

Anhydrosis in the diabetic foot: a comparison of two urea creams

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ARTICLE POINTS

1 Anhydrosis compromises the barrier function of the skin, leaving it open to infection which may eventually lead to ulcer formation and ultimately amputation.

2 This study compared the efficacy of a cream containing 10% urea and a cream containing 25% urea in the treatment of anhydrosis.

3 Thirty participants applied 10% urea cream to their right foot and 25% urea cream to their left foot for 6 weeks.

4 Both urea creams led to an increase in skin hydration, but the 25% urea cream resulted in a greater increase.

5 The study suggests that creams with approximately 25% urea will be significantly more effective than preparations with 10% or less urea content.

KEY WORDS

- Anhydrosis
- Urea cream
- Hydration
- Pilot study

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Introduction

A study was carried out to compare the efficacy of two urea creams of different percentages in controlling anhydrosis in the diabetic foot. A total of 30 outpatients with evidence of bilateral anhydrosis participated in a double-blind incidental study. The study comprised a 6 week treatment regimen, with the application of 10% urea cream to the right foot and 25% urea cream to the left foot of participants. Analysis of results showed that both urea creams resulted in a statistically significant increase in skin hydration. However, the 25% urea cream produced a significantly greater increase in skin hydration than the 10% cream.

Diabetes is a metabolic disorder which is emerging as the world's commonest disease (Scott, 2002). It has been suggested that complications associated with the diabetic foot have major medical, social, and economic problems of global proportions (Boulton and Vileikyte, 2000). Diabetic foot problems are a common complication of diabetes; 23–42% of people with diabetes develop neuropathy, 9–23% develop vascular disease and 5–7% develop foot ulceration (Williams and Airey, 2000).

The coexistence of vascular, neurological and structural dysfunction may potentially lead to amputation. A person with diabetes has 15 times the risk of requiring amputation than a person without diabetes. Approximately 4% of people with diabetes will have undergone some form of amputation, ranging from a single digit to major below or above knee surgery (Scott, 2002).

Causes of anhydrosis

Neuropathy, which refers not only to sensory and motor dysfunction but also to autonomic compromise, is a common and often distressing complication of diabetes. The Rochester Diabetic Neuropathy Study (Dyck et al, 1992) found that 6% of the study population presented with autonomic neuropathy. Diabetic autonomic neuropathy can affect any organ innervated by the autonomic nervous system (Ziegler, 2001). This autonomic defect can be evident in the eccrine sweat glands of the skin. This abnormality in the body's thermoregulation

process results in anhydrosis in the foot (Ziegler, 2001). Anhydrosis refers to an integument with a dry, rough or scaly appearance that may be red, cracked, and /or itchy (Corcoran-Flynn et al, 2001). It should be noted that the presentation of anhydrosis in the diabetic foot does not necessarily result from autonomic neuropathy, but may be a consequence of a number of factors including the ageing process.

Consequences of anhydrosis

Regardless of cause, the corneo-desmosomes within the stratum corneum must be degraded for desquamation to occur. This process is controlled by the amount of available water within the stratum corneum. Any disturbance to the process of desquamation causing an increase in transdermal water loss will reduce the efficacy of the skin to function as a barrier, leaving it anhydrotic in appearance (Harding, 2000). The hydration of the surface tissue on the plantar aspect of the foot relies solely on the secretions from the sweat glands. It is generally believed that decreased autonomic function in the feet leads to drying and cracking of the skin and fissure formation (Green et al, 1999). In normal skin the stratum corneum acts as a protective barrier and prevents against desiccation, environmental damage and excess water loss (Harding et al, 2000). As a consequence of anhydrosis the barrier function of the skin is compromised, leaving the skin open to infection which may eventually lead to ulcer formation and

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1 It is widely recognised that the treatment of anhydrosis should be aimed at the restoration of the epidermal water balance.

2 There seems to be general agreement that in the treatment of anhydrosis, moisturisers containing urea maintain the skin's flexibility and prevent the development of fissuring, thereby ensuring that the integrity of the skin as a barrier is not broken.

3 Participants were given a protocol which included instructions about how to apply the creams once per day to the plantar aspect of the foot, and about how to ensure that the each cream was applied to the appropriate foot as indicated on the tube.

4 Prior to the application of either cream, a measurement of the baseline skin hydration levels was obtained from each participant.

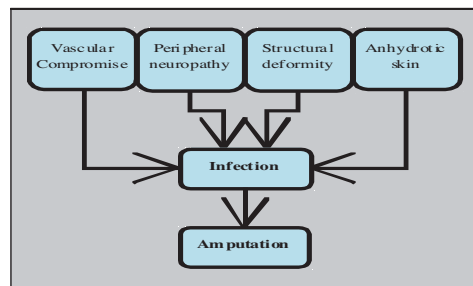


Figure 1. Pathways to amputation

ultimately amputation. It is widely believed that if the dry anhydrotic skin becomes open and/or infected, it will predispose ulceration and possible gangrene (Aye and Masson, 2002). Additionally, the anhydrosis may deteriorate due to environmental factors, e.g. cold weather, air conditioning, and external forces such as footwear and walking (Corcorran-Flynn et al, 2001). If anhydrosis is coupled with other well known risk factors the patient may be at greater risk of infection and ultimately amputation if the anhydrosis is left untreated (see Figure 1).

