seen every 14 days during the course of treatment and then follow up for two months. The patients were examined clinically; also the scoring of feet odor was done at each visit.

**Results:** Group A: Twenty five patients 9 (36%) females and 16 (64%) males were included in this group were treated by Zinc Sulphate solution , and their ages ranged between  $27-73(47.8\pm12.18)$  years. and the duration of that illness was ranged from  $1-120(43\pm46.61)$  months. Clinical response after one month of the treatment was 10(40%) patients with complete clearance, 5(20%) patients had partial clearance while 10(40%) patients showed no response.

Group B: Twenty five patients treated by clotrimazole solution, and their ages ranged from  $24-65(43.2\pm11.83)$  years, and the duration of the illness was ranged from  $1-180(30.24\pm44.9)$  months. Clinical response after four weeks of treatment was 19(76%) patients with complete response, 2(8%) patients had partial response, while 4(16%) patients have no response.

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There was no statistical significance difference at two weeks in comparison between group A and B (chi square 5.37 P value =0.07) but was slightly significant at four weeks (chi square 6.65, P value =0.04). Side effects of treatment were mild which included itching and burning sensation in 4(16%) patients of group A and in 1(4%) patients of group B. These side effects did not require discontinuation of the treatment. **Conclusion:** Clotrimazole solution was superior to15% Zinc sulphate solution as effective as topical treatment for Athlete's foot. **Keywords:** Tinea pedis, topical zinc sulphate, clotrimazole

# Introduction

Athlete's foot or tinea pedis is one of the commonest fungi that infect the skin in the humans being. Also its common superficial fungal infection in developed countries. The most frequent dermatophytes that cause it Trichophyton rubrum(the most common and the most stubborn). T. mentagrophytes var. interdigitale and less by Epidermophyton floccosum, and the most cases are caused by that one of three organisms. The infected individual acts as a carrier, since when the infection occur, the organism may lasting as long as in the host [1]. Athlete's foot is more common in the adult than in children and more in males than women. The infection with tinea pedis occurs by the contact directly with arthroconidia (that produced by the filaments of dermatophyt), wearing of the tightly-fitting shoes also enhance the infection and it's spreading (spores in occlusive footwear encourage relapses) [2]. The sharing of wash places, like the swimming pools, gymnasia, changing rooms of sports clubs and the public showers predisposes to infection [3]. Athlete's foot considered as chronic fungul infection that often with remission with treatment and relapse thereafter, so the management is consider usually not so easy. There are many systemic drugs and include; terbinafin,,, itraconazole, and fluconazole. Topical antifungal medications like, allylamine,

azole, ciclopirox, tolnaftate and undecenoic acid have been used in the treatment of Athlete's feet [4]. Many of the drugs are used as antifungal drugs (azoles group and allylamines) that used currently in general practice for treatment of Athlete's foot have been shown to be less than satisfaction in eliminating the disease, even with good compliance from the treated patient. Azoles group that act as  $14\alpha$ -demethylase inhibitor of fungi and prevent the synthesis of the ergosterol; however, azoles group also inhibit the cytochrome P450 enzymes of mammalian. Allylamines the prevent formation of squalene epoxidase, that enzyme is crucial for the formation the cell membrane of the fungi, and have no effect on the mammalian cytochrome P450-dependent enzymes [5, 6].

Odor in the Athlete's feet which is a common socio-medical issue, that could be caused either by the fungi of tinea pedis itself or by the associate microorganism like Brevibacteria( most one impotant for feet odor), as these microorganisms take the dead corneocytes on the feet and produce a cheesy odor and the sulfuric aroma, by the process that produce methanethiol from an amino acid (methionine). While Propionibacteria which present in the sebaceous glands ducts of the adolescent and adult it has vinegar-like odor as a result of propionic acid which result



from the breakdown product of amino acids. Another microorganism that contributes to the feet odor is the Staphylococcus epidermidis that produce isovaleric acid by the degradation of the leucine that present in the sweat and give a strong cheesy odor [7, 8].

