Open study on the topical treatment of interdigital fungal infections in diabetic patients

A high proportion of diabetic patients experience fungal infections, and pharmaceutical strategies have varying success rates. A new alternative method, hydrophobic interaction, may provide a valuable treatment for these infections

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A. Johansson, Department of Diabetic Foot Care, Norra Älvsborg Länssjukhus, Trollhättan Sweden;
Å. Ljungh, MD, PhD, Associate Professor, Department of Laboratory Medicine University hospital of Lund, Sweden;
J. Apelqvist, MD, PhD, Associate Professor, Department of Endocrinology, University Hospital of Malmö, Sweden.
Email: jan.apelqvist@skane.se

A high proportion of diabetic patients (up to 84%) develop topical inter-digital fungal infections. The most commonly found fungus in these infection is *Trichophyton rubrum*, which is present in approximately 70% of cases.[1-3] The increased susceptibility of patients with diabetes is believed to be related to decreased immunodefence menchanisms, hyperglycaemia and the change in skin condition.

The most common treatment strategy is pharmaceutical, either topically or systematically administrated, but these have had varying success rates. They also cause potential adverse effects (toxicity or allergy) and risk development of resistance.[4,5] New treatment methods are, therefore, widely sought. In this pilot study, we evaluate a new, non-pharmaceutical strategy based on the theory of hydrophobic interaction.

Hydrophobic interaction

Hydrophobic interaction occurs when two hydrophobic (water-repellent) surfaces bind to each other in the presence of water or, in the case of wounds, exudate. An important mechanism by which microorganisms, fungi and bacteria adhere to surfaces is the expression of cell surface hydrophobicity.[6] The vast majority of pathogenic microorganisms are hydrophobic.[7]

The Sorbact dressing range uses the principles of hydrophobic interaction to bind and eliminate bacteria and fungi from dry to moist wounds. It can be used on all skin types and in fungal infections in skin folds. Microorganisms bind to the dressing's hydrophobic surface and are then inactivated and eliminated. No side-effects or microbial resistance have been reported.[8] Sorbact is manufactured in Sweden by Abigo Medical and distributed in the UK by BSN Medical as Cutimed Sorbact Ribbon.

Few studies have investigated the non-pharmaceutical treatment of fungal skin infections in diabetic patients. This pilot study evaluated the effect of Sorbact in the treatment of interdigital skin infections in people with diabetes mellitus.

Material and methods

Consecutive diabetic patients attending the diabetic foot clinic at the hospital NÄL (Norra Älvsborgs Länssjukhus, Trollhättan, Sweden) who were diagnosed with a topical inter-digital fungal infection were included in the study over a 14-month period. Patients where excluded from the study if the lesion was assessed as non-fungal, the initial culture was negative or they could not follow study protocol. All patients gave informed consent, and ethics committee approval was received.

Intervention

The treatment intervention comprised daily application of Sorbact ribbon gauze (2 x 50cm) for 10 days, in accordance with the manufacturer's recommendations and based on previous *in vitro* studies. All patients had experienced previous interdigital infections, for which were given topical antifungal pharmaceuticals.

The investigating podiatrist applied the test dressing during the patient's first visit at the outpatient clinic. Patients were given written and oral instructions to wash their feet, dry them carefully, apply the test dressing and change their socks daily.

Assessment

On days 1, 5 and 10, all patients attended the clinic where the infection was assessed by the investigator, by visual inspection. The lesion was evaluated using a four-grade scale:

- Deteriorated
- Unchanged (defined as <50% reduction in the size of the ulcer)
- Improved (defined as >50% reduction in the size of the ulcer)
- Healed.

Significant change was considered if the lesion had increased or decreased in size by more than 50%. The wound was defined as healed if the skin

Table 1. Results of the assessments made by the study investigator and the blinded observer

Assessment	Day 5	Day 10*
Deteriorated	2	1 (1)
Unchanged (<50% reduction in size)	7	4 (7)
Improved (>50% reduction in size)	11	5 (2)
Healed	0	10 (10)

* Bracketed figures relate to the photo evaluations

Declaration of interest
This study was sponsored by Abigo Medical AB

was intact with no localised reaction.

The same assessments where performed by the patient on days 2, 3, 4, 6, 7, 8 and 9.

The investigator photographed the lesions on days 1, 5 and 10 for an independent evaluation, which was performed by a blinded observer. The blinded observer had no relation to the investigator or patient; the assessment followed the same protocol as outlined above.

Cultures sample were taken before inclusion and on days 1, 5 and 10. Before inclusion, the swab was placed on the infected area for 10 minutes, whereas on days 1, 5 and 10 it was taken from the wound-contact surface of the test dressing. The samples were frozen and sent to the Department of Medical Microbiology, Dermatology and Infection, University of Lund for culture.[8]

The investigator and patients assessed their perception of the treatment (defined as ease of application), on days 1, 5 and 10. The treatment was graded as:
- Very easy
- Easy
- Difficult.

Results

Twenty patients were recruited into the study, as recommended by the ethics committee. The sample consisted of 14 males and 6 females aged between 26 and 74 years of age. All patients completed the study and no adverse reactions were recorded.

Assessments

Fifteen patients (75%) had improved or healed by day 10. Four patients (20%) remained unchanged and one patient (5%) deteriorated. In the latter patient, the fungal skin reaction improved but the ulceration on the fourth phalanx worsened, perhaps due to mechanical stress from inappropriate footwear (Table 1).

