Observational Evaluation of Sertaconazole Nitrate Cream 2% in the Treatment of Pruritus Related to Tinea Pedis

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Tinea pedis typically presents as a pruritic, erythematous, and scaly eruption on the foot, with symptoms correlated with the severity of infection. Although many clinical studies have assessed the antifungal action of various agents, relatively little attention has been devoted to evaluating if antifungal agents are capable of improving subjective symptoms while treating the infection. A single-center, open-label, observational, proof of concept study was conducted in 21 participants (age range, 16–74 years) to evaluate if sertaconazole nitrate cream 2% used twice daily for 7 days was able to reduce participants' perceived itching while treating the infection. Findings included participants' overall assessment of quality of life (QOL) with the Dermatology Life Quality Index (DLQI) and participants' overall satisfaction with treatment. The pruritus visual analog scale (VAS) was used to assess the subjective symptom of itching. Results indicated the mean total score of changes in perception of QOL was 8.95 at baseline and 3.38 at day 7, a within-group change of −5.57 (P<.0001), and the mean reduction in reported itching from baseline to day 7 was −63.10% (P<.0001). Fifteen of 21 participants (71.4%) were somewhat or very satisfied with the results of their treatment. The implication of these findings is that successful elimination of the inflammatory symptoms of tinea pedis, such as pruritus, may promote adherence to therapy by directly affecting participants' perception of QOL. Furthermore, early and rapid relief of symptoms, as seen in this study, may encourage patients to continue therapy for the full recommended period of 4 to 6 weeks, thereby reducing the risk for relapse that leads to chronic disease.

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Tinea pedis, or athlete's foot, is a common condition and also is a disease that frequently is self-treated with over-the-counter preparations, often at the risk for recurrence and chronicity.[1] The lifetime risk for acquiring tinea infection, including tinea pedis, is 10% to 20% in the United States. In fact, diagnosis of tinea infection is second only to acne as the most commonly reported skin disease.[2,3] Causal agents are dermatophyte species of the *Trichophyton*, *Epidermophyton*, and *Microsporum* genera.[3] Although males and females of all ages have been reported with the condition, men aged 20 to 40 years most frequently are affected.[3]

Tinea pedis usually presents as a pruritic, erythematous, and scaly eruption on the foot.[4,5] Symptoms can range from mild scaling to a painful, erosive, inflammatory process, with the most familiar presentation, interdigital tinea pedis, characterized by scaly soggy toe webs accompanied by pruritus and foul odor.[5] Other presentations include the moccasin variant, which affects the soles and sides of the feet and is characterized by scale and some erythema.[2,3]

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As a general rule, cutaneous fungal infections are characterized by irritated skin and subjective symptoms, such as itching, stinging, or burning sensations; the presence of pruritus is correlated with the severity of infection.[6,7] The combined effect of fungal infection and the inflammatory response provoked by dermatophytes is known to impair skin barrier function. Traditionally, symptoms associated with inflammation, such as pruritus, have been addressed by concomitant use of corticosteroids with antifungal agents, but long-term corticosteroid use may cause skin atrophy and therefore should be avoided.[7] Optimal treatment of tinea pedis should address symptoms and eradicate the fungus associated with the infection.

The efficacy of sertaconazole nitrate cream 2%, an antifungal agent introduced in the United States in December 2003, in the treatment of tinea pedis has been well established.[8-11] Although many clinical studies have assessed the antifungal action of various agents, relatively little research of antifungal agents with demonstrated efficacy has addressed the ability to improve participants' subjective symptoms, including itching, stinging, and burning sensations. A small observational study was designed to measure the ability of sertaconazole nitrate cream 2% to reduce these symptoms while treating tinea pedis. In this proof of concept study, the extent to which symptoms affected participants' perceptions of quality of life (QOL) were measured at baseline, day 3, and day 7.

Methods

The goal of this study was to determine if the established clinical efficacy of sertaconazole nitrate cream 2% to treat tinea infection and related symptoms corresponded with improvement in participants' assessment of QOL. To evaluate participants' subjective experiences of treatment, a single-center, open-label, observational study was conducted in 21 participants (age range, 16–74 years). This study was approved by an institutional review board and informed consent was obtained from each participant or a guardian if the participant was younger than 18 years.