Zinc is an important micronutient that is an essential component for more than 300 metalloenzymes that involved in a variety in metabolic pathways and cellular functions, that include the antioxidant enzymes. superoxide dismutase and affects their stability, conformity, and activity [9]. Zinc sulphate was effective in the treatment of many skin diseases, where it used in the topical, intralesional or systemic formula, acne vulgaris [10], recurrent oral like aphthus [11], cutanous leishmaniasis [12,13], many form of viral warts like plane warts [14], other viral infections [15,16], Tinea versicolor [17], and dermatophytes fungal infections [18]. The action of zinc sulphate by the different mechanism of action that may be as antioxidant. immunomodulator, antiviral, anti-fungal, while it is cytotoxic in high astringent, concentration [19].

So, objective of the study is to compare the efficacy of topical 15% zinc sulphate solution in the managment of Athlete's feet in versus the topical clotrimazole solution.

# **Patients and Methods**

# Study protocol

The single-blind, comparative therapeutic study using topical 15% zinc sulphate solution with 1% clotrimazole solution for the management of tinea pedis was executed in the Unit of Dermatology, BaqubaTeaching Hospital between March 2020- July 2021.Fifty patients, 31 males and 19 females with tinea pedis were involved in this work. **Study design** 

The chief compliant is the tinea pedis (interdigital type) in all patients that attending to the Unit of Dermatology were only included regardless the age and sex. Full history were including: age of patients, sex, marital status, residence, social status, job, and history of the disease itself, including the duration, complaint of the patient, duration, associated with odor, family history, any seasonal variations and what is the aggravating factors. A socks

type that been used, frequency of changes per day and type of the shoes also asked to all patients. In addition to history of drug intake that associated with sweating including aspirin, fluoxetin and insulin.

The assessment of severity of the disease in all cases was performed including :clinical examination to the lesion, and address the site, any changing in color, presence any of the dry scales, wet scales ,maceration , erythema and skin scraping test .Also the associated feet odor was assessed and scored. Evaluation of the patients was done every two weeks for one month and follow up was carried out. Photo for all lesions of the patients were taken by a digital camera (Sony:Cyber shoot with resolution 9 mega pixels), as a first visit(baseline) and then every other 14 days, in the same circumstances (place with fixed illumination and distance).

### Study population

Exclusion criteria: patients were received no therapy for tinea pedis in the last two months prior the study. Patients with diabetes mellitus or atherosclerosis that may cause



complications in the feet; deformity and malformation of the feet and immunosuppressant conditions were also excluded from the study.

## Preparations

Fifteen percent of the zinc sulphate solution 15% (W/V) was produced by thawing zinc sulphate crystals (ZnSO4 7H2O=287.54 It is manufactured by: Thomas Bekar India), 15 grams in 100 ml of Distilled Water, and kept in cleaned container at the room temperature of hospital and Clotrimazole(1%) solution is obtained from MEDICO LABS\_SYRIA.

#### **Clinical response score**

No clearance: - If there is no any response while clinically examine and no change in scoring of feet odor.

Partial clearance: - If there is some clinical improvement,like change of wet scales into dry scales, abscence in scales and change in feet odor.

Complete clearance: - There is complete clearance of rash and odor

### Scoring of feet odor

The scoring system had been used to assess the patients with bared feet and any odor and to evaluate the odor intensity in that case and involve four points:

*Score 0*: No any odor.

<u>Score1</u>: mild; the odor is smell only when the patient's finger put between the toe webs of his sole.

<u>Score2</u>: Moderate; when the doctor in close to the patient can smell the odor.

*Score 3:* Severe; the surrounding people can smell the odor.

# **Statistical Analysis**

It done by Excell 2010, SPSS version 20 statistical program.P\_value is considered

significant when less than 0.05, It done by Excell 2010, SPSS version 20 statistical program.

# Results

Group A: Twenty five patients 16 (64%) males, 9 (36%) females involved in this group, with ages ranged from 27-73 and a mean± SD of 47.8±12.18 years. While the disease duration ranged between 1-120 and a mean $\pm$  SD of 43 $\pm$ 46.61 months. Also repeated foot washing ranged from 2-10 with a mean $\pm$  SD of 5.24 $\pm$ 2.66 times/day. Twenty four (96%) patients had a feet odor and the manner of feet odor was cheesy odor in 20 (80%) patients and vinegar odor in 4 (16%) cases while 8 (32%) patients had itching. 17 (68%) of cases presented with seasonal variation with tinea pedis that worsened during the summer time, while 16(64%) of had associated with patients plantar hyperhydrosis.While 10 (40%) cases madet drying of foot after the washing as a habit while others were not.

