

# The Use of 40% Urea Cream in the Treatment of Moccasin Tinea Pedis

Boni E. Elewski, MD; Heather R. Haley, MD; Courtney M. Robbins

*Moccasin tinea pedis is a chronic dermatophyte infection of the foot that is recalcitrant to topical antifungal therapy. Furthermore, most patients with moccasin tinea pedis also have onychomycosis, thus adding to the recalcitrant nature of the infection. The topical antifungals used as sole therapy are generally ineffective because the scale on the plantar surface impedes or limits the absorption of the antifungal agent. The aim of this study was to evaluate the efficacy of 40% urea cream as an adjunct to topical antifungals in the treatment of moccasin tinea pedis. Patients with untreated moccasin tinea pedis were selected from the general dermatology clinic. The diagnosis of moccasin tinea pedis was made clinically and confirmed with a potassium hydroxide test or a positive fungal culture. A total of 12 patients with moccasin tinea pedis were treated with 40% urea cream once daily and ciclopirox cream twice daily. Patients then were evaluated after 2 to 3 weeks of treatment for the presence of erythema, scaling, and pruritus. After 2 to 3 weeks, a 100% cure rate was achieved in the 12 patients treated with topical 40% urea cream and ciclopirox cream concomitantly.*

*Cutis.* 2004;73:355-357.

Accepted for publication December 3, 2003.

Dr. Elewski is Professor of Dermatology, and Dr. Haley is a resident in Dermatology, Department of Dermatology, University of Alabama at Birmingham. Ms. Robbins is a medical student at the University of Mississippi, Oxford.

Dr. Elewski is a consultant for Novartis Pharmaceuticals Corporation, Bradley Pharmaceuticals, and Pfizer Inc. Dr. Haley and Ms. Robbins report no conflict of interest.

Reprints: Boni E. Elewski, MD, Department of Dermatology, University of Alabama at Birmingham, 1530 3rd Ave S, EFH 414, Birmingham, AL 35294-0009 (e-mail: beelewski@aol.com).

Dermatophytosis of the feet has long been the most common fungal disease. *Trichophyton rubrum*, the most common etiologic agent, is responsible for a dermatophytosis known as *moccasin tinea pedis*, which usually affects the entire plantar surface and sides of the foot.<sup>1,2</sup> Patients with moccasin tinea pedis present with a chronic “dry type” infection with varying but often severe erythema and thick, hyperkeratotic scale. The infection is commonly recalcitrant to topical antifungal therapy alone. Involvement is most frequently bilateral and commonly associated with onychomycosis, thus adding to the vexing nature of the infection.<sup>1</sup>

Common treatment options for tinea pedis include topical antifungals, usually for up to 4 weeks.<sup>3</sup> However, the efficacy of topical antimycotics as sole therapy often is limited in moccasin tinea pedis. The thick scale on the plantar surface of the foot, which impedes absorption of the antifungal agent, is the common culprit.<sup>4</sup> Consequently, adjunctive oral therapy for 1 to 4 weeks is often necessary, thereby contributing to the potential adverse effects and interactions of the drug.<sup>1,5</sup>

In searching for better topical treatment of recalcitrant moccasin tinea pedis, the characteristic thick scale must be addressed. Topical keratolytics, such as 40% urea cream, are a practical approach to this problem. By dissolving the intercellular matrix and augmenting the shedding of scale, topical urea cream is a potent tissue softener for skin and nails. Through this keratolytic mechanism, topical urea cream may work synergistically with and increase the efficacy of topical antifungals in the treatment of moccasin tinea pedis. Several studies have, in fact, shown the usefulness of 10% to 20% urea cream and various topical imidazoles in the treatment of onychomycosis and tinea pedis.<sup>6-10</sup> In addition, 40% urea cream alone has been found to possess antifungal properties in reducing fungal counts of *T rubrum*.<sup>11</sup>