At baseline, medical history was recorded, including concomitant medications and treatments, and all participants received both potassium hydroxide tests and fungal cultures for tinea infection. To be included in the study, participants had to report a score of 5 or more on the pruritus visual analog scale (VAS), an 11-point scale ranging from 0 (no itching) to 10 (itching frequently interferes with daily activities).

Patients were excluded from the study if they were pregnant, breastfeeding, or not practicing birth control; if they were allergic to the test medication; if they were unable to comply with terms of the study; if they had a medical condition that contraindicated their participation or a skin disorder that might interfere with diagnosis or evaluation of tinea pedis; if they had a history of noncompliance or unreliability; or if they had participated in any investigational drug study within 30 days of baseline visit. Once admitted into the study, participants were instructed to apply sertaconazole nitrate cream 2% to affected areas of the feet twice daily for 7 days. Participants were evaluated at baseline, day 3, and day 7. Participants' overall assessment of QOL was measured with the Dermatology Life Quality Index (DLQI) at baseline and day 7, while pruritus VAS was administered at all 3 visits. Adverse events were assessed at day 3 and day 7. Participants' overall satisfaction was measured on a 5-point scale ranging from −2 (very dissatisfied) to +2 (very satisfied) at day 7.

Statistical analysis was conducted on the intention-to-treat population, which included all participants who were enrolled and received study medication. A paired *t* test/Wilcoxon signed rank test (according to normality of variable) was used to measure change from baseline in DLQI and pruritus VAS scores. Participant overall satisfaction scores were measured with the Wilcoxon signed rank test.

Results

Participants—Twenty-one participants completed the study (12 males and 9 females). Of these 21 participants, 17 were white, 2 were black, 1 was Hispanic/Latino, and 1 did not specify.

Dermatology Life Quality Index—The DLQI was designed to assess the impact of symptoms on QOL and consisted of 10 questions. It was administered to all participants at baseline and on day 7. Responses to each question were scored on a scale from 0 (not at all) to 3 (very much), which yielded a total score of 0 to 30 with higher scores indicating greater impairment of QOL.

When all participants' scores for all questions were aggregated, the total DLQI scores showed a considerable change from baseline to day 7 with a mean total score of 8.95 at baseline and 3.38 at day 7, a within-group change of −5.57 ($P<.0001$)(Table 1).

Pruritus VAS—At all 3 visits, participants self-administered the pruritus VAS to describe the subjective symptom of itching on a scale of 0 (no itching) to 10 (itching frequently interferes with

Table 1.

Responses to the Dermatology Life Quality Index (N=21)[a]

Aggregated Scores of Effect on QOL	Participants, n (%)
Baseline	
0–1 (no effect)	0 (0)
2–5 (small effect)	7 (33.3)
6–10 (moderate effect)	9 (42.9)
11–20 (very large effect)	4 (19.0)
21–30 (extremely large effect)	1 (4.8)
Day 7	
0–1 (no effect)	9 (42.9)
2–5 (small effect)	7 (33.3)
6–10 (moderate effect)	3 (14.3)
11–20 (very large effect)	2 (9.5)
21–30 (extremely large effect)	0 (0)

Abbreviation: QOL, quality of life.
[a]Change in scores from baseline to day 7: mean (SD), −5.57 (4.17); median (P25, P75), −4.00 (−8.00, −2.00); range, −15.00 to 0.00; *P* value (within group), <.0001 (paired *t* test).

Table 2.

