

A randomised trial of honey barrier cream versus zinc oxide ointment

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Intertrigo is an inflammatory condition of skin folds, induced by skin-to-skin contact, heat, moisture and friction (Mistiaen and van Halm-Walters, 2010; Verpleegkundigen & Verzorgenden Nederland (V&VN), 2011). The condition is most commonly found in the larger skin folds of the body (V&VN, 2011). Intertrigo is characterised by blanching erythema in the skin folds, and can easily progress to severe inflammation, including maceration, erosions, fissures and crusting (Janniger et al, 2005; V&VN, 2011, see *Figure 1*); however, the exact pathophysiology of intertrigo is not known.

In 2011, in the Netherlands the prevalence of intertrigo in the large skin folds in hospitalised patients, nursing homes, and those who were nursed at home was 8.5% (Halfens et al, 2011). Major symptoms are: irritated skin, pruritus, pain and burning sensation (Mistiaen and van Halm-Walters, 2010; V&VN, 2011). Immobilised and obese patients are especially at risk. Other predisposing factors include high body temperature, perspiration and poor hygiene (Janniger et al, 2005; Yosipovitch et al, 2007). Intertrigo in the groin is often prolonged and/or exacerbated by urinary and faecal incontinence (Farage et al, 2007). When skin erosions occur, bacteria and fungi of the skin flora can colonise the folds and prolong the inflammatory process (Janniger et al, 2005; Bardsley, 2008), although the role of bacteria and fungi in maintaining or worsening intertrigo is not yet clear. Intertrigo may become a chronic disease, especially for patients that need special care. Intertrigo more frequently affects women, probably owing to the presence of inframammary skin folds.

Management of intertrigo consists of a combination of preventive measures and treatment strategies. By regular control of skin folds, intensive skin care, mobilisation, good hygiene, and minimising friction and moisture, development or worsening of intertrigo may be prevented (Mistiaen and van Halm-Walters, 2010; V&VN, 2011). Results can be positively influenced by intensive skin care, but this is often omitted, owing to the high daily workload of health professionals. There is a wide amount of variation in topical

Abstract

In this single-blind multicentre, intervention study, 31 patients with symmetrical intertrigo in large skin folds were included to study the clinical effect of two topical treatments, i.e. standard therapy with zinc oxide ointment versus honey barrier cream. Patients were treated twice daily for 21 days, and the severity of intertrigo was scored in an observation period of 21 days. Patients were used as their own controls by treating symmetrical skin folds, on the left and right side. There was no significant difference in treatment effect between both intervention groups. For the majority of patients, both treatments were effective. The use of honey barrier cream showed lower pruritus complaints (12.9% versus 29.0%). Honey barrier cream is a suitable alternative in the treatment of intertrigo, and promotes patient comfort.

Key words: Honey barrier cream ■ intertrigo ■ pruritus ■ skincare ■ zinc oxide ointment

Table 1. The intertrigo-severity scale

	0	1	2	3
Erythema	None	Mild: light pink	Moderate: red	Severe: bright red
Moisture	None	Mild: softening	Moderate: maceration	Severe: green/yellow/exudate
Skin	None	Fissures: red border	Moderate: erosions	Severe: infected, damaged skin
<i>Table 1</i> 0–3 Intertrigo 4–6 Intertrigo of moisturised skin 7–9 Intertrigo of infected skin				

treatments for skin conditions like intertrigo. The treatment of intertrigo is not standardised and differs between hospitals and nursing homes, and even between health professionals. The most frequently used treatment is application of a standard barrier, such as zinc-oxide ointment or Sudocrem®.

A band of cotton between skin folds may also be beneficial to patients with intertrigo (Janniger et al, 2005; Mistiaen and van Halm-Walters, 2010). Secondary infections should be treated with antifungals, corticosteroids or a combination preparation.

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Figure 1 Intertrigo in the groin area, Deventer Hospital

Zinc oxide ointment acts like a skin-drying agent and has skin protective capacity. It acts like a barrier, stimulates wound healing and probably also has anti-inflammatory effects. This is owing to the fact that inflammatory disorders, including erythematous skin conditions, are reported to be associated with decreased plasma zinc levels (Rosta et al, 2002).

MediHoney™ Barrier Cream is a registered cream, based on honey, for protection and healing vulnerable skin. Honey has been known for its healing properties in wounds for years (Simon et al, 2007). Honey has antibacterial and anti-inflammatory properties (Cooper et al, 2010). It improves wound healing and reduces pain complaints (Simon et al, 2007). Some forms of honey have antifungal activity (Irish et al, 2006).

The objective of the present clinical study was to compare the beneficial effect of honey barrier cream (MediHoney) to standard treatment with zinc-oxide ointment in patients with chronic intertrigo. The authors hypothesised that honey barrier cream, would improve wound healing of intertrigo, be more user-friendly and improve patients comfort.

