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Evaluation of Wound Care Options in Patients with Recessive Dystrophic Epidermolysis Bullosa: A Costly Necessity

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Abstract: **Recessive dystrophic epidermolysis bullosa (RDEB) is a genetic disorder in which mutations in collagen VII, the main component of the anchoring fibril, lead to skin fragility and to the development of acute and chronic wounds. Wound care and dressing changes are an important part of the daily lives of individuals with RDEB. Ideal wound care should improve wound healing, minimize pain, and improve quality of life. The objective of the current study was to review wound care options that might be used in a patient with RDEB and calculate the cost of these various options based on publicly available pricing of wound care products. There is a wide range of costs for wound care options in patients with RDEB. For example, a 1-day supply of dressing for a neonate boy with RDEB ranges from $10.64 for the least expensive option to $127.54 for the most expensive option. Wound care in patients with severe, generalized RDEB has not only a significant economic effect, but also directly affects quality of life in this patient population. Although randomized controlled trials evaluating different wound care products in patients with RDEB are lacking, small studies and expert opinion support the use of specialized nonadherent dressings that minimize skin trauma and promote wound healing. Until there is a cure, prospective studies are needed to assess pain, quality of life, and wound healing associated with the use of specialized wound care products for this life-altering condition.**

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Epidermolysis bullosa (EB) refers to a diverse group of inherited skin fragility disorders. Recessive dystrophic epidermolysis bullosa (RDEB) results from mutations in the gene encoding collagen VII, the main component of the anchoring fibril, which maintains adherence between the dermoepidermal junction and the dermis. Severe, generalized RDEB results from truncation mutations in the collagen VII gene, leading to absent or rudimentary anchoring fibrils. Patients with severe, generalized RDEB develop acute and chronic wounds that cause pain, disability due to joint contractures and mitten-hand deformity, and ultimately a shortened life span with premature death due to squamous cell carcinoma arising within chronic wounds (1).

Despite intense research (2,3), no effective treatment has been found for EB. A groundbreaking trial of allogeneic stem cell transplantation in seven patients with RDEB demonstrated better wound healing and less blistering after transplantation, but two patients died as a consequence of the transplant conditioning regimen or posttransplantation infection, and no cure has been found (4).

Given the lack of effective therapies, wound care remains the cornerstone of treatment in these patients. Although there are no randomized controlled trials (RCTs) comparing wound care options, expert consensus is that the use of sophisticated, nonadherent dressings in patients with RDEB decreases pain and improves wound healing. The goal of this study was to examine a variety of wound care options that might be used in a patient with severe generalized RDEB and calculate the cost of these options based on publicly available pricing. Knowledge of wound care costs is important in planning health care for patients with RDEB and for planning future studies of wound care products in these patients.

MATERIALS AND METHODS

The cost of daily wound care supplies was determined by calculating the amount of wound supplies necessary to cover the body surface area (BSA) affected with wounds in a hypothetical neonate, infant, and 10-year-old child with severe generalized RDEB. The BSA in each age group was calculated using the Mosteller formula (5) or the Centers for Disease Control and Prevention nomograms for weight and height (6). BSA was then divided into specific body sites based on modified Lund and Brower burn charts appropriate for each age group (7). Finally, BSA involvement with wounds on each body site was extrapolated from published composite anatomic diagrams created using data from the National EB Registry from 1986 to 2002 (8). In that study, the frequency of different anatomic site involvement was determined based on physical examinations of patients with different forms of EB, including severe generalized RDEB. Using these published diagrams, we grouped the frequency of wound involvement at each body site into tertiles (<1%–10%, 11%–50%, and 51%–100%). Given the practical limitations of bandaging an affected area and avoiding trauma to surrounding intact skin, we assumed that bandaging would be required for the upper limit of the amount of affected skin in each tertile (10%, 50%, and 100% respectively). A schematic of the methods used in our calculations can be found in Fig. 1.