### In Vitro Activity of 40% Urea Cream and Ciclopirox Cream Against *Trichophyton rubrum*<sup>11</sup>

Sample	Control Count	Count After 2 Hours (% reduction)	Count After 6 Hours (% reduction)	Count After 24 Hours (% reduction)	Count After 3 Days (% reduction)
40% Urea	$3.95 \times 10^5$	$2.5 \times 10^4$ (93.6)	$1.8 \times 10^3$ (99.5)	$7.0 \times 10^3$ (98.2)	<10 (>99.9)
Ciclopirox	$3.95 \times 10^5$	$4.5 \times 10^5$ (0.0)	$7.0 \times 10^5$ (0.0)	$3.5 \times 10^4$ (91.0)	<10 (>99.9)
40% Urea + Ciclopirox	$3.95 \times 10^5$	$5.5 \times 10^2$ (99.8)	<10 (>99.9)	<10 (>99.9)	<10 (>99.9)

Topical ciclopirox is a synthetic broad-spectrum antimycotic agent with inhibitory activity against pathogenic dermatophytes, including *T rubrum*. In addition to being effective in curing tinea pedis, it is generally well tolerated. Most reported side effects (eg, mild pruritus and burning) are minor and localized.<sup>12</sup>

The objective of the present study was to evaluate the efficacy of 40% urea cream as an adjunct to topical antifungals in the treatment of recalcitrant moccasin tinea pedis. With its low adverse effect profile, broad-spectrum coverage, and large quantity available to adequately last for one month, ciclopirox cream was chosen for study in conjunction with 40% urea cream.

#### Methods

Patients with previously untreated moccasin tinea pedis were selected from the general dermatology clinic. The diagnosis of moccasin tinea pedis was made clinically and confirmed with either a potassium hydroxide test from skin scrapings revealing septate hyphae or a positive fungal culture showing dermatophyte. At baseline, all patients had thick scale on the plantar surfaces of their feet. Some patients also had dry, red, scaly toe web spaces, and most patients also had onychomycosis. A total of 12 patients were treated with a combination of 40% urea cream and ciclopirox cream. The 40% urea cream was applied once daily and the ciclopirox cream twice daily. After 2 to 3 weeks of treatment, patients were evaluated for the presence of erythema, scaling, and pruritus.

#### Results

A positive fungal culture was obtained in 9 of the 12 patients. *T rubrum* was isolated in 8 patients, and

*Epidermophyton floccosum* was isolated in 1 patient. On a potassium hydroxide test, septate hyphae were diagnosed in the other 3 patients. Of the 12 patients with moccasin tinea pedis treated concomitantly with topical 40% urea cream and ciclopirox cream, a 100% cure rate was achieved. After 2 to 3 weeks of combination therapy, all patients were free of erythema, scaling, and pruritus. In comparison, one patient with documented *T rubrum* used a topical antifungal agent only for one month. This patient had resolution of most of the pruritus but continued to complain of scaling on the feet. By adding 40% urea cream, the scaling was cleared. All patients completed the full course of treatment. One patient did complain of minor irritation in the toe web spaces, but it was not significant enough to discontinue therapy.

#### Comment

Urea is a known keratolytic agent that assists in the clinical resolution of scale and crusting. It also has been shown to enhance the absorption of other agents, including antifungals, into the skin, which is often thickened with a hyperkeratotic scale in moccasin tinea pedis.<sup>13</sup> An additional property of topical urea is its inherent antifungal activity. This property was shown in an in vitro study on the relative antifungal activity of 40% urea cream alone, ciclopirox cream alone, and a combination of both 40% urea and ciclopirox creams. In this study, all 3 groups were capable of reducing the fungal counts of *T rubrum*, as shown in the Table. The most effective reduction in *T rubrum* counts for both 40% urea cream alone and ciclopirox cream alone occurred 3 days after exposure, and, indeed, the combination of 40% urea cream with ciclopirox cream was capable of eliminating the fungus completely after only 6 hours of exposure.<sup>11</sup> Thus, 40%

urea cream not only has antifungal activity but also seems to act synergistically with topical antifungals against *T rubrum*.