The socks types were nylon in 17(68%), cotton 6(24%) and wool 1(4%) patient. Frequency of socks changes around the day of was presented in 15(60%) patients. The shoes types of were leather 9(36%), sandal 10(40%), and rubber 6(24%) patients. Histories of drugs were aspirin in 5(20%) patients while 7 (28%) patients presented with positive family history of tinea pedis. The factors that aggravating of tinea pedis were the hyperhidrosis present in 7(28%), occlusive the feet wear in 10(40%) and nylon socks 8(32%) patients Table (1).

Scoring of feet odor before treatment was Score 0: in 1(4%) patients, Score 1: 20(80%) patients and Score 2: 4(16%) patients Table (2).



Group B: Twenty five patients presented with tinea pedis were involved in this study, 10(40%) females and 15 (60\%) males. The ages were ranged from 24-65 with a mean± SD of 43.2±11.83 years, and the disease duration were ranged from 1-180 months, and the mean± SD of 30.24±44.9 months. Also repeated foot washing ranged from 1-10 and the mean± SD of 4.84±2.15 times/day.

Twenty (80%) of patients had feet odor and also the tinea pedis, while 8 (32%) patients reported a positive family history of tinea pedis, itching was found in 9 (36%) patients. The quality of odor was cheesy odor in 20 (80%) patients and vinegar odor in 2 (8%) patients.While 12 (48%) of caseshad history of variation around the seasons with worse odor during the summer time, and 19(76%) of patients had associated with plantar hyperhidrosis,and 12 (48%) patients had drying habit to the feet after washing while others were not.

Types of the socks that used by patients were nylon in 10(40%) patients, cotton 6(24%) and wool 4(16%) patients. Daily changed frequency of the socks were presented in 10(40%) patients and others not. Types of the shoes were: leather 10(40%), sandal 12(48%) and rubber 3(12%) patients. History of drugs was: aspirin in 2(8%)patients.

Factors that may aggravate of the feet odor were occlusive feet wear 10(40%), hyperhidrosis in 10(40%) patients, and nylon socks 5(20%) patients Table (1).

Scoring of the odor before starting the therapy was Score 0: in 3 (12%) cases, Score 1: in 20 (80%) cases and Score 2: in 2 (8%) cases Table (3)

# The clinical assessment among tinea pedis patients

Group A: Clinical scoring of the odor in the tinea pedis after 2 weeks of treatment was Score 0: 1 (4%) patient. Score 1: 20 (80%) patients that changed into score 0 in 10(50%) patients, and not changed in 10(50%) patients. Score 2: 4 (16%) patients changed into score 0 in 2(50%) patients, and not changed 2(50%).

Scoring of the Athlete's feet odor after one month of treatment was:

Score 0: 1 (4%) patient. Score 1: 20 (80%) patients changed into score 0 in 12(60%) patients, and not changed in 8(40%) patients. Score 2: 4 (16%) of patients that changed into score 0 in 2(50%) patients, and score 1 in 1(25%) patient and no change 1(25%) Table (2).

After two weeks of treatment, 2(8%) patients showed complete clearance, 9(36%) patients had partial of clearance and 14(56%) patients that showed no response Table (4).

While clinical response after four weeks of the treatment was 10(40%) patients was complete clearance, 5(20%) patients had partial clearance and 10(40%) patients showed no response.

The clinical response in that patients have the difference between two weeks and four weeks and was significant (chi square 7.14 P value =0.03).

Itching and burning sensation in 4(16%) patients on treatment were mild side effects and these did not require discontinuation of the drugs.

<u>Group B:</u> Scoring of the odorin tinea pedis foot after 2 weeks of treatment was

*Score0*: 3 (12%) patients. *Score1*: 20 (80%) patients that changed into the *score 0* in 15



(75%) patient, and thre is no clinical diffrence in 5 (25%) of cases. *Score2*: 2 (8%) patients changed into *score 1* in 1(50%) patient and no difference in 1 (50%).

Scoring of the odor of feet after one month of treatment was:

Score 1: 20 (80%) patients changed into score 0 in 17 (85%) of the cases, and no changed in 3(15%) patients. Score2: 2 (8%) changed into score1 in 2 (100%) patients Table (3).

