Ammonium Lactate 12% Lotion *versus*a Liposome-Based Moisturizing Lotion for Plantar Xerosis
A Double-Blind Comparison Study

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Two emollients, ammonium lactate 12% lotion and a liposome-based moisturizing lotion, were compared in a double-blind test for efficacy in the treatment of plantar xerosis. A total of 43 out of 57 participants (75%) with bilateral plantar xerosis followed instructions completely and applied the lotions (one to each foot) twice daily for 4 weeks. Each participant was evaluated once a week for 6 weeks (the final 2 weeks for evaluation of post-treatment regression) to determine xerotic grade (degree of dryness) and treatment effectiveness. With both lotions, significant improvement began during the second week of treatment and continued into the fourth week. There were no significant differences between the two lotions in the 6-week patterns of either xerotic grade or treatment effectiveness. (J Am Podiatr Med Assoc 89(10): 502-505, 1999)

Xerosis (dry skin) and hyperkeratosis (callus formation) are often associated with biomechanical disorders of the foot, autonomic dysfunction, or vasculopathy in patients with diabetes mellitus.1, 2 If treatment is delayed or avoided, more complicated medical problems often arise, including skin fissures, ulcerations, and infections resulting from severe xerosis. Xerosis-associated damage to the foot therefore represents a serious challenge for podiatric physicians and their patients, especially patients with diabetes, who are already prone to infections. Indeed, 85% of the roughly 60,000 lower-extremity amputations performed annually in the United States result from morbidity of the diabetic foot.3 Standard treatments for xerosis include a variety of commercial emollients (moisturizers), some of which contain alpha-hydroxy acids (eg, lactic acid) and some of which contain lipid-soluble substances. This study compared the clinical efficacy of treatment with a conventional ammonium lactate 12% lotion (Lac-Hydrin, Westwood-Squibb Pharmaceuticals, Buffalo, New York) with that of treatment with a liposome-based moisturizing lotion (Lypha-Zome, Fountain Pharmaceuticals, Inc, Largo, Florida).

Xerosis results from a decrease in moisture level of the stratum corneum. In transepidermal water loss, water migrates upward through the epidermis, hydrating the stratum corneum before evaporating into the atmosphere.4 Humectants such as lactic acid prevent transepidermal water loss by attracting water to the stratum corneum.5 Occlusives also pre-

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vent transepidermal water loss by physically blocking the epidermis with a lipid such as petrolatum. To be clinically effective, emollient systems must provide precise combinations of occlusives and humectants. Currently, lactate emollient systems provide the most effective treatment for moderate-to-severe xerosis, including hyperkeratotic disorders.

Lactic acid, an alpha-hydroxy acid, is a natural humectant that increases skin moisture and reduces transepidermal water loss. Lactic acid is commercially available in lotions of 5% to 12% lactic acid with ammonium hydroxide in a nonionic glycol base. Ammonium lactate reduces the thickened stratum corneum and removes thick scales seen in hyperkeratotic conditions. At higher concentrations, this alpha-hydroxy acid has a normalizing effect on the stratum corneum.

The choice of delivery system is an important consideration when choosing a lipid-based emollient to ensure penetration of the stratum corneum. A new preparation of petrolatum, paraffin, and mineral oil in natural soy lecithin (LyphaZome) has recently been developed. This delivery system utilizes microscopic spheres called liposomes to encapsulate water-soluble and lipid-soluble emollients for penetration of the stratum corneum to increase skin hydration (W Crow, Technical Director, Food, Drug, Chemical Services, Sarasota, Florida, personal communication, 1998).

The purpose of this study was to examine the clinical effects of ammonium lactate 12% lotion compared with those of a liposome-based moisturizing lotion. If both substances are associated with similar clinical response and effectiveness, then the preference of either the patient or the clinician might be the only serious consideration in choosing an emollient for the treatment of xerosis.

Materials and Methods

Fifty-seven individuals volunteered to participate in a randomized, double-blind, bilateral, paired comparison study. “A” and “B” formulations of ammonium lactate 12% lotion (Lac-Hydrin) and a liposome-based moisturizing lotion (LyphaZome) were packaged in identical containers marked with the study number, lotion letter, and side of application. Each lotion was applied twice daily for 4 weeks; this was followed by a 2-week post-treatment period in which neither lotion was applied.