Patients and methods

Study design

The study was designed as a multi-centre, randomised cross-comparative (left-right comparison) study of the therapeutic efficacy of honey barrier cream versus zinc-oxide ointment. Nurses received instructions for application of both medications. Both products were applied twice daily for 3 weeks to the symmetrical skin folds with intertrigo. By consistent application of the products on the same side, patients were used as their own controls.

Patients

The study included 31 patients, from four nursing homes. An annual survey of the prevalence of care problems, including intertrigo, in participating nursing homes in the Netherlands were used to recruit patients (LPZ, Dutch National Prevalence Survey of Care Problems). The inclusion

criterion was symmetrical intertrigo. Exclusion criteria were wounds or unilateral intertrigo. Previous treatment of intertrigo had to be stopped before entering the study. The majority of patients had not received any treatment. The patients in this study had symmetrical intertrigo in the larger skin folds (inframammary, between skin folds of the abdomen or the groin). One patient had symmetrical intertrigo in the elbow folds. Informed consent was obtained before participating in the study. The study protocol was approved by an independent medical ethics committee (METC).

Therapies

Each patient received a randomised numbered envelope with one tube containing 50g of honey barrier cream, and one jar containing 100g of zinc-oxide ointment. A centralised random-number table gave allocation information as to which treatment should be administered, left or right. The two therapies were applied by instructed nurses. Double-blinding of the trial was not possible, because of the difference in the consistency of both medications. In order to maximise the blinding of the study, nurses were instructed to clean the skin carefully, and remove all zinc-oxide ointment residue on the skin with oil before examination by the single-blinded investigator.

Measurements

At baseline, the severity of intertrigo was scored by a newly designed non-validated intertrigo-severity scale, based on the definitions in the new treatment guideline and Clinical Erythema Assessment (Del Rosso et al, 2007; V&VN, 2011). A review of the literature showed that, at present, there is no scale available to measure the severity of intertrigo. The severity scale is based on erythema, moisture and impaired skin. On day 1 the severity of symmetrical intertrigo on the left and right side was scored with a 0–9 pointscale (see Table 1). Twenty-one patients had exact symmetrical intertrigo at the start. The randomised treatment regime with honey barrier cream and zinc-oxide ointment to either the left or right side was performed continuously for the study period.

On days 7, 14 and 21, the severity of intertrigo was examined. The severity of the symptoms, i.e. pruritus, pain, burning or odour, was evaluated with a 4-point scale (never, seldom, sometimes, often). Severity of intertrigo on day 7 after starting treatment was chosen as the primary endpoint of this study. The treatment preference of patient and nursing staff was evaluated at day 21.

Statistical analysis

The intertrigo scores are categorical variables and repeated measurements in time. Power analysis showed the need, by continuity correction, of 26 patients to detect a difference of 40% ($\alpha=0.05$, $\beta=0.2$) at 80% power. Despite the lack of hard evidence owing to the lack of research, the expectation was a 40% higher proportion of improvement to the honey side in comparison to the zinc side. Data were analysed by the non-parametrical test, the Wilcoxon signed-ranks test. Honey barrier cream was considered to be more effective than zinc-oxide ointment, when a 2-point difference in score was registered, with a minimal improvement of 25%

on the intertrigo severity scale (2 points) defined as relevant. For the paired measurements of the primary endpoint and the difference between both therapies, data were analysed by the McNemar's test. Cohen's kappa was used to measure the agreement between both treatments by its efficacy. Differences were considered statistically significant for $p < 0.05$. All statistical analyses were conducted using SPSS (v18.0; PASW).

Results

In total, 31 patients were enrolled in this study, of which 21 had exact symmetrical intertrigo (left vs right), and 10 had non-exact symmetrical intertrigo at baseline. The majority of patients were women (90%; $n=28$), who had intertrigo in inframammary skin folds (55%). The mean age was 81.7 ± 7.9 years (range 68–98 years). The majority of patients suffered chronically from intertrigo, this is because it is a recurring problem.

The patients were treated on both sides and were followed for a mean period of 21 days. The mean intertrigo scores on both sides showed a significant decrease in scores over time (see Figure 2 and Figure 3). In total 17 patients (55%) had a positive 2-point difference for the honey barrier side on day 7 and 12 patients (39%) on the zinc-oxide ointment side. The difference between scores based on primary endpoint was not significant (McNemar's test, $p=0.180$).

At day 7, a total of 21 patients showed some degree of healing on the honey-treatment side, compared with 26 patients on the zinc-oxide side. In 6 patients, results were better with the standard therapy, compared to treatment with honey barrier. Contrarily, one patient benefited more from honey barrier cream. Twenty-four patients responded equally to both medicines. There was a moderate agreement between both treatments (Cohen's $\kappa=0.441$), this suggests that there is no difference between the efficacy of the two treatments. Spearman's rho correlation coefficient showed a significant moderate positive correlation between the differences at day 7, compared with the baseline score, on the honey barrier side and the zinc-oxide side ($r=0.493$, $p=0.05$). The majority of patients experienced healing of the skin on both sides over time, regardless of which treatment was applied.