The cost of several nonadherent wound care products was obtained from an online search engine (Amazon. com) to simulate the experience of a patient without insurance and lacking access to wholesale distributors (Table 1). The analysis of dressing choices was modeled on the elegant review of the principles of wound care for patients with EB by Lara-Corrales et al (9). The cost of a 1-day supply of dressings was calculated for four wound care options chosen to reflect a range of wound care costs and real-life choices for individuals with RDEB. Each layer of dressing material used on an individual body site was assumed to cover the entire affected BSA (e.g., if a silicone wound dressing and gauze wrap were used together, the amount of silicone wound dressing and gauze used was assumed to be equivalent for that affected area).

Institutional review board project review was waived because all calculations were performed using publicly available data and no patient evaluation or chart review was performed.

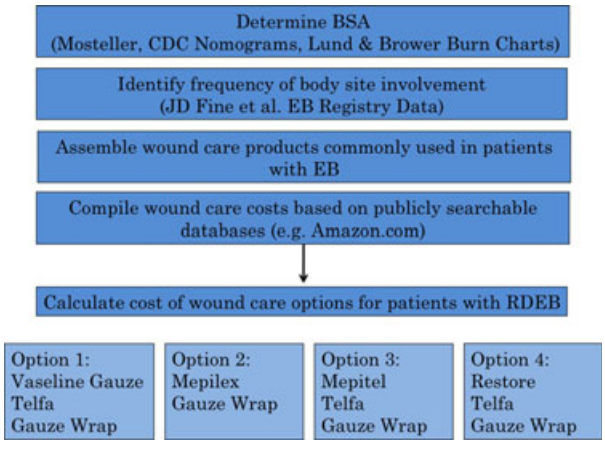

Figure 1. Methods and materials schematic.

RESULTS

Daily wound care costs for select wound care options are displayed in Table 2. Wound care costs for a single dressing change for a neonatal boy ranged from $10.43 for the least expensive option to $127.54 for the most expensive option. Wound care costs ranged from $22.15 to $270.92 daily for an infant boy and from $54.54 to $668.23 for a 10-year-old boy.

DISCUSSION

Physicians are often asked to justify the high cost of nonadherent wound care products for their patients with severe generalized RDEB. Optimizing wound healing, preventing infection, and reducing pain are routine aspects of proper wound care for all patients. For individuals with RDEB with inherent skin fragility, multiple wounds, and a propensity for progressive debilitating scarring and contractures (Fig. 2A, B), reducing skin trauma associated with dressing changes is an especially important argument for advocating for the medical necessity of advanced wound care products.

Although RCTs comparing different wound care products in RDEB are lacking, we can extrapolate from data that support the efficacy of nonadherent dressings in other patient populations. One study compared the force needed to remove dressings in normal volunteers; silicone dressings were less adherent than other dressings such as acrylates, polyurethane, and hydrocolloids (10). As expected, adhesion to skin significantly correlated with the pain of dressing removal. Several RCTs and multicenter trials in individuals with burns and ulcers have demonstrated less pain and less traumatic dressing changes using silicone wound dressing than with traditional dressings (11,12).

Atraumatic dressing changes are especially important not only for wound healing, but also for pain and quality of life. Patients with severe generalized RDEB experience significant pain related to their condition (13), and dressing changes are one of the most significant sources of pain and anxiety in patients with RDEB (14). Despite the widely acknowledged association between dressing changes and pain, little research has focused directly on this topic. A retrospective study of anesthesia management in 25 patients with RDEB who underwent 121 procedures at Stanford University demonstrated that 21% of procedures requiring anesthesia were dressing changes (15). Furthermore, 10% of the patients in this study were treated with methadone for chronic pain, emphasizing the complex nature of the pain that this population experiences.

