**Extended Abstracts Tolnaftate**

**High W.A., Fitzpatrick J.E. (2008). Chapter 219. Topical Antifungal Agents. In K. Wolff, L.A. Goldsmith, S.I. Katz, B.A. Gilchrest, A.S. Paller, D.J. Leffell (Eds), *Fitzpatrick's Dermatology in General Medicine*, 7e. Retrieved July 8, 2012 from http://www.accessmedicine.com.proxy2.lib.uwo.ca/content.aspx?aID=2969866.**

Source description

- This textbook is published by The McGraw-Hill Companies in 2008
- This textbook is written is written by experts in the field of dermatology, mostly physicians
- The information provided is supported by primary literature

Summary

The authors stated that based on repeated studies tolnaftate and undecylenic acid have demonstrated to be approximately equal in efficacy and that they are both less efficacious than topical imidazoles, allylamines, benzylamines, and ciclopirox olamine. Topical tolnaftate and topical undecylenic acid share the same risks and precautions inherent to all topical medications. Monitoring for treatment failure is indicated when using these medications as they are less efficacious than imidazoles. The authors state that early studies demonstrated a cure rate for tinea pedis as high as 73% to 93%, but later studies demonstrated lower efficacy that is equivalent to that of undecylenic acid.

Comments/Critical Appraisal

This source has good internal validity as the authors provided valid recommendations that were supported by primary literature. It also has good external validity as they comment on the effectiveness of tolnaftate compared to other agents available in patients with tinea pedis. In addition, they provided information with regards to tolnaftate's efficacy in comparison to other anti-fungal agents. This information in turn will aid in the selection of anti-fungal agents for patients experiencing tinea pedis.

**Canadian Pharmacists Association. Patient Self-Care: Helping You Patients Make Therapeutic Choices. In: Mallin,A. Athlete's Foot. 2nd ed. Ottawa, ON: Canadian Pharmacists Association; 2010: 489-493.**

Source Description

- This book is published by the Canadian Pharmacist Association in 2010 (this is the second edition of the book)
- Each chapter is written by experts in the field
- The information in each chapter is supported by primary literature and practice guidelines.
- Credible source; used by most pharmacists to obtain information about self care therapeutic choices

Summary

The author of this chapter states that non-prescription topical agent such as tolnaftate is effective in providing symptom relief and curing infection. Furthermore, it should be applied twice daily to the affected area (plus 2 cm beyond on clean, dry feet for up to 4 weeks, including 1-2 weeks after the lesion has disappeared, to prevent recurrences). The author states that tolnaftate is generally well-tolerated with the most common adverse reactions being minor local symptoms (burning, stinging). It should not be used in children less than 2 years old unless otherwise directed by a physician. The authors also state that tolnaftate (antifungal powder formulation) can be used as a preventative measure in individuals with a history of athlete's foot.

Comments/Critical Appraisal

This source has good internal validity as the author provided valid recommendations that were supported by primary literature and guidelines. However, the authors did not include any information with regards to their research strategy (i.e. how they obtained the information) which may in turn affect the internal validity of the source. This source does not have good external validity as it does not provide clear guidelines with regards tolnaftate's place in therapy and therefore it's difficult to know when tolnaftate should be used in comparison to the other antifungal agents. In addition, it does not provide any information with regards to the cure rates for tolnaftate and the other agents.

**Markova, T. 2002. What is the most effective treatment for tinea pedis (athlete's foot)? The Journal of Family Practice. Vol. 51 No.1. Accessed online on July 8, 2012 via** http://www.jfponline.com/Pages.asp?AID=1080#bib2

Source Description

- The Journal of Family Practice
- This particular journal is written by a physician
- The date of last update was on January 2002

Summary

The authors state that the two topical OTC antifungals: tolnaftate and miconazole, require at least 2 to 4 weeks to achieve slightly lower cure rates compared to terbinafine, but are considerably less expensive. The author makes a reference to a Cochrane Review that included 72 placebo-controlled trials of topical agents that yielded the following cure rates: undecenoic acid, 72%; allylamines (terbinafine, naftifine, butenafine), 70%; tolnaftate, 64%; azoles (miconazole, clotrimazole, ketoconazole, econazole, oxiconazole), 47%. Furthermore, the author makes a reference to a meta-analysis of 11 RCTs that suggests that allylamines are slightly more effective than azoles.