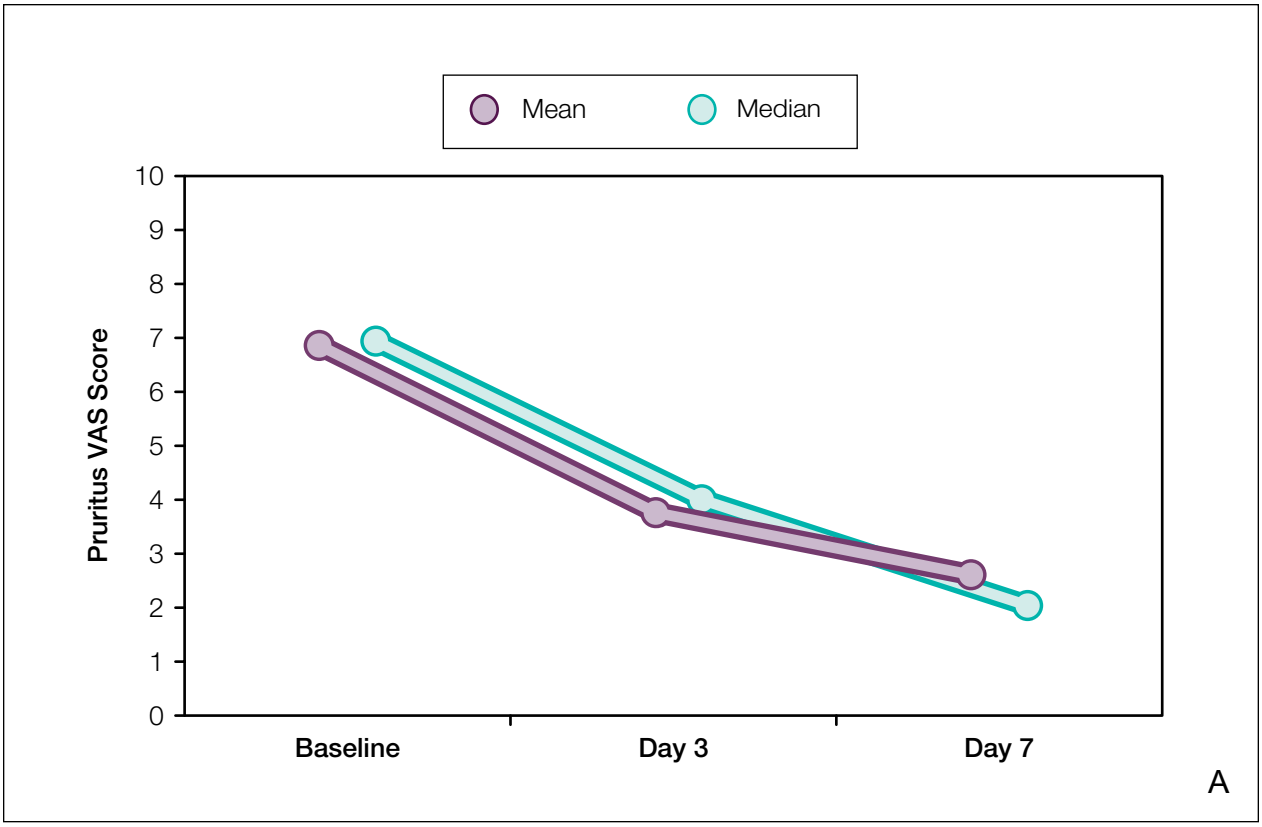
Participants' Overall Satisfaction at Day 7 (N=21)[a]

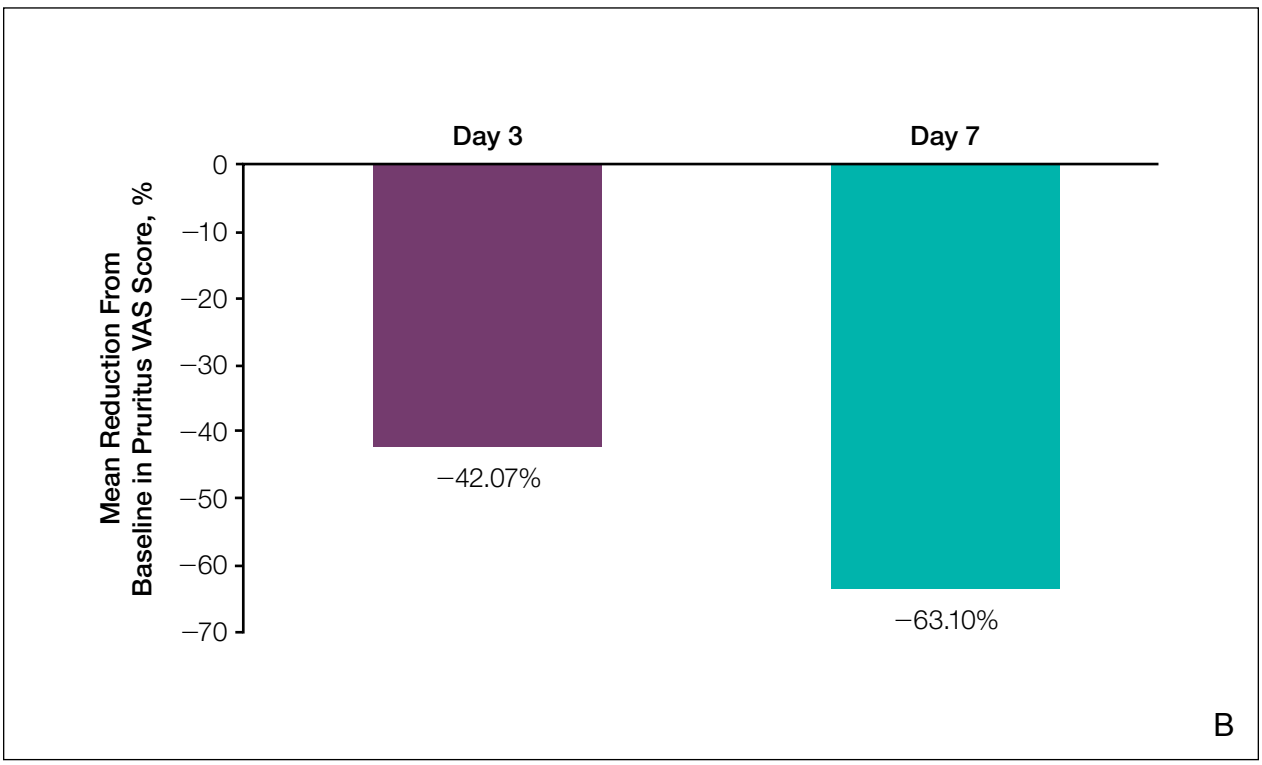
Overall Satisfaction Score	Participants, n (%)
−2 (very dissatisfied)	1 (4.8)
−1 (somewhat dissatisfied)	2 (9.5)
0 (neutral)	3 (14.3)
+1 (somewhat satisfied)	3 (14.3)
+2 (very satisfied)	12 (57.1)

