A Novel Treatment for Onychomycosis in People Living With HIV Infection: Vicks VapoRub™ is Effective and Safe

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Onychomycosis is a common nail disease caused by fungal infection with yeasts and molds (Westerberg & Voyack, 2013). Over time, affected nails, which can be superficially, distally, or proximally infected, become discolored and thickened (Gupta et al., 2000). With advanced infection, cosmetic changes are accompanied by functional problems and an increased risk of cellulitis due to the loss of surrounding skin integrity (Surjushe, Kamath, Oberai, Saple, & Dharmshale, 2007). For many people, the appearance of affected nails causes concern and embarrassment, which can then result in changes to the person's usual activities, such as going to a pool or beach, and may also influence the choice of shoe (Potter, Mathias, Raut, Kianifard, & Tavakkol, 2006). Toenails are more frequently affected than fingernails, and the prevalence of onychomycosis ranges from 3% to 8% in the general population (Gupta, Ryder, & Johnson, 2004). Risk factors for onychomycosis include water contact, infection in other family members, tinea pedis, diabetes mellitus, peripheral vascular disease, and immune-compromised states (Gupta et al., 2000; Gupta et al., 2004; Surjushe et al., 2007; Westerberg & Voyack, 2013).

Onychomycosis is found four times more frequently in persons with HIV-related immune compromise, but data are limited (Moreno-Coutiño, Arenas, & Reyes-Terán, 2011). Infection is associated with more advanced immunodeficiency and usually presents as proximal onychomycosis, which is often harder to diagnose and treat than other forms of the disease (Gupta et al., 2000; Moreno-Coutiño et al., 2011).

Treatment of onychomycosis is difficult overall. Antifungal therapies are the mainstay of treatment and can be administered topically or orally (Gupta et al., 2000; Werschler, Bondar, & Armstrong, 2004). Tavaborole, a topical treatment, has recently been approved by the U.S. Food and Drug Administration for onychomycosis and has been shown in two Phase-III clinical trials to have a complete cure rate (a completely clear nail and negative mycology) in 6.5% and 9.1% of participants, respectively (Lexi-Comp, Inc., 2015). While tavaborole offers a treatment option with minimal side effects and drug interactions, it is cost prohibitive for many in the socioeconomic group studied here. The cost for a 1-month supply is currently $589.45

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(Lexi-Comp, Inc., 2015). Topical treatment is not as effective as oral therapy, but both are associated with high rates of treatment failure and relapse (Eisman & Sinclair, 2014; Westerberg & Voyack, 2013).

At present, oral terbinafine is the first-line treatment for onychomycosis (Gupta et al., 2004); it has a clinical cure rate (negative follow-up mycology cultures and clinical resolution) of 60% and a recurrence rate of 20% to 50% (Eisman & Sinclair, 2014; Westerberg & Voyack, 2013). Alternative antifungals, the azoles (itraconazole and fluconazole), and griseofulvin have even lower clinical cure rates (Westerberg & Voyack, 2013). All antifungal agents also have the potential for hepatotoxicity and azole-mediated inhibition of the cytochrome P450 system, which can result in significant drug-drug interactions, especially with antiretroviral therapies (Lexi-Comp, 2009).

Treatment of toenail onychomycosis usually requires 12 weeks of oral antifungal administration and can be expensive (Gupta et al., 2004; Westerberg & Voyack, 2013). A 4-week supply of terbinafine, itraconazole, or griseofulvin costs $392.99, $239.99, and $54.13, respectively (Gupta et al., 2004; Lexi-Comp, 2009; Lexi-Comp, Inc., 2015). Insurance companies will not cover the cost of treatment unless mycological evidence of infection is confirmed (Westerberg & Voyack, 2013). High treatment costs and lack of health insurance can prohibit treatment of this condition in people living with HIV infection (PLWH), who are often socioeconomically disadvantaged. In our clinic population, for example, 47% of persons in HIV-related care have an annual income of less than $10,000 (Gupta et al., 2000). For these reasons, there is a need to find an alternative, inexpensive treatment option that is well tolerated, shown to be effective, and has minimal drug-drug interactions.

Vicks VapoRub™ (The Procter & Gamble Company, Cincinnati, OH) is a medicinal ointment commercially used for the relief of cold symptoms and muscle aches when rubbed over the chest or affected area (Procter & Gamble, n.d.). It contains three active ingredients (camphor, eucalyptus oil, menthol), and can be purchased over the counter for as little as $3.00 (Procter & Gamble, n.d.). Increasing anecdotal evidence supports the use of Vicks VapoRub in the treatment of onychomycosis, and topical Vicks VapoRub is commonly used as an alternative to traditional antifungal therapies in persons who are unable to afford usual medical treatments (Gupta et al., 2004). Broad-spectrum antifungal properties of all three active ingredients in Vicks VapoRub have been demonstrated, and some have been shown to be superior to those of established medical antifungal agents (Al-Bayati, 2009; Ashour, 2008; Singh, Bwhawana, Kumar, & Dubey, 2008). Furthermore, an animal study of 1% essential oil and menthol versus bifonazole for the topical treatment of experimentally induced onychomycosis demonstrated greater efficacy than the former regimen, with complete cure on day 29 after treatment in all rats (Al-Bayati, 2009).