Treatment of anhydrosis

It is assumed that by maintaining the skin in an optimally hydrated condition it is possible to maintain the skin's flexibility, prevent the development of fissuring and ensure that the integrity of the skin's barrier to infection is not broken. The level of hydration of the stratum corneum has been shown to influence the skin's ability to act as a protective barrier (Harding, 2000; Corcorran-Flynn, 2001). It is widely recognised that the treatment of anhydrosis should be aimed at the restoration of the epidermal water balance. This may be accomplished by the use of moisturising agents which increase the skin's hydration (Serup, 1992). In order to enhance the water binding capacity of the stratum corneum, urea (which acts as a humectant) can be added to the moisturising cream (Corcorran-Flynn, 2001). Urea is a physiological substance which is widely distributed within human tissue, as well as being a major constituent of the stratum corneum as part of the skin's natural moisturising factor (Kuzmina et al, 2002). There seems to be general agreement that in the treatment of anhydrosis, moisturisers containing urea maintain the skin's flexibility and prevent the development of fissuring, thereby ensuring that the integrity of the skin as a barrier is not broken (Loden, 1996).

Study aim

The aim of this double blind pilot study was to compare the efficacy of a cream containing 10% urea and a cream containing 25% urea in the treatment of anhydrosis in the diabetic foot. We aimed to determine:

- If each cream demonstrated a significantly hydrating effect.
- If the higher concentration of urea produced a significant greater hydrating effect.

Materials and method

Ethical approval was obtained from both Glasgow Caledonian University and South Glasgow University Hospitals NHS Trust. The sample comprised 30 outpatients (14 male and 16 female; 12 with type 1 diabetes and 18 with type 2 diabetes) who attended the Centre for Diabetes and Metabolism or the Department of Podiatry, Southern General Hospital, Glasgow, during the period January 2003–March 2003. All patients presenting with evidence of bilateral anhydrosis (visual appearance only) were included. Patients with hypersensitivity to urea and any previous dermatological conditions were excluded.

Urea creams of different percentages were dispensed to patients in 100 g tubes which were labelled right and left foot, respectively. The participants and the lead researcher were unaware which cream had been dispensed in each tube.

All participants were given a written protocol regarding the application of the two creams. The protocol included instructions about how to apply the creams once per day to the plantar aspect of the foot, and about how to ensure that the each cream was applied to the appropriate foot as indicated on the tube. To minimise the risk of cross contamination the patient was instructed to use the left hand to apply the cream to the right foot and vice versa.

Prior to the application of either cream, baseline skin hydration levels were measured in each participant. The skin hydration level may be determined by measuring the skin's electrical resistance (Atkins and Thompson, 2001). Subsequent skin hydration levels were obtained after a period of 6 weeks. All

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1 The electrodes were applied in such a way that the pressure did not alter the tissue structure or was so weak that some of the contact area was lost.

2 The skin hydration monitor is a device powered by a 9 volt battery designed to measure skin resistance, using a wheatstone bridge circuit.

3 The inter-repeatability and intra-repeatability of the system was checked over a 2 week period and the system was found to be highly repeatable with an inter-day repeatability of 0.6% and an intra-day repeatability of 0.1%.

4 There was a mean increase in skin resistance levels following the application of the 10% and 25% urea cream.

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measurement values were obtained from as near possible the same site in all patients. The medial plantar aspect of the heel was chosen as the standard site for measurement. This area in the foot is recognised as a site prone to anhydrosis and fissuring in the people with diabetes (Tyrrell, 2002; Aye and Masson, 2002). When applying the electrodes to the skin the application of pressure was not critical (Lindholm-Sethson et al, 1998). However, the electrodes were applied in such a way that the pressure did not alter the tissue structure or was so weak that some of the contact area was lost.

Analysis of creams

An independent assay of the two creams was carried out to determine the weight by weight (w/w) total nitrogen as urea in the two creams used in the study. The results revealed that the cream applied to the right foot contained an average of 12.38% w/w total nitrogen as urea, and the cream applied to the left foot contained an average of 25.22% w/w total nitrogen as urea.

Measurement of outcomes

The measurement system was constructed by the technical department associated with the School of Health and Social Care, Glasgow Caledonian University. The skin hydration monitor is a device powered by a 9 volt battery designed to measure skin resistance, using a wheatstone bridge circuit. The system comprised a hand-held portable instrument which measured the electrical resistance of the stratum corneum. The level of hydration can be assessed by measuring the changes in the skin's electrical resistance and can be referred to as the 'galvanic skin response'. The degree of skin resistance was

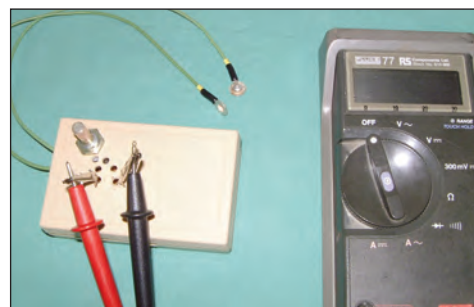


Figure 3. Skin hydration measurement system.

recorded in volts. The volt meter was set with a base value of 1.600 V. This value was used because of the sensitivity of the resistors used in the construction of the meter. The greater the degree of skin resistance (hydration), the higher the voltage recorded (Atkins and Thompson, 2001).