All of the participants had at least a moderate degree of plantar xerosis, hyperkeratosis, or both, with equal dryness bilaterally. Participants who did not apply the lotions twice daily were eliminated from the study. Participants were instructed not to apply over-the-counter or prescription products to their feet or use any means of debridement such as pumice stones for the duration of the study.

The effects of both lotions on xerosis and hyperkeratosis of the feet were evaluated with numerical measurement scales. A grading system with numbers indicating xerotic stage, corresponding to qualitative descriptions of xerosis or hyperkeratosis, was used to evaluate participants at week 0 through week 6 (Table 1). The incidence and severity of side effects were noted weekly. Overall treatment effectiveness was determined globally by the clinicians at the end of week 4 and week 6 according to the following scale: 1 = worse, 2 = no change, 3 = slight improvement, 4 = moderate improvement, 5 = excellent, 6 = clear.

Statistical Analyses

The numerical results obtained for the 57 participants included data on clinical grade of xerosis and the measure of effectiveness at the end of weeks 4 and 6. Complete data were obtained from 43 of the participants (75%). All statistical methods used in this study were those of Sokal and Rohlf, and all tests used the \( \alpha = .05 \) level to indicate statistical significance.

Mean, median, and sample rank for xerotic grade per treatment were calculated for each of the 6 weeks. The mean xerotic grades for ammonium lactate 12% lotion and the liposome-based moisturizing lotion for each week were compared using a paired \( t \)-test, and the median and rank for xerotic grade for each treatment per week were compared using the Wilcoxon signed rank test.

Changes over time in mean, median, and sample rank for each treatment were assessed with one-way analysis of variance of treatment means (by weeks) and the Kruskal-Wallis one-way analysis of variance on rank (by weeks). Week 0 (pretreatment) was used as a control, and Dunnett’s post-test (for treatment means) and Dunn’s post-test (for sample rank) were used to compare xerotic grade at week 0 with xerotic grade at weeks 1 through 6.

Mean, median, and sample rank for effectiveness per treatment were calculated for each of the 6 weeks. As with xerotic grade described above, for sample ef-
fectiveness the paired t-tests, the Wilcoxon signed rank tests, and an analysis of variance on means and the Kruskal-Wallis tests on rank were performed for each treatment.

Results

Of the 57 participants in the study, only 43 were evaluated. Ten participants were noncompliant and were eliminated from the study. Four additional participants had adverse reactions (itching and irritation) to both lotions within the first 2 weeks and were therefore eliminated. Of the 43 participants, 17 (40%) had diabetes mellitus. The mean age of participants was 42 years, with ages ranging from 13 to 72 years. The mean weight of participants was 87 kg, with weights ranging from 52 to 136 kg. Of the 43 participants, 20 were self-reported as “Caucasian,” 12 as “black,” 6 as “Hispanic,” and 5 as “Asian.”

Xerotic Grade

There were no significant differences in sample median or ranking between ammonium lactate 12% lotion and the liposome-based moisturizing lotion in any of the weeks of treatment (Fig. 1). For both treatments there were significant changes in median and rank between week 0 and week 6 (ammonium lactate 12% lotion, Kruskal-Wallis statistic $H = 109.7$, $df = 6$, $P < .001$; liposome-based moisturizing lotion, $H = 123.3$, $df = 6$, $P < .001$).

The mean xerotic grade before treatment with either ammonium lactate 12% lotion or the liposome-based moisturizing lotion (week 0) was between “moderate” and “severe” (mean, 2.2). By the end of week 4, the mean values for both treatments decreased to just below the boundary between “none” and “slight” (mean, 0.8). At the end of post-treatment week 5, the grades for both treatments rose to just above the boundary between “none” and “slight” (mean, 1.1). At the completion of the study (week 6), the mean grades for both treatments rose again, close to the midpoint between “slight” and “moderate” (mean, 1.6).