Comments/Critical Appraisal

The internal validity of this article is good as the author makes reference to high quality level of evidence such as a Cochrane review and a meta-analysis. The external validity of this article is good as it provides information about the cure rates for each anti-fungals which would then help in the selection of antifungals for patients presenting with athletes' foot.

**Ongley R. Efficacy of topical miconazole in the treatment of tinea pedis. *CMAJ*. 1978; 119: 353 – 354.**

**Study Objective**
The author's main objective was to determine the efficacy of 2% miconazole cream in the treatment of bilateral tinea pedis, as compared to 1% tolnaftate cream and placebo.

**Methods**
**Design:** randomized, placebo-controlled, double-blind trail
**Allocation:** The preparations were assigned numerically in coded tubes, and patients were randomized equally to each of the tubes (each foot was treated differently; 20 feet per tube)
**Blinding:** Double-blind
**Follow-up period:** Clinical assessment was recorded on days 14 and 28 during therapy, and at 6 weeks after therapy. Mycologic examination was performed at the completion of therapy and at the follow-up visit
**Setting:** An extended care hospital
**Participants:** 30 males who were patients at the hospital were enrolled in this study; these patients had bilateral, chronic, non-blistering tinea pedis, proven by examination of scales in KOH and by culture. None had received therapy for tinea pedis in the preceding 6 months.
**Intervention:** 2% Miconazole cream compared to 1% tolnaftate cream and placebo, each applied twice daily for 28 days.
**Outcomes:** The primary outcomes in this trial were the efficacy (clinical and mycologic improvement) of the creams after 28 days of therapy
**Patient follow-up:** All 30 patients were followed up at 6 weeks after the start of therapy
**Main Results:** At day 14 of therapy, treatment with tolnaftate had the highest clinical improvement numbers, 20 out of 20 treated feet, compared to 8 in the placebo group and 19 in the miconazole arm. When therapy was completed, clinical and mycological examination showed that 19 out of 20 feet in the miconazole arm were cured, as compared to 10 in the placebo group and 15 in the tolnaftate group. At the six week follow up, all of the patients who had a cure at the 4 week mark with miconazole had remained free of infection, whereas only 2 in the placebo group and 13 in the tolnaftate group remained free of infection.
**Conclusions**
Tolnaftate proves to be a useful agent in the treatment of tinea pedis, however, it was shown to be slightly inferior to miconazole.

**Comments**
The authors in this study wanted to compare the efficacy of miconazole to tolnaftate and then, compare both agents to placebo. This study concluded that miconazole has an exceptional cure rate and a lower relapse rate as compared to tolnaftate and placebo, making the tolnaftate an inferior option for athlete's foot and azoles superior.

The strengths of the study are: study design (double blinded, placebo controlled trial, randomization). The patient population was small, all participants were males and no other demographic information was provided. Follow up was appropriate given the condition being treated (Follow up occurred on day 14 and day 28 of therapy and then, at 6 weeks after initiating treatment). None of the participtants dropped out which increases the external validty of this study. For the patients who got two active creams for their feet, the effects of inter-patient variability were non-existent for the anti-fungals and it gave a clearer comparison. Each foot was analyzed with respect to all the feet in the same treatment arm. The presence of cure in the placebo arm was most likely due to the fact that the placebo cream contained ethylene glycol, which has some antimicrobial properties.

This paper also gives evidence for the placement of these two agents in the treatment hierarchy for athlete's foot; if tolnaftate does not work, miconazole would be an option. Alternatively, miconazole could be used as the first-line agent.

**Crawford F et al. Athlete's Foot and Fungally Infected Toenails. *BMJ*. 2001; 322: 288 – 289**

**Study objectives**

To determine the effectiveness and safety concerns of different topical treatments for athlete's foot and fungally infected toenails.

**Scope**

The main outcomes for the studies that were reviewed were the rates of fungal eradication and the clinical improvement of symptoms.

For allylamines, the authors looked at a systemic review dealing with 12 randomized controlled trials for agents like terbinafine against placebo for 4 weeks. 1433 patients with athlete's foot were included in this trial and follow-up was 6 – 8 weeks. A smaller randomized control trial compared allylamines to one another for treatment efficacy in 60 patients.

For azoles, 17 randomized controlled trials containing 1259 patients with athlete's foot were looked at. The duration of treatment was for 4 weeks and all were against placebo. Follow up was 6 – 10 weeks. Another 12 randomized controlled trials compared the azoles to each other; 584 patients were treated for 3 – 4 weeks and follow up was from 3 – 10 weeks. Finally, azoles were also compared against the allylamines; 12 randomized controlled trials were found. 1487 patients with athlete's foot either had 4 weeks of azole therapy or 1 – 6 weeks of allylamine therapy.