Repeatability of measurement system

In order to assess the repeatability of the measurement system, known values of resistors (1KΩ, 100 KΩ 330 KΩ, 560 KΩ and 660 KΩ) were connected to the electrodes and the resultant voltage was recorded. The inter-repeatability and intra-repeatability of the system was checked over a 2 week period and the system was found to be highly repeatable with an inter-day repeatability of 0.6% and an intra-day repeatability of 0.1%.

Results

Following completion of the study, it was revealed that the tube labelled 'right' contained 10% urea cream and the tube labelled 'left' contained 25% urea cream. Table 1 shows the mean (and standard deviation) skin resistance by treatment stage (before and after treatment) and urea concentration (10% vs 25%). There was a mean increase in skin resistance levels following the application of the 10% and 25% urea cream.

Data were analysed using a repeated-measures ANOVA with both treatment stage

Table 1. Skin resistance measurements for 25% and 10% urea cream

| | Mean skin resistance before treatment (V) | Mean skin resistance after treatment (V) |
|----------|---|--|
| 10% urea | 1.627 0.048 (sd) | 1.645 0.057 (sd) |
| 25% urea | 1.633 0.068 (sd) | 1.664 0.080 (sd) |

sd = standard deviation

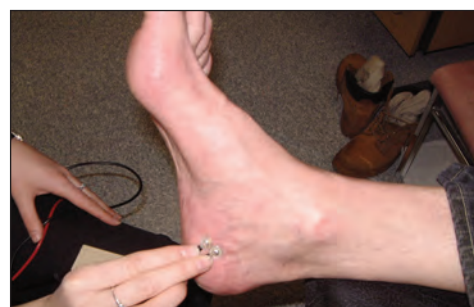


Figure 2. Site of hydration measurement.

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1 After treatment there was significantly greater skin hydration for feet treated with the 25% cream compared with the 10% cream.

2 Following the completion of the study no adverse reactions to the application of either creams were reported by the participants.

3 It is recognised that the study was underpowered regarding the number of patients recruited for this pilot and that the results may have been influenced by the participants not adhering to the protocol for the application of the creams.

4 From the results found in this pilot study, we can recommend the use of urea cream in the treatment and prevention of anhydrosis in the diabetic foot.

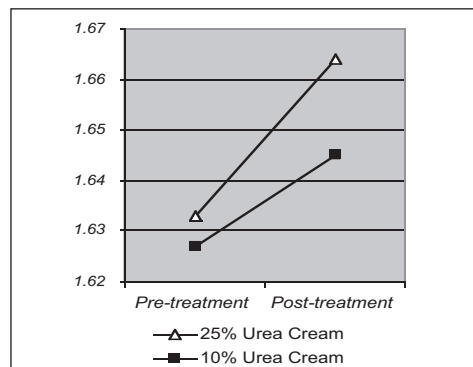


Figure 4. Comparative mean skin resistance levels utilising 25% and 10% urea cream before and after treatment.

and urea concentration as within-participant factors. Overall, a significant main effect of both treatment stage ($p < 0.001$) and urea concentration ($p < 0.05$) were observed, along with a significant interaction ($p < 0.001$).

At baseline, there was no significant difference in skin resistance between left and right feet ($p = 0.269$). Both the 10% ($p < 0.001$) and 25% ($p < 0.001$) urea cream resulted in significantly greater skin resistance. After treatment we observed a significantly greater skin hydration for feet treated with the 25% cream compared with the 10% cream ($p < 0.005$; Figure 4).

Discussion

Both the 10% and 25% cream resulted in a significant increase in skin hydration (as measured by skin resistance levels). The 25% cream increased skin hydration significantly more than the 10% cream.

Following the completion of the study no adverse reactions to the application of either creams were reported by the participants. It is recognised that the study was underpowered in terms of the number of patients recruited, and that the results may have been influenced by the participants not adhering to the protocol for the application of the creams. There was a statistically significant increase in skin hydration with the 25% urea cream when measurements of the percentage change in baseline skin resistance level were observed (Figure 4). There was a greater level of skin rehydration following the continual application of the cream containing 25% urea when compared with the continual application of the cream containing 10% urea.

Areas for potential error include: participant compliance, style of footwear;

type of hosiery worn throughout the study; and the frequency of foot washing carried out by participants during the trial period.

Conclusion

On the basis of the results found in this pilot study, we can recommend the use of urea cream in the treatment and prevention of anhydrosis in the diabetic foot. We acknowledge that this study has only compared the efficacy of two urea creams and has not included the effectiveness of other creams which may be purchased by the public. However, this study suggests that creams with approximately 25% urea will be significantly more effective than preparations with 10% or less urea. ■

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