Effectiveness

There were no significant differences in sample median or ranking between ammonium lactate 12% lotion and the liposome-based moisturizing lotion at the end of either week 4 or week 6 (Fig. 2). For both treatments there were significant changes between the post-treatment weeks in sample median (ammonium lactate 12% lotion, $H = 15.5$, $df = 1$, $P < .001$; liposome-based moisturizing lotion, $H = 16.3$, $df = 1$, $P < .001$).

Figure 1. Mean xerotic grade achieved with ammonium lactate 12% lotion and a liposome-based moisturizing lotion by week (error bars are 95% confidence interval estimates of the mean grade per treatment). The number above each pair of bars shows the Wilcoxon-test probability of there being no significant difference between median values from the paired samples. Mean xerotic grade is as follows: 0 = none, 1 = slight, 2 = moderate, 3 = severe.

Figure 2. Mean effectiveness of ammonium lactate 12% lotion and a liposome-based moisturizing lotion by week (error bars are 95% confidence interval estimates of the mean grade per treatment). The number above each pair of bars is the Wilcoxon-test probability of there being no significant difference between median values from the paired samples. Mean effectiveness is as follows: 1 = worse, 2 = no change, 3 = slight improvement, 4 = moderate improvement, 5 = excellent, 6 = clear.
The clinical mean effectiveness at the end of week 4 for ammonium lactate 12% lotion was between “moderate improvement” and “excellent” (mean, 4.7); the mean for the liposome-based moisturizing lotion was also between “moderate improvement” and “excellent” (mean, 4.6) (Fig. 2). At the end of the study (end of week 6), the mean effectiveness for the ammonium lactate 12% lotion had decreased to between “slight improvement” and “moderate improvement” (mean, 3.7), as had the mean for the liposome-based moisturizing lotion (mean, 3.5).

Discussion

Plantar xerosis and hyperkeratosis have many etiologies, including biomechanics, footwear, environmental factors, genetics, and systemic factors such as diabetes.1 According to the 1997 Diabetes Survey conducted by the American Podiatric Medical Association,10 approximately 95% of podiatric physicians treated diabetic patients for skin fissures and 97.9% prescribed skin creams or lotions. The current standard of care for mild-to-moderate hyperkeratosis involves increasing the moisture content of the stratum corneum with an emollient system.

All participants in this study initially had at least moderate xerosis and hyperkeratosis bilaterally. At the end of the treatment period, the 43 participants who completed the course of treatment had either no xerosis or only slight xerosis remaining. There were no significant clinical differences between ammonium lactate 12% lotion and the liposome-based moisturizing lotion. These participants were treated safely and effectively with ammonium lactate 12% lotion and the liposome-based moisturizing lotion twice daily for 4 weeks. After 2 weeks of no treatment, the degree of xerosis had increased markedly bilaterally, as determined by the return of dry, scaly, and thickened plantar skin.

Only four participants had adverse reactions after applying the two lotions. These participants complained of burning and itching of both feet within the first 2 weeks of use of the lotions. These adverse reactions resolved soon after the application of the lotions was discontinued. The participants were excluded from further evaluation.

Conclusion

In this study, ammonium lactate 12% lotion and a liposome-based moisturizing lotion were compared in a randomized, double-blind evaluation. Forty-three participants with at least moderate plantar xerosis and hyperkeratosis bilaterally applied the lotions for 4 weeks; this was followed by a 2-week post-treatment regression period. By week 4, both lotions equally and significantly reduced the xerosis and hyperkeratosis to a slight clinical grade or appearance with a global effectiveness rating of moderate improvement to excellent. The post-treatment regression period saw the return of dryness, scales, and thickening of the plantar skin; by week 6, there was slight-to-moderate xerosis and hyperkeratosis, with a global effectiveness rating of slight-to-moderate improvement. There were four reported cases of adverse reactions affecting both feet, and these reactions were resolved by the discontinuation of the lotions. Statistical and clinical evidence indicates that there were no significant differences between the ammonium lactate 12% lotion and the liposome-based moisturizing lotion. Therefore, the choice of one or the other treatment should be a matter of personal preference of clinician and patient.

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