After two weeks of beginning of the treatment, 4 (16%) patients showed complete clearance, 15 (60%) patients had partially clearance and 6 (24%) patients with no response Table (4).

While clinical response after four weeks from the treatment was 19 (76%) patients was complete response, 2 (8%) patients had partially responded, and 4 (16%) patients showed no response Table (4).

The clinical response was also significant (chi square 20.12 P value =0.000043) in that patients between two weeks and four weeks of treatment.

Side effects of treatment were mild which included itching and burning sensation in 1(4%) patient. These side effects did not require discontinuation of the medicine.

There was no significant difference statistically in two weeks (chi square 5.37 P value =0.07) in the comparison between group A and B ,but was slightly significant at four weeks (chi square 6.65, P value =0.04).

	Grou	p (A)	Group (B)		
	Number	(%)	Number	(%)	
1- Family history	7	28	8	32	
2-Iching	8	32	9	36	
4-Type of odor					
Cheesy odor	20	80	20	80	
- Vinegar odor	4	16	2	8	
5- Associated with sweating	17	68	19	76	
6-Season variation	16	60	12	48	
7-Drying of feet	10	40	12	48	
8-Types of socks					
-Nylon	17	68	10	40	
-Cotton	6	24	6	24	
-Wool	1	4	4	16	
-Daily changing	15	60	10	40	
9-Types of shoes					
- Leather	9	36	10	40	
-Sandal	10	40	12	48	
-Rubber	6	24	3	12	
10-Drugs history					
-Aspirin	5	20	2	8	
11-Aggravating factors					
-Hyperhydrosis	7	28	10	40	
-Occlusive footwear	10	40	10	40	
-Nylon socks	8	32	5	20	

**Table (1):** Study groups description the (tinea pedis)



Scoring before therapy	Scoring	Score 0 (1) pt	%	Score1 (2) pt	%	Score2(4) pt	%	total	%
Scoring	Score0	1	100	15	75	2	50	18	72
after	Score1	0	0	5	25	1	25	6	24
Therapy	Score2	0	0	0	0	1	25	1	4

\*p value=0.0000001

Table (3): Feet odor scoring of the (Group B) after one month of treatment

Scoring before treatmen t	Scoring	Score 0 (3) pt	%	Score1(2 0) pt	%	Score2 (2) pt	%	total	%
Scoring	Score0	3	100	17	85	0	0	20	80
after	Score1	0	0	3	15	2	100	5	20
Therapy	Score2	0	0	0	0	0	0	0	0

 Table (4): Clinical response among patients with tinea pedis

	At two weeks						At four weeks						
	No clearance		Partial clearance		Complete clearance		No clearance		Partial clearance		Complete clearance		
	n.	%	n.	%	n.	%	n.	%	n.	%	n.	%	
Group A	14	56	9	36	2	8	10	40	5	20	10	40	
Group B	6	24	15	60	4	16	4	16	2	8	19	76	



Figure (1A): Tinea pedis(interdigital type) before 15% topical zinc sulfate solution application





Figure (1B): Same patient above after one month of 15% topical zinc sulfate solution application

### Discussion

Athlete's foot considers the commonest form of dermatophyt skin infection in the North America, United Kingdom, and probably throughout the developed world [20]. It is common in adults than more in children, but may also occur in children younger age 6years or more [21]. The chance for presenting with tinea pedis in adult males probably about 20%, while among women to become chronically infected with tinea pedis only about 5% [21]. It is a common problem seen among males and housewives, in Iraqi patients it accounted about (4.3%), with a mean age of 29 years and ranged from 17-53 years [22].

Three species of fungi are together responsible for the vast majority of cases of Athlete's foot throughout the world. Trichophyton rubrum, Trichophyton mentagrophytes var. interdigit ale, and also Epidermophyton floccose. The Trichophyton consider the most common rubrum is pathogen that associated with stubborn and chronic Athlete's foot [1].

Trauma, with the excessive moisture, and occlusive shoes, and also the frequent usage of public showers and pools these factors that might contribute to increase risk of infection: [23].

There are generale measurement in treatment of tinea pedis like wash of feet daily with drying thoroughly, avoid tight footwear, especially in the summer and avoid walking barefoot in the public areas, wear cotton socks and change them frequently and also wearing the plastic shoes or other of the footwear that do not allow sweat to be evaporate easily best to be avoided [24].