Other topical anti-fungal medications, like undecenoic acid and tolnaftate, were also addressed in one systemic review. One randomized controlled trial compared ciclopiroxolamine to placebo in 144 patients with a fungal foot infection for 4 weeks, with a follow up in 6 weeks. Another randomized controlled trial looked at topical griseofulvin against placebo in 94 patients. Undecenoic acid against placebo was found in 4 randomized controlled trials; 223 patients were treated. Lastly, a four week therapy of tolnaftate versus placebo was in 3 randomized controlled trials that included 148 people and a follow up of 5 – 8 weeks.

In nail infections, only one systematic review was found, containing two randomized controlled trials with a total patient population of 153 people. These studies unfortunately did not report the blinding or the method of randomization.

**Methods**

**How studies were identified:** The authors searched Medline, Embase and the Cochrane Controlled Trials Register for systematic reviews and randomized control trials

**Number and type of trials included:** Systematic reviews, containing randomized controlled trials, and other randomized controlled trials were included. Papers that did not use microscopy and culture for diagnosis or as an outcome measure were excluded, as were any studies that did not contain information pertaining to the feet.

**Other relevant information:** As noted by the authors, some of the trials looked at did not report patient demographic information or the method of randomization.

**Main results**

For allylamines, the larger systematic review found that they reduced the risk of treatment failure; the absolute risk reduction was 54% and the relative risk reduction was 67%. The number needed to treat was 2 after six weeks. The authors found that for comparing one allylamine to the other, there was no significant difference between naftifine and terbinafine (absolute risk of treatment failure was

75% and 81% respectively). Although this review did not report the frequency of side effects, the authors found that topical allylamines had few reports of severe local irritation.
The authors found that azoles also reduced the risk of treatment failure; the absolute risk reduction was 42% and the relative risk reduction was around 69%. The number needed to treat was 2. There were no significant differences between the azoles and as compared to the allylamines, azoles had similar efficacy. It was noted, however, that allylamines could be applied for a shorter duration (1 week) to get the same results as a 4 week azole treatment. Again, this review did not specify adverse effects, but the authors found reports of local irritation.
For the other topical agents, ciclopiroxolamine also reduced the risk of treatment failure; its absolute risk reduction was 48%, with a relative risk reduction of 52%. Griseofulvin had similar results with an absolute risk reduction of 47% and a relative risk reduction of 71%. Undecenoic acid also had similar numbers with an absolute risk reduction of 46% and a relative risk reduction of 59%. Finally, tolnaftate had an absolute risk reduction of 44% and a relative risk reduction of 63%. All of these agents had a number needed to treat of 2. These studies also did not report adverse events.
In nail infections, the systematic review had insufficient evidence to draw conclusions.

**Conclusions**
In short, the authors categorized the different topical agents in terms of their effectiveness. Those that entered the "Beneficial" category included the allylamines, the azoles, undecenoic acid and tolnaftate. Those that were placed in the "Likely to be Beneficial" category were topical ciclopiroxolamine and topical griseofulvin. Finally, for fungal nail infections, the topical treatments looked at were placed in the "Unknown Effectiveness" category, due to the authors' inability to draw conclusions on the insufficient evidence presented.

**Comments**
Systematic review based in the United Kingdom, the authors' looked at the clinical cure rates and the resolution of symptoms at follow up for different anti-fungals.
Although a smaller scope of databases was searched, the trials were up to May 2000, making it more current. There was no mention of MESH terms or patient demographics. Tolerability was not included in this review, but the authors did mention that from a few trials, only mild, local irritation was reported with the topical products. This review did not give many details in terms of its methods and this is a huge drawback. However, the sample size from all the trials looked at was relatively large for most of the agents. In addition to this, the only included trial types were randomized controlled trials and systematic reviews, which are very reputable sources. There were multiple trials that were assessed: most versus placebo, but the allylamines and azoles did have head-to-head studies. Numbers needed to treat were included in this study along with absolute risk reduction and 95% confidence intervals. In this review, there was more evidence for tolnaftate and its effectiveness for treating athlete's foot. Although allylamines had faster cure rates than azoles, there was a discrepancy in whether or not allylamines have a significant improvement in the rate of cure.