Eight patients (44%) found the test dressing 'very easy' to use and seven 39% found it 'easy'. Three patients (17%) found it 'difficult'. Of these three patients, one found it difficult to dispose of the dressing material and two had difficulty applying the dressing, due to a stiff back and poor vision in one case and an ankle joint injury in the other.

The investigator found the dressing 'very easy' and 'easy' to use in 88% and 12% of the patients respectively.

Microbiology

The microbiology findings showed a broad variation of fungi present in the treated area:
- *Trichophyton*
- *Penicillium* (mould)
- *Fusarium*
- Dermatophyte
- *Candida*.

In a number of cases, no fungi were recorded at day 10. Full details are given in Table 2. There was a strong correlation between no growth on day 10 and healed or improved lesions. In the cases with growth of fungi on day 10, the lesions where either healed, improved or unchanged.

Photo evaluation

The evaluation of the photographs was complicated in four patients due to the poor quality of the pictures.

On day 10, the blinded assessor considered that two patients (10%) had improved, 10 patients (50%) had healed, seven patients (35%) were unchanged before treatment start, and one patient's wound had deteriorated. (Table 1).

Discussion

This small, non-comparative, open pilot study showed that the hydrophobic test dressing was an effective treatment for interdigital fungal infections in diabetic patients, with no reported adverse events. According to assessments, 75% of the infections had improved or healed after 10 days of treatment. In 55% of patients, the culture showed no growth of fungi after 10 days of treatment. Furthermore, the investigator and most of the patients found the dressing easy to apply. However, the sample size is too small to determine if the hydrophobic dressing is more effective than other treatments, and a randomised controlled trial (RCT) would be needed to determine this.

There are limited data on the treatment of fungal infections in diabetic patients against which these data can be compared. In a double-blind clinical trial, Schopf et al. randomised 429 patients with tinea pedis (athlete's foot) to topical treatment with either terbinafine and lotrimazole. In the subgroup of patients without any protocol violations, 164/173 (95%) given terbinafine healed compared with 159/174 (91%) given clotrimazole. A local skin reaction was reported in 4% and 5% in each group respectively.[9] In the present study, no side-effects or resistance was reported for the hydrophobic treatment.

The weakness of this pilot study lies in its open, non-randomised, non-comparative design and small sam-

ple size. A strength of the study is that photographs of the lesions were assessed by a blinded observer, although the focus of four images was too poor to assess reliably. Nevertheless, the results support those of an earlier, unpublished pilot study on interdigital infection, and the current pilot is intended to be a precursor to a RCT with a longer follow-up period.

Conclusion

The results of this pilot study indicate that this hydrophobic treatment may be a valuable alternative treatment for interdigital fungal infections in the diabetic foot. However, more robust evidence, ideally in the form of a RCT, is needed to confirm this finding. ■

Table 2. Microbiology findings for the patients on days 1, 5 and 10.

Patient	Finding	Assessment	Patient	Finding	Assessment
Patient 1:			**Patient 11:**		
• Day 1	No growth		• Day 1	*Fusarium*	
• Day 5	No growth		• Day 5	*Fusarium*	
• Day 10	*Trichophyton*	Unchanged	• Day 10	No growth	Healed
Patient 2:			**Patient 12:**		
• Day 1	No growth		• Day 1	No growth	
• Day 5	*Fusarium*		• Day 5	No growth	
• Day 10	*Candida*	Improved	• Day 10	No growth	Healed
Patient 3:			**Patient 13:**		
• Day 1	No growth		• Day 1	No growth	
• Day 5	*Candida*		• Day 5	*Trichophyton*	
• Day 10	No growth	Healed	• Day 10	*Candida*	Healed
Patient 4:			**Patient 14:**		
• Day 1	*Candida*		• Day 1	No growth	
• Day 5	*Candida*		• Day 5	*Fusarium*	
• Day 10	No growth	Deteriorated	• Day 10	*Candida*	Unchanged
Patient 5:			**Patient 15:**		
• Day 1	No growth		• Day 1	*Penicillium*	
• Day 5	*Candida*		• Day 5	*Penicillium*, Trichosporon	
• Day 10	No growth	Improved	• Day 10	No growth	Healed
Patient 6:			**Patient 16:**		
• Day 1	*Penicillium*		• Day 1	No growth	
• Day 5	*Penicillium*		• Day 5	*Penicillium*, Trichosporon	
• Day 10	*Candida*	Improved	• Day 10	*Penicillium*	Healed
Patient 7:			**Patient 17:**		
• Day 1	*Candida*		• Day 1	No growth	
• Day 5	No growth		• Day 5	*Penicillium*	
• Day 10	No growth	Improved	• Day 10	No growth	Unchanged
Patient 8:			**Patient 18:**		
• Day 1	*Penicillium, Candida*		• Day 1	*Penicillium*	
• Day 5	*Penicillium, Candida*		• Day 5	No growth	
• Day 10	No growth	Improved	• Day 10	Dermatophyte	Healed
Patient 9:			**Patient 19:**		
• Day 1	*Trichophyton*		• Day 1	No growth	
• Day 5	*Trichophyton*		• Day 5	No growth	
• Day 10	No growth	Healed	• Day 10	*Candida*	Unchanged
Patient 10:			**Patient 20:**		
• Day 1	No growth		• Day 1	*Trichophyton*	
• Day 5	*Penicillium*		• Day 5	*Trichophyton*	
• Day 10	No growth	Healed	• Day 10	*Trichophyton*	Healed

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