Many of the systemic drugs like terbinafine,, itraconazole, and fluconazole, also topical antifungal drugs like, allylamine, azole, ciclopirox, benzylamine, tolnaftate and undecenoic acid have been used to treated the tinea pedis [4].

Feet odor is common sociomedical problem among males and it's etiology and pathogenesis is not well understood but there are multifactorial agents that play a role like weather,sweating,with bacterial, and fungal



infections, wearing closed shoes and socks [7].

The study showed that zinc sulfate was good agent in clearance of feet odor and probably work through its antibacterial and antifungal actions.

Zinc is an essential trace element that has direct anti-dermatophytes action in vivo and vitro [25] ,and had been shown to be an effective remedy in the treatment of pityriasis versicolor,Sharquie et al observed complete clinical and mycological clearance after 3 weeks treatment with 15% of zinc sulphate in the treatment of tinea versicolor [17].and other superficial fungal infection [18].Sharquie et al in a single blinded placebo controlled therapeutic trial studied the efficacy of 15% zinc sulphate solution for the treatment of foot odor [27].

## Conclusions

Topical solution of 15% zinc sulphate was an effective treatment for tinea pedis and clearance of feet odor.

### Recommendations

Our knowledgement To be better, the study that carried out and were observe the Zinc sulphate is an effective mode of treatment that used in the management of tinea pedis as 40% of patients had complete clearance but it was less superior than clotrimazole solution which gave76% clearance rate.

To increase the effectiveness of topical zinc sulphate a higher concentration like 25% is recommended [26].

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**Ethical clearance:** Ethical approval was obtained from the College of Medicine /

University of Diyala ethical committee for this study.

# Conflict of interest: Nil

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# دراسة منفردة التعمية مقارنة لعلاج سعفة القدم بسلفات الزنك 15% مقارنة بمحلول الكلوتريمازول 1%

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### الملخص

خلفية الدراسة: سعفة القدم هو عدوى فطرية جلدية تبدء بين اصابع القدمين عادة و هي شائعة لدى الاشخاص الدين تصبح اقدامهم شديدة التعرق اثناء انحشار ها داخل الاحدية الضيقة. اهداف الدراسة: لتقييم فعالية سلفات الزنك 15% في علاج سعفة القدم بالمقارنة مع محلول الكلوتريمازول 1%. يعقوبة التعليمي والطرائق: تجربة منفردة التعمية ومقارنة املاح سلفات الزنك 15% مقارنة ب الكلوتريمازول 1%, في مستشفى بعقوبة التعليمي قسم المرضى ال مجموعتين, مجموعة (ا) عواجت بسلفات الزنك 15% مرتين يوميا , مجموعة (ب) عواجت بمحلول الكلوتريمازول 1% مرتين يوميا. مع المتابعة كل اسبوعين. المنتابع: مجموعة (ا) 25 مريض مدة المرض 1-200 شهر عواجت بسلفات الزنك وبعد المتابعة باربعة اسابيع من العلاج كان الشفاء التام 40% و 40% لم يستجيبوا العلاج , ومجموعة (ب) 25 مريض علاجها بمحلول الكلوتريمازول و 21% الشفاء التام 40% و 40% لم يستجيبوا العلاج , ومجموعة (ب) 25 مريض علاجها بمحلول الكلوتريمازول و كانت مدة المرض بين 1-180 شهر , وبعد اربعة اسابيع من العلاج كان الشفاء التام 76% و 16% لم يستجيبوا للعلاج . المرض بين 1-180 شهر , وبعد اربعة اسابيع من العلاج كان الشفاء التام 70% و 16% لم يستجيبوا للعلاج. الاستنتاجات: املاح سلفات الزنك 11% فعالة في علاج سعفة القدم , لكن الكلوترمازول فعال اكثر . البريد الاكتروني: 100% منه العلاج في علاج سعفة القدم و الكالوترمازول فعال اكثر . المرض بين 1-100 شهر , وبعد اربعة اسابيع من العلاج كان الشفاء التام 76% و 16% لم يستجيبوا للعلاج. المرض بين 1-100 شهر . وعد اربعة العابيع من العلاج كان الشفاء التام 16% و 16% لم يستجيبوا للعلاج . المري الاكتراني المقتلوية : سعفة القدم ، كبريتات الزنك الموضعية، كلوتريمازول

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