In the present study, the ciclopirox cream was chosen arbitrarily from the antifungals indicated in the treatment of tinea pedis. In combination with 40% urea cream, ciclopirox cream cleared all cases of moccasin tinea pedis in 2 to 3 weeks. However, more potent topical antifungals, such as terbinafine or butenafine, which, when used alone, have a 69% cure rate in moccasin tinea pedis when used for 2 weeks, may be more effective.<sup>5</sup> Nevertheless, the adverse effect profiles of these agents, with their slightly greater incidence of allergic contact dermatitis than ciclopirox, partially negate their potential increased efficacy in the treatment of moccasin tinea pedis.<sup>14</sup>

The etiology of the minor irritation of the toe web spaces in one patient in the study is uncertain because allergic contact dermatitis has been reported in a small percentage of subjects with both topical urea and ciclopirox creams.<sup>15,16</sup> However, the irritation was not significant enough to stop the treatment, and the combination therapy was well tolerated by the other patients.

As the type of tinea pedis most recalcitrant to therapy, moccasin tinea pedis commonly is treated with oral antifungals, such as terbinafine and itraconazole, in addition to topical antifungals, thus adding the potential complications of systemic therapy. Therefore, topical treatments with urea cream and an antifungal, shown in this study to be effective in about the same time interval as that indicated for topical plus systemic therapy, are an advantageous and efficacious alternative. Thus, with its inherent antifungal activity, as well as its ability to work synergistically with topical antifungals, 40% urea cream is a useful adjunct and an excellent addition to the arsenal in the treatment of chronic, recalcitrant moccasin tinea pedis.

Further studies with larger numbers of patients are needed to better define the rate of cure.

## REFERENCES

- Richardson M, Elewski B. *Superficial Fungal Infections*. Oxford: Health Press Limited; 2000.
- Kemna ME, Elewski BE. A U.S. epidemiologic survey of superficial fungal diseases. *J Am Acad Dermatol*. 1996;35:539-542.
- Rand S. Overview: the treatment of dermatophytosis. *J Am Acad Dermatol*. 2000;43(suppl 5):S104-S112.
- Leyden JL. Tinea pedis pathophysiology and treatment. *J Am Acad Dermatol*. 1994;31(suppl 3, pt 2):S31-S33.
- Rupke SJ. Fungal skin disorders. *Prim Care*. 2000;27:407-421.
- Tanuma H, Doi M, Sato N, et al. Bifonazole (Mycospor cream) in the treatment of moccasin-type tinea pedis. Comparison between combination therapy of bifonazole cream + 10% urea ointment (Urepearl) and occlusive dressing therapy with the same agents. *Mycoses*. 2000;43:129-137.
- Bonifaz A, Ibarra G. Onychomycosis in children: treatment with bifonazole-urea. *Pediatr Dermatol*. 2000;17:310-314.
- Syed TA, Ahmadpour OA, Ahmad SA, et al. Management of toenail onychomycosis with 2% butenafine and 20% urea cream: a placebo-controlled, double-blind study. *J Dermatol*. 1998;25:648-652.
- Tanuma H, Tanuma M, Abe M, et al. Usefulness of lanconazole (Astat) cream in the treatment of hyperkeratotic type tinea pedis. comparative study of monotherapy and combination therapy with 10% urea ointment (Pastaron). *Mycoses*. 2001;44:181-190.
- Torres-Rodriguez JM, Madrenys N, Nicolas MC. Non-traumatic topical treatment of onychomycosis with urea associated with bifonazole. *Mycoses*. 1991;34:499-504.
- Carmol 40 [package insert]. Fairfield, NJ: Bradley Pharmaceuticals, Inc; 2004.
- Aly R, Maibach HI, Bagatell FK, et al. Ciclopirox olamine lotion 1%: bioequivalence to ciclopirox olamine cream 1% and clinical efficacy in tinea pedis. *Clin Ther*. 1989;11:290-303.
- Takahashi K, Suzuki T, Sakano H, et al. Effect of vehicles on diclofenac permeation across excised rat skin. *Biol Pharm Bull*. 1995;18:571-575.
- Lacy CF, Armstrong LL, Goldman MP, et al. *Drug Information Handbook*. 9th ed. Hudson, Ohio: Lexi-Comp Inc; 2001.
- Cramers M, Thormann J. Skin reactions to a urea-containing cream. *Contact Dermatitis*. 1981;7:189-191.
- Foti C, Diaferio A, Bonamonte D. Allergic contact dermatitis from ciclopirox olamine [case reports]. *Australas J Dermatol*. 2001;42:145.