Three patients showed a minimal aggravation of intertrigo at day 7 on the honey treated side, compared to 2 patients on the zinc-oxide-treated side. In one patient intertrigo worsened during both treatments. Two patients did not show any improvement at both sides at day 7. There were four patients who showed minimal healing for the zinc-oxide-treated side on day 7, while the honey side did not show any improvement. All patients showed healing of intertrigo in both treatment sides over time on day 14 and 21. There was one patient, whose scores of intertrigo on day 21 were lacking. During the study the intertrigo was nearly healed by day 14; however, increasing incontinence problems, led to a new episode of intertrigo in the groin, which caused her withdrawal.

On day 1, the patients were asked if they experienced complaints due to intertrigo. The prominent complaint of intertrigo was pruritus (32%), followed by pain (6.5%) and burning sensation (3.2%). The percentage of patients with no

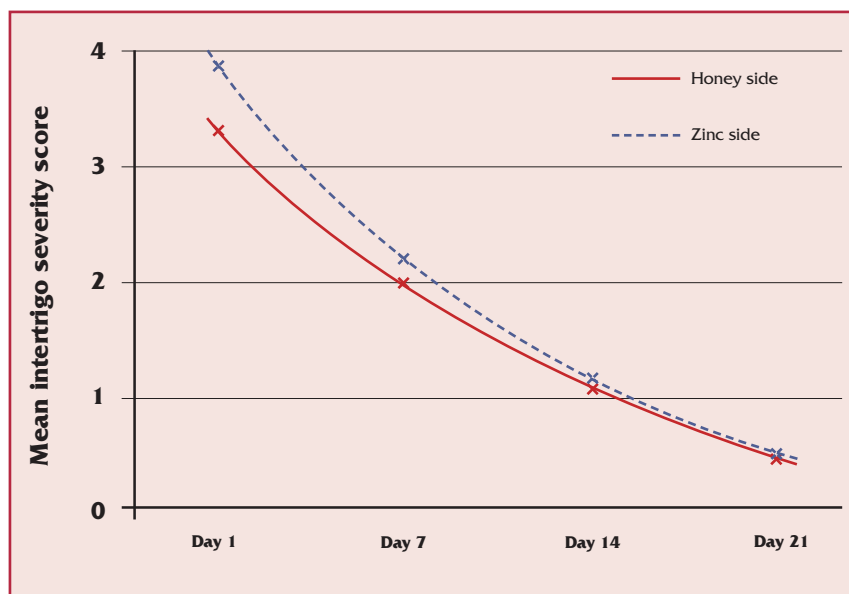


Figure 2 Mean intertrigo severity score for both sides over time (0–9 point scale)

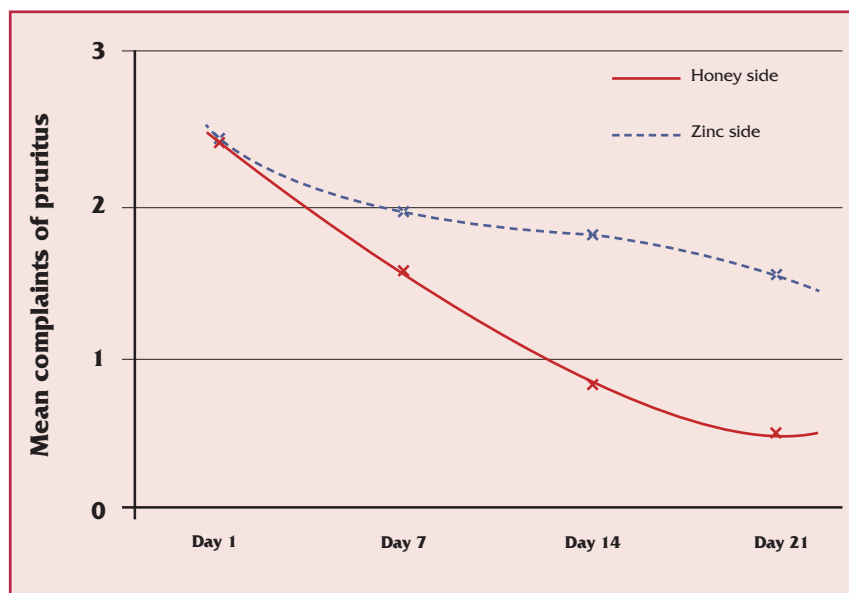


Figure 3 Number of patients reporting the sensation of pruritus (0 never, 1 seldom, 2 sometimes, 3 often)

complaints at all was 23%. The longitudinal measurements showed a decrease in symptom severity for both treatments over time. In total 12 patients experienced pruritus (39%). A decrease of pruritus sensation for both sides in time is shown in Figure 3. With regard to the sensation of pruritus, a significant decrease was found for the honey treated side over time (Wilcoxon signed-ranks test, $p < 0.05$).