The purpose of our study was to determine the efficacy and safety of Vicks VapoRub in the treatment of onychomycosis in PLWH using clinical resolution and quality-of-life measures.

Methods

This was a single-site, prospective pilot study of PLWH with onychomycosis who attended the outpatient care clinic at Washington University's Infectious Disease Clinic and AIDS Clinical Trials Unit. The Institutional Review Board of Washington University approved the study. Study participants were recruited through posters placed in the waiting rooms and clinical areas of these facilities.

During screening visits, the study investigators assessed potential study participants. If assessment of the affected nail clinically suggested onychomycosis, informed consent was obtained for study participation. Digital photographs of affected nails were taken using a white background under artificial lighting conditions; images were downloaded and stored in a password-protected file. Affected nails had an overlay of transparent film applied so that an outline of the nail plate, as well as involved portion of the nail, could be assessed longitudinally. After the nail tracing was taken, the transparent film was applied to an index card. The outline of the nail was then separated into eight segments, each representing 12.5% of the nail. If 50% of the segment had an area of infection, the entire segment was counted as

area of involved nail. These segments were compared at each visit to monitor response to treatment.

Using disposable sterile nail clippers and a blunt scalpel blade, nail clippings, scrapings, and subungual debris from the affected nail(s) were collected for culture at Barnes Jewish Hospital mycology laboratory. Midway through the study it was found that mycological cultures had yielded few positive results with patients who had clinical manifestations of disease. A switch was made to a dermatophyte test medium (DTM), which was used in the office to detect infection. The DTM was found to be more effective at detecting infection and could be read in a matter of days as opposed to weeks with cultures in the mycological laboratory. The disadvantage of DTM testing was the inability to identify the fungal species.

Participants were also asked historical questions related to opportunistic infections, possible risk factors for onychomycosis, and the natural history of their nail disease; they also completed the OnyCOE-t questionnaire to assess quality-of-life measures. The OnyCOE-t questionnaire was designed to show patient-reported impact on quality of life associated with onychomycosis infection. It has been studied for validity and reliability in this population (Potter et al., 2006). A significant impact on quality of life is found in those with an 8.5-point increase in scoring on the questionnaire. This directly correlated with a 25% increase in clearing of nail infection (Potter et al., 2006). Historical data regarding the infection and opportunistic infection were recorded in a data collection sheet created by the study team for recording purposes. A demonstration of how to topically apply Vicks VapoRub to affected nails, using petroleum jelly, was performed for participants. The participants then gave a return demonstration of the technique. Time was allowed for each participant to ask questions about study procedures and technique.

Results

Twenty subjects were recruited to the study between May 2010 and April 2012. The participants were mostly male (90%) and predominantly African American (55%), with a mean age of 46 years (Table 1). Nineteen (95%) were on combination antiretroviral therapy, with HIV RNA levels of fewer than 50 copies/mL in 61%. Median CD4+ T cell count was 399 cells/mm^3 (interquartile range = 278–666). Of the 20 subjects, one was lost to follow-up at the week-24 visit. Difficulty with adherence to study treatment and visits was reported due to length and number of treatments. The majority of missed visits occurred at the 36- and 48-week visits. At each visit, adherence to medication was assessed. At study week 24, 80% of participants were found to be adherent to treatment. Eighteen subjects were seen at week 24; of these 18 subjects, 83% had improvement of their affected nails (median clearance 25%; range 6.3% to 87.5%), and 2 of those subjects had total resolution of their infections (Figure 1, A and B). Two of 3 subjects with no clearing of the affected nail were nonadherent to treatment, with one reporting adherence but no change to infection. No side effects were reported. By week 48, 8 (53%) of 15 assessed subjects had stable or improved clearance of their affected nails. Five (25%) of the 20 subjects were lost to care by week 48. The participants lost to care were excluded from the final analysis.

