Use of a Keratin-Based Wound Dressing in the Management of Wounds in a Patient with Recessive Dystrophic Epidermolysis Bullosa

Robert S. Kirsner, MD, PhD; Sharon Cassidy, RCpN, PGDip (Prof Nsg); Clive Marsh, PhD; Alejandra Vivas, MD; and Robert J. Kelly, PhD

ABSTRACT

Recessive dystrophic epidermolysis bullosa is a rare, autosomal recessive blistering condition. The authors successfully treated a patient with a novel keratin-based dressing. Starting at 11 months, 1 hand and 1 foot of the patient was treated, and significant improvement was observed. Thereafter, keratin treatment was applied to both hands and feet.

KEYWORDS: wound healing, keratin, recessive dystrophic epidermolysis bullosa

ADV SKIN WOUND CARE 2012;25:400–3

BACKGROUND

Although caused by mutations in the same gene, two major types of dystrophic epidermolysis bullosa (DEB) exist, the most severe autosomal recessive type and the milder form, autosomal dominant type.[1] Wound care for patients with recessive dystrophic epidermolysis bullosa (RDEB) represents a therapeutic challenge. Recessive dystrophic epidermolysis bullosa is caused by a defect in the gene for type VII collagen, and as a result, patients fail to produce functional collagen VII protein. Type VII collagen normally provides support between dermis and basal lamina, forming the major component of the anchoring fibrils.[2] Thus, RDEB patients have poor adhesion of the epidermis to the dermis and are susceptible to resultant blistering after minor trauma. Wound care in these patients typically consists of using nonadherent (often silicone-based) dressings to provide moist wound healing, prevent infection, protect the patient from trauma, and allow removal without disturbance to the wound bed. However, in this standard mode of care, healing is slow, and skin durability is poor. Furthermore, the patient is compromised in activities able to be undertaken without recurrent blistering and wounding. Patients with RDEB have a diminished life span, often as a result of their developing squamous cell carcinoma at a high rate.[3]

RESEARCH FINDINGS

Recent advances have been made in the understanding of the role of keratin in wound healing.[4] For example, when the skin is wounded, keratin 17 is up-regulated, and in keratin 17 knockout mice, poor healing is observed.[5] Given its now appreciated role in healing, it was hypothesized that exogenous keratin might have a beneficial effect. Keratin-based wound dressings have been developed, and the keratin protein is isolated in a manner that retains its functionality. This functionality has been demonstrated by both in vitro tests showing that keratinocyte proliferation and migration rates are enhanced[6] and by in vivo tests conducted in a porcine partial-thickness wound healing model[7] showing accelerated epithelialization rates. Molecular analyses suggest that keratin formulations lead to keratinocyte activation and epidermal migration by up-regulating keratin gene expression.[7,8] Based on data available in 2009 and problems of wound healing in patients, the authors chose to use a novel keratin-based dressing for treatment of a patient with RDEB. As care progressed, further data on the healing properties of these keratin-based dressings reinforced their potential.

CASE EXAMPLE

The patient was a vaginally delivered boy born at full term. Shortly after his birth, the infant rubbed his heels together, which peeled back the epidermal layer to expose the dermis, as illustrated in Figure 1. Twelve years earlier, one of the patient's cousins had