[a]Change in scores from baseline to day 7: mean (SD), 1.10 (1.26); median (P25, P75), 2 (0, 2); range, −2 to 2; *P* value (within group), .0018 (Wilcoxon signed rank test).

daily activities). Results conclusively showed that participants reported significantly less itching at both day 3 and day 7 compared to baseline. Scores from the 3 visits were compared. The mean reduction from baseline to day 3 was −42.07% (6.86 to 3.86, respectively; $P<.0001$), and the mean reduction from baseline to day 7 was −63.10% (6.86 to 2.61, respectively; $P<.0001$)(Figure).

Participants' Overall Satisfaction—Participants' overall satisfaction was assessed at day 7 using a 5-point scale ranging from −2 (very dissatisfied) to +2 (very satisfied). Of the 21 participants in this study, most (15/21 [71.4%]) were somewhat or very satisfied with the results of their treatment, whereas 3 (14.3%) were neutral and 3 (14.3%) were either very or somewhat dissatisfied ($P=.0018$)(Table 2).





Pruritus visual analog scale (VAS) scores (mean and median) at baseline and day 3 and day 7 after treatment with sertaconazole nitrate cream 2% in 21 participants (A), and mean percentage reduction from baseline to day 3 and day 7 in pruritus VAS scores (B). One participant was not available at day 3; therefore, these findings are based on 20 participants. The pruritus VAS scores ranged from 0 (no itching) to 10 (itching frequently interferes with daily activities).

Safety—No adverse events were reported and no participants discontinued participation before the end of treatment.

Comment

This study demonstrated that sertaconazole nitrate cream 2% for the treatment of tinea pedis was effective in reducing pruritus in participants using the cream for 7 days. Most participants were very satisfied with the results of the treatment and reported that the early and rapid relief of their symptoms enhanced their QOL. The implication of these findings is that successful and rapid elimination of the inflammatory symptoms of tinea pedis, such as pruritus, may promote adherence to therapy. Furthermore, early and effective relief of symptoms, as seen in this study, may encourage patients to continue therapy for the full recommended period of 4 to 6 weeks, thereby reducing the risk for relapse that leads to chronic disease.

A proof of concept study design was used to validate the premise that effective antifungal therapy can provide the added benefit of symptom relief, thereby increasing the likelihood that patients will continue the therapy long enough for it to be completely effective. We recognize that placebo-controlled randomized clinical trials are the gold standard for medical research and lack of placebo control is one of the limitations to this study. However, proof of concept studies without placebo control may provide early evidence of the potential of a therapeutic agent to show clinical efficacy. These studies have been used to test the efficacy of various dermatologic products in the treatment of pruritus, including uremic pruritus in patients on chronic dialysis therapy[12] and chronic pruritus associated with atopic dermatitis and other conditions.[13]

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