Quality-of-life data as they pertained to the infection were assessed at each study visit. Of the 20 subjects enrolled, 75% reported feeling embarrassed

Table 1. Participant Characteristics

Variable	*n* (%)
Male sex	18 (90%)
Racial minority	13 (65%)
Mean age in years (interquartile range)	46 (33–56)
Mean years since HIV diagnosis (interquartile range)	8.5 (1–16)
History of opportunistic infection	6 (30%)
Nadir CD4+ T cells/mm^3 (interquartile range)	200 (76–301)
Baseline CD4+ T cells/mm^3 (interquartile range)	399 (293–631)
ART use	19 (95%)
HIV RNA < 50 copies/mL	12 (60%)
Comorbidity[a]	8 (40%)
History of nail trauma	3 (15%)

Note. Racial minorities = African American, Hispanic, American Indian; ART = antiretroviral therapy.

a. One or more of the following: cardiovascular disease, hypertension, chronic hepatitis C, chronic hepatitis B, diabetes mellitus, peripheral neuropathy, chronic kidney disease.

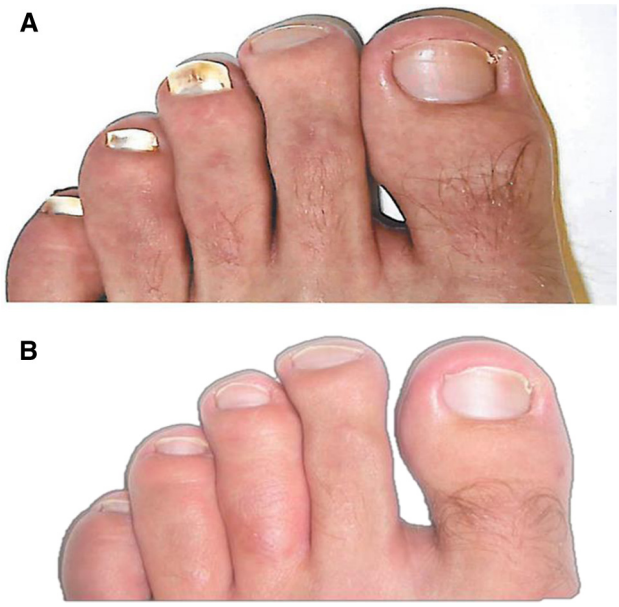

Figure 1. (A) Baseline photograph of study subject showing area of nail affected. (B) Week 48 photo of the same study subject showing continued clearance of onychomycosis after 24 weeks of successful treatment.

by the appearance of their toenails in the 4 weeks preceding the baseline visit, and 53% reported discomfort or pain due to the infection. This was decreased to 61% and 39%, respectively, by the week 24 visit. Additionally, 94% of subjects reported being satisfied by the condition of their toenails and by the overall results of the treatment by the week-24 visit.

Discussion

Vicks VapoRub was shown to be an effective and safe treatment of onychomycosis in the PLWH in our study. Onychomycosis is a difficult disease to treat in immune-suppressed patients. It puts individuals at an increased risk for opportunistic infections and possible life-threatening complications. No research has been completed on alternative treatment options for onychomycosis in PLWH. Providing a treatment option for PLWH that will have minimal side effects and lack contraindications with antiretroviral medications would offer favorable management for a difficult-to-treat condition in a high-risk group.

Current treatment options for PLWH with onychomycosis are limited, not only by medication contraindications, but also by cost. Treatment with Vicks VapoRub could provide effective clearance of infection at the cost of as little as $5.38 per jar. Terbinafine, the current standard of treatment, costs approximately $392.99 for a 4-week supply; with the average length of treatment being 6–12 months, it could cost as much as $3,959.88 to fully treat the infection. PLWH are economically disproportionally disadvantaged, making terbinafine an unobtainable option for many. Participants in our study found clinically significant clearance of infection at as little as 24 weeks and a cost of $5.38.

Our study was limited by its small sample size, difficulty with follow-up, and adherence problems. We suspect that a larger sample size with longer treatment duration would yield even greater infection clearance. Our study did not attempt to isolate the components of Vicks VapoRub that might be effective. Additional studies should be completed to compare this treatment option to placebo or standard of care to gain a better understanding of treatment efficacy. This could allow components of the treatment to be isolated and give a true understanding of the mechanisms of action in this alternative therapy.

Despite the limitations of our study, it is undeniable that this treatment option for PLWH has promise as a cost-effective and safe remedy for a common infection. It has the opportunity to improve the quality of life for patients, as well as to prevent health complications. Participants in our study expressed satisfaction with the treatment and the results.

Conclusion

Vicks VapoRub is a safe alternative treatment for onychomycosis in PLWH. We found that, of the 18 subjects evaluated at 24 weeks, 83% had improvements in affected nails (median clearance 25%; range 6.3% to 87.5%), with 2 subjects having total resolution of the infection. Two of 3 subjects with no clearing of the affected nail were nonadherent. By week 48, 8 of 15 subjects assessed had stable or improved clearance of their affected nails. No side effects were reported.

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Disclosures

The authors report no real or perceived vested interests related to this article that could be construed as a conflict of interest.

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