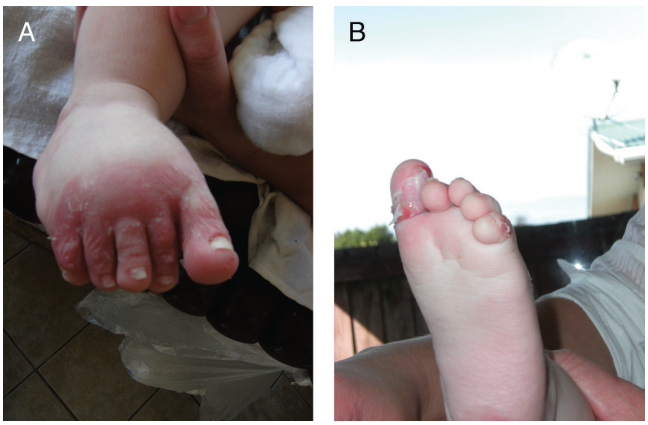
Robert S. Kirsner, MD, PhD, is Chief of Dermatology, University of Miami Miller School of Medicine, and Professor, Vice Chairman & Stiefel Laboratories Chair of the Department of Dermatology and Cutaneous Surgery, University of Miami, Florida. Sharon Cassidy, RCpN, PGDip (Prof Nsg), is Nurse/Manager and EB Nurse Specialist, SOS Nursing, Christchurch, New Zealand. Clive Marsh, PhD, is Development Engineer, Keraplast Technologies LLC, San Antonio, Texas. Alejandra Vivas, MD, is Postdoctoral Associate, Wound Healing Research Clinic, University of Miami Miller School of Medicine, Florida. Robert J. Kelly, PhD, is Research Director, Keraplast Technologies LLC, San Antonio, Texas. Dr Kirsner has disclosed that he is/was an advisor to Keratec, Ltd. Dr Cassidy has disclosed that she is a consultant advisor for Keraplast Technologies, LLC. Dr Vivas has disclosed that she has no financial relationships related to this article. Drs Marsh and Kelly have disclosed that they are employees of Keraplast Technologies, LLC. The authors disclose that Keragel T dressings used on the reported patient were provided by Keraplast, San Antonio, Texas, and that portions of the article were presented in poster formats at conferences (Society for Pediatric Dermatology, Portland, Oregon, 2010; DEBRA, Cincinnati, Ohio, 2010; and New Zealand Dermatology Society, Christchurch, New Zealand, 2010). Submitted October 6, 2011; accepted November 4, 2011.

Figure 1.
PHOTO SOON AFTER BIRTH IN PATIENT WITH RDEB

been diagnosed with RDEB but had since died. Histology and electron microscopy confirmed a diagnosis of RDEB.

Before keratin-based dressings were initiated, the infant experienced blisters all over his body, particularly on his hands and feet. Treatment included cleansing with saline and applying a soft silicone-based, nonadherent primary dressing (Mepitel; Mölnlycke Health Care, Norcross, Georgia) and a secondary dressing—for the feet, an absorbent foam dressing (Mepilex; Mölnlycke), and for the hands, a tubular gauze bandage wrap. Dressing changes were performed 4 times per week. Blisters, on average, took 2 weeks to heal, and the skin would break down repeatedly the next week (Figures 2A and B). The care was provided by a multidisciplinary team involving a wound care clinician, trained caregivers, and the family of the patient.

Figure 2.
RIGHT FOOT AND LEFT FEET PRIOR TO TREATMENT



A keratin-based wound dressing (Keragel T; Keraplast, San Antonio, Texas) was applied directly to the wounded areas on the left hand and left foot and was covered with the same secondary dressings used as part of standard care. The right foot and hand continued with standard care and acted as controls. All dressings continued to be changed 4 times per week. Log sheets were kept to monitor the occurrence and severity of blisters, and faster healing (reduced from 14 to 7 days) was recorded. More robust skin was also observed on the treated areas during the 6 months following the start of treatment with decreased number of blisters recorded on the treated side (6 and 5 blister episodes on treated foot and hand, respectively, and 12 and 14 on control foot and hand, respectively) (Figures 3A and B, 4A and B, and 5A and B).

After observing faster healing and less reblistering on the treated hand and foot after 6 months, treatment with the keratin-based wound dressing was initiated on the right hand and foot at the request of the parents and caregivers. Subsequently, these areas also became more durable with less frequent and less severe blistering (Figures 6A and B). Use of the keratin-based wound dressing made the skin of the hands and feet sufficiently robust, so that the soft silicone-based, nonadherent primary dressing was no longer needed, and a thinner absorbent foam secondary dressing was used on the feet. This change made the wound dressings less bulky, which improved the patient's dexterity and quality of life.

