



Tinea Pedis/Gram-Negative Toe Web Infection Treated with a Dilute Povidone-Iodine and Dimethylsulfoxide Preparation

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Abstract

Interdigital toe web infection is most frequently a polymicrobial complex disease process being caused by fungal, yeast or bacterial etiological factors, with a wide range of clinical manifestations. Treatment can prove to be difficult if the mixed etiology is not readily identified and furthermore more than one prescription is often required for eradication. There are many reported effective therapies, but none have been curative for mixed infection with a single topical formulation. This case report describes a 62-year-old man with a history of diabetes mellitus that presented with a polymicrobial infection of the interdigital spaces that was treated successfully with a novel topical formulation. This is the first case report of a broad-spectrum topical anti-microbial gel (2% povidone-iodine) in a dimethylsulfoxide vehicle eradicating a mixed fungal/gram-negative bacterial infection.

Keywords

Dimethylsulfoxide, Gram-negative toe web infection, Povidone-iodine

Introduction

Interdigital toe web infection is most frequently a polymicrobial disease process caused by fungal, yeast or bacterial infections with a wide range of clinical manifestations. Typically dermatophyte infections are more chronic in nature presenting as asymptomatic erythema and desquamation in the interdigital space. Bacterial infections are often more acute in nature marked by exudate, maceration, malodor and painful inflammation between toes extending onto soles of feet [1]. Dermatophyte infections may precede other infections. Dermatophytes are often able to damage the stratum corneum and promote gram-negative bacterial infections because they produce natural antibiotic products than can affect the composition of the resident bacterial flora and promote the selection of antibiotic-resistant bacteria which in turn can aggravate the initial infection [2]. In other cases, gram-negative interdigital toe web infection appears independently and is favored by pre-existing local conditions such as marked hyperhidrosis and cutaneous maceration, often caused by closed shoes or the practice of wet sports [3,4]. Candida infection often occurs secondarily to fungal or bacterial infections. Successful therapy can be prolonged if the polymicrobial aspect of infection is not readily identified. Topical and oral anti-fungal, anti-yeast and anti-bacterial agents are often utilized in combination to combat the often mixed infection.

Case Report

A 62-year-old man with a history of diabetes mellitus presented with a 1-week history of a painful rash on the right foot. He stated his primary care physician had diagnosed him with a fungal infection upon routine physical exam 4 weeks prior to onset of rash and had

prescribed a topical antifungal (econazole) cream, which he used twice daily for 2 weeks without complication. Shortly after finishing the cream he went on a long hike with his grandchildren during a hot day wearing hiking boots. Several days after the hike his right foot became very painful and weepy, continually worsening each day. On physical exam the second, third and fourth interdigital spaces along with surrounding plantar skin demonstrated erythema, vesiculopustules, maceration, weeping and malodor. Both bacterial and fungal cultures were collected. Based on the clinical history and physical exam, a presumed polymicrobial diagnosis of tinea pedis and gram negative toe web infection was made. Cultures subsequently were positive for *Pseudomonas aeruginos* and *Trichophyton mentagrophytes*.

The patient was prescribed a topical gel comprised of 2% povidone-iodine (PVP-I, w/w) in dimethyl sulfoxide (DMSO) that was mixed by a licensed compounding pharmacy. The patient was instructed to apply a thin layer of the gel to all involved areas twice daily for two weeks. At the one week follow-up the infection was

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almost completely cleared with only a small amount of maceration and erythema remaining. At the two week follow-up there was no trace of infection. The patient reported the gel was well tolerated and denied any side effects. Tests of curebacterial and fungal cultures obtained at the two-week visit were negative.

Discussion

Polymicrobial infection of the interdigital spaces and surrounding skin can be difficult to eradicate and can require several different treatment mechanisms to adequately cover the differing causative organisms. A combination of behavioral adjustments such as keeping the feet dry and socks that wick away moisture, along with topical and sometimes oral or systemic therapies may be necessary. There are a variety of treatments available for fungal and yeast infections, but there currently is not a standard of care for gram-negative bacterial toe web infections, which can lead to acute cellulitis and sepsis if left untreated in some patient populations [5]. Topical treatments such as dilute silver nitrate soaks, gentamycin cream, Castellani's paint and debridement have been utilized, however gramnegative bacterial toe web infections often require oral antibiotics along with behavioral modification to eradicate infection, with one study reporting fifteen patients treated with a third generation cephalosporin twice daily intramuscularly demonstrating a complete response [6,7]. This is the first case report of a broad-spectrum antimicrobial topical treatment-demonstrating efficacy in a mixed fungal/bacterial infection. PVP-I is used in the dermatology primarily as a pre-operative surgical scrub due its well-known broad-spectrum anti-microbial coverage. Though the mechanism of action is incompletely understood, free iodine is believed to non-selectively poison electron transport and cellular respiration, destabilize membranes, inhibit protein synthesis and denature nucleic acids in a broad range of infectious organisms rather than working selectively on a specific bacterial subunit or unique structural element of a particular virus.

PVP-I lends itself to a broad range of treatment options for many cutaneous infections but has not gained widespread recognition [8].

DMSO is a well-characterized, safe, effective pharmaceutical vehicle, known for decades to enhance penetration of small, uncharged molecules through the skin and mucous membranes [9]. DMSO is in fact such an effective penetration enhancer for small molecules that a topically applied diclofenac/DMSO gel is found to be equally effective as oral diclofenac for the treatment of osteoarthritis [10]. We are the

first group to report the use of DMSO as a transdermal penetration agent for the large, polymeric, charged polyvinylpyrrolidone-iodine complex on volar skin surfaces where the thickened, condensed stratum corneum has previously rendered transdermal drug delivery to be difficult.

Conclusion

This is the first case report of a broad-spectrum topical antimicrobial gel utilizing a DMSO-vehicle to enhance the penetration of a polymeric complex through volar skin in eradicating a mixed fungal/gram-negative bacterial infection. The lack of prescription FDA-approved treatment for gram-negative toe web infections coupled with the lack of need for multiple topical and/or oral treatment modalities makes our novel treatment system a potential armamentarium for many cutaneous infections. This novel combination warrants further investigation in randomized, controlled trials to assess its clinical potential.

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