On day 21, a survey was conducted in 93 respondents to evaluate users opinions. The result was that 61 respondents (66%) preferred honey treatment over the standard, compared to 8 (8.6%) who preferred the standard. A percentage of 80% preferred honey for its moisturising features, compared to 20% who experienced no difference between both treatments. In total, 43 respondents (46%) found zinc-oxide ointment difficult to clean from the skin and painful for the patients on the irritated skin (12%). The patients did not favour one therapy over the other.

KEY POINTS

- Intertrigo is a chronically, inflammatory condition of skin folds, that can cause an irritated, painful skin and pruritus sensation.
- There is a wide amount of variation in treatment of intertrigo, the most important part of treatment is: attention to skin hygiene and skin care.
- Topical treatment with a barrier cream like zinc oxide ointment can stimulate wound healing due to skin protective aspects and anti-inflammatory effects. Although application of zinc oxide ointment is labour intensive and removal of zinc rests can be painful on irritated skin.
- MediHoney barrier cream, a natural cream based on honey, can be a suitable, patient-friendly, alternative in the treatment of intertrigo. It improves wound healing, reduces pain complaints and even contains anti-pruritic properties.

Discussion

Management of intertrigo consists of preventive measurements and treatment options (Janniger et al, 2005; Mistiaen and van Halm-Walters, 2010; V&VN, 2011). New barrier creams (such as MediHoney) are increasingly being used, although clinical evidence for efficacy is lacking.

The present study showed that honey barrier cream and zinc-oxide ointment both improve the skin condition over time. A group of patients responded equally over time, which suggests that honey barrier cream can be a suitable alternative in the treatment of intertrigo.

Application of zinc-oxide ointment to the skin is labour intensive, because it needs to be stirred thoroughly before use and zinc-oxide residue has to be removed from the already irritated skin, which can be painful for the patient. Honey barrier cream is a natural product, is easy to apply without side-effects and leaves no residue on the skin (Simon, Traynor and Santos et al, 2007).

The friction forces to the skin caused by cleansing of zinc rests could have influenced the outcomes of this study in favor to honey barrier cream. Honey barrier cream is delivered in tubes and is hygienic to use. However, it is more expensive than the standard.

This study did not reveal that honey barrier cream was more effective than the standard. These results have to be confirmed in a larger study population for definitive comparative efficacy assessment.

Some patients experienced worsening of intertrigo at the beginning of treatment, followed by healing over time. Continuous skin-to-skin contact by immobilisation, e.g. in bed or wheelchair, is a clinical indicator that may prolong intertrigo. However, preventive hygiene and mobilisation measures such as increasing patient activity, may be beneficial for these patients too.

The majority of patients experienced pruritus as the main complaint of intertrigo, but this was more prevalent with zinc-oxide treatment during the study. This suggests that honey barrier cream may contain anti-pruritic properties. Although the study was not blinded for the patients, the authors do not think that this has influenced the outcomes positively for the use of honey barrier cream. The majority

of patients were not interested in the therapy they were receiving owing to their mental state. On the other hand, over time, the results of less pruritus complaints on the honey barrier cream side were consistent.

A limitation of the present study is that the number of evaluable patients is low. Therefore, the results have to be confirmed in a larger study population. Only three men were included in this study, which means gender differences analysis is not possible. However, the majority of intertrigo patients are female and they are known to be at greater risk of developing intertrigo. Another limitation of this study is the use of a non-validated scale for scoring, this limits the research finding significance.

The survey shows that the majority of nursing staff preferred honey barrier cream over the standard, because it moisturises the skin and eliminates the need to clean it after use. The use of honey barrier cream negates the need for a second, often painful cleansing act. This reduces workload and improves skin care.

Conclusion

Improved hygiene and skin care are important aspects in the treatment of intertrigo. It has been proven that attention to skin hygiene, and increasing patient activity and mobility, can prevent the development or worsening of intertrigo. In addition, daily use of barrier creams or ointments positively contribute to the treatment of intertrigo. The present study demonstrates that honey barrier cream is as effective as the standard treatment, with the advantage of not needing to be cleansed from the skin, which is required with zinc-oxide ointment. Moreover, honey barrier cream reduces pruritus complaints and is comfortable for patients. Nevertheless, the efficacy of the honey barrier cream has to be confirmed in a larger study population with special attention to its antibacterial and antifungal properties (Bardsley, 2008). **BJN**

Conflict of interest: none.

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