Use of the keratin-based dressing also cut care costs through reduced time at dressing changes and reduced costs of other

Figure 3.
CONTROL RIGHT FOOT AND TREATED LEFT FOOT, RESPECTIVELY, AFTER 4 MONTHS—WITH TREATED FOOT DEMONSTRATING LESS SEVERE AND FREQUENT BLISTERING

Figure 4.
TREATED HAND WITH TYPICAL BLISTER AFTER 4 MONTHS AND 1 WEEK LATER WITH RAPID HEALING

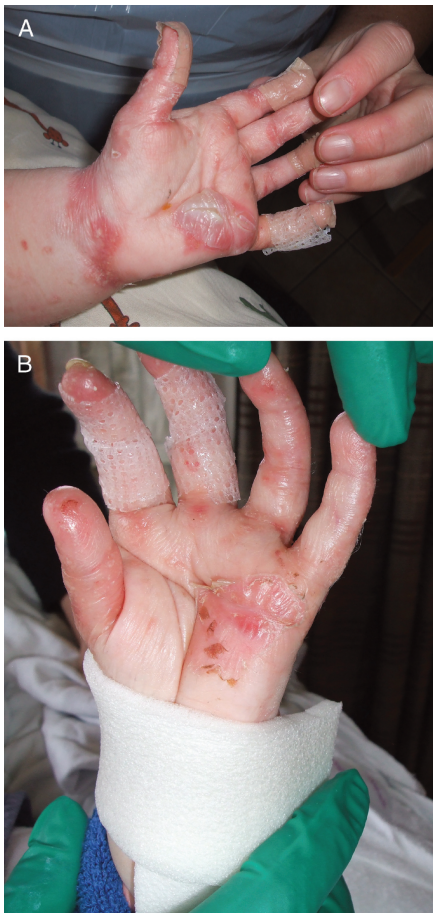


Figure 6.
LEFT AND RIGHT HANDS, RESPECTIVELY, 2 YEARS AFTER THE STUDY COMMENCED, WITH IMPROVED STATE SINCE START OF TREATMENT

Figure 5.
CONTROL RIGHT HAND AND TREATED LEFT HAND, RESPECTIVELY, AFTER SEVERE TRAUMA THAT OCCURRED AFTER 4½ MONTHS—LESS SEVERE BLISTERING OF LEFT HAND PRESUMED DUE TO IMPROVED SKIN ROBUSTNESS

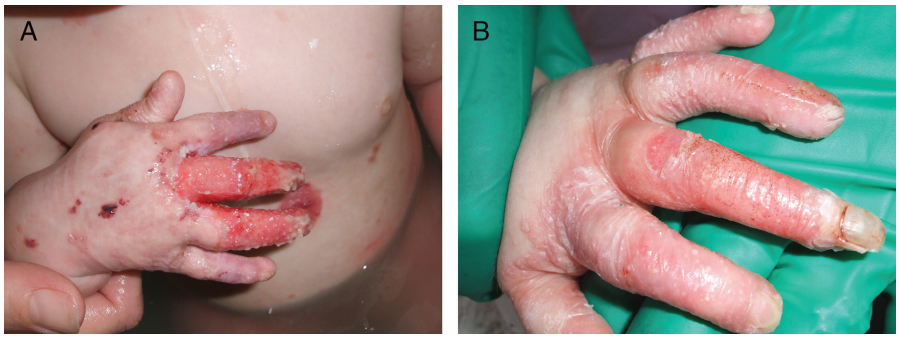


Table 1.

COMPARISON OF COSTS[a] BEFORE AND AFTER THE KERATIN-BASED WOUND DRESSING WAS USED

	Each Foot			Each Hand			Total Costs per Dressing Change for Both Hands and Both Feet	
		Costs per Dressing Change			Costs per Dressing Change			
	Dressings Used	Dressing	Labor	Dressings Used	Dressing	Labor	Dressing	Labor
Before the keratin-based dressing was used	Soft silicone-based, nonadherent primary dressing and an absorbent foam secondary dressing	$36.16	$12.60	Soft silicone-based, nonadherent primary dressing and a tubular gauze bandage wrap	$9.32	$8.40	$90.96	$42.00
After the keratin-based dressing was used	¼ tube of keratin-based dressing and a thin, absorbent foam secondary dressing	$13.26	$10.50	¼ tube of keratin-based dressing and a tubular gauze bandage wrap	$7.70	$6.30	$41.92	$33.60

	Each Foot		Each Hand		Total: Both Hands and Both Feet		
	Dressing Cost	Labor Cost	Dressing Cost	Labor Cost	Dressing Cost	Labor Cost	Total Cost
Cost savings, per dressing change, made by using the keratin-based dressing	$22.90	$2.10	$1.62	$2.10	$49.04	$8.40	$57.44
Annual cost savings made by using the keratin-based dressing	$4763.20	$436.80	$336.96	$436.80	$10,200.32	$1,747.20	$11,947.52

[a]Costs for the dressings are based on the price paid by the providing health institution at the time of the study; labor costs are $16.80 per hour. All cost figures are in US dollars.

dressings (estimated to be approximately US $12,000 annually) needed, as quantified in Table 1. The reported observations of this patient are consistent with the hypothesis that the keratin-based wound dressing enhances keratinocyte activity (migration and proliferation rates) in wounds and accelerates healing. The authors' findings also reinforce that keratin proteins are critical in wound healing.

SUMMARY

In summary, the authors observed faster healing and improved skin robustness from the use of the keratin-based dressing. This supports the hypothesis that keratin dressings enhance keratinocyte activity and accelerate epithelialization and wound closure.[9] In this young patient, keratin-based dressings improved his quality of life and reduced the cost of care. ●

REFERENCES

1. Dystrophic epidermolysis bullosa. Genetics Home Reference. http://ghr.nlm.nih.gov/condition/dystrophic-epidermolysis-bullosa. Accessed June 7, 2012.
2. McMillan JR, Long HA, Akiyama M, Shimizu H, Kimble RM. Epidermolysis Bullosa (EB) – diagnosis and therapy. Wound Practice & Research, Journal of the Australian Wound Management Association 2009;17(2):62-70.
3. Kirsner RS, Hu S. Recessive dystrophic epidermolysis bullosa and squamous-cell carcinoma: the role of type VII collagen. J Invest Dermatol 2007;127:2292.
4. Omary MB, Ku NO. Cell biology: skin care by keratins. Nature 2006;441:296-7.
5. Kim S, Wong P, Coulombe PA. A keratin cytoskeletal protein regulates protein synthesis and epithelial cell growth. Nature 2006;18;441:362-5.
6. Van Dyke M, Blanchard C, Timmons S, Siller-Jackson A, Smith R. Soluble Keratin Peptide. US patent 6,270,79. San Antonio, TX: Keraplast Technologies, Ltd; 2001.
7. Perez R, Kirsner R, Gil J, Valdes J, Davis S. Evaluation of the effects of two keratin formulations on wound healing and keratin gene expression in a porcine model. Proceedings of Symposium on Advanced Wound Care, April 26-28, 2009, Dallas, TX.
8. Davis SC, Perez R, Rivas Y, Gil J, Valdes J, Kirsner R. The effect of a keratin-based dressing on the epithelialization of deep partial thickness wounds. Proceedings of American Academy of Dermatology Meeting, March 6-10, 2009, San Francisco, CA.
9. Pechter PM, Gil J, Valdes J, et al. Keratin dressings speed epithelialization of deep partial thickness wounds. Wound Repair Regen 2012;20:236-42.