TABLE 1. *Cost of Several Nonadherent Dressing Options for Treatment of EB Based on Amazon.com Search Performed in August 2012. Selection Modified from Products in Reference 9*

Product	Manufacturer	Available sizes (inches)	Amazon price ($)
Hydrocolloids			
Restore contact layer dressing with TRIACT technology	Hollister	4 × 5	124.42
Restore hydrocolloid dressing		4 × 4	24.84
		6 × 8	55.99
		8 × 8	79.49
Foams			
Mepilex	Mölnlycke	4 × 4	27.35
		4 × 8	86.10
		6 × 6	72.20
		8 × 8	203.15
Mepilex border		3 × 3	17.10
		4 × 4	27.99
		6 × 6	38.80
		6 × 8	45.95
Mepilex border lite		2 × 5	22.50
		3 × 3	21.70
		4 × 4	24.35
		6 × 6	45.95
Hydrogels			
Duoderm hydroactive sterile gel	ConvaTec	15 g	80.94
		30 g	33.95
IntraSite gel	Smith & Nephew	8 g	71.20
		15 g	109.73
		25 g	127.99
Alginates			
Kaltostat	ConvaTec	2 × 2	78.94
		4 × 8	274.94
SeaSorb	Coloplast	2 × 2	152.97
		4 × 4	109.75
		6 × 6	275.97
Silicone mesh			
Mepitel	Mölnlycke	2 × 3	59.95
		3 × 4	72.95
		8 × 12	199.95
Silver dressings			
Aquacel Ag	Convatec	2 × 2	83.10
		6 × 6	107.10
Mepilex Ag	Mölnycke	4 × 4	53.95
		4 × 8	164.21
		6 × 6	179.83
		8 × 8	233.00
Acticoat	Smith & Nephew	4 × 4	153.00
		4 × 8	208.00
Restore Ag	Hollister	4 × 4	91.95
		6 × 8	481.94
Gauze			
Vaseline petrolatum gauze	Covidien	1/2 × 72	27.14
		1 × 36	16.36
		3 × 9	47.61
Telfa		3 × 4	10.89
		3 × 6	13.21
		3 × 8	12.86
Kerlix		4.5 yards × 4 yards	3.70

TABLE 2. *Summary of Select Estimated Wound Care Costs for Select Age Groups with Epidermolysis Bullosa*

	Option 1: Vaseline gauze, Telfa, gauze wrap	Option 2: Mepilex, gauze wrap	Option 3: Mepitel, Telfa, gauze wrap	Option 4: Restore, Telfa, gauze wrap
Neonate male	$10.43	$70.39	$100.57	$127.54
Neonate female	$10.03	$67.72	$96.75	$122.69
Infant male	$22.15	$149.46	$213.62	$270.92
Infant female	$20.89	$140.94	$201.45	$255.45
Child male	$54.64	$368.26	$526.96	$668.23
Child female	$54.86	$369.75	$529.09	$670.94

The Restore with TRIACT technology was chosen for the pricing listed in option 4. Other nonadherent Restore hydrocolloid dressing options are available with pricing comparable with options 2 and 3 (data not shown).

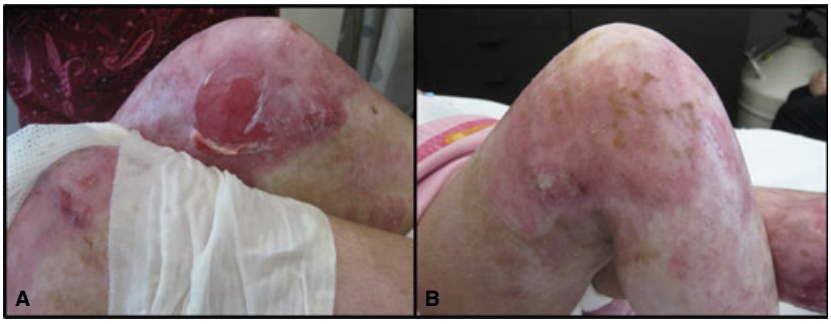

Figure 2. (**A**) Skin fragility and acute erosion overlying a chronically scarred left knee joint in a patient with severe generalized RDEB. The right knee is partially covered with nonadherent dressings (petrolatum-impregnated gauze and silicone wound dressing). (**B**) Largely reepithelialized erosions that continue to require nonadherent protective dressings.

The European Wound Care Association (EWCA) undertook an international survey of clinicians from 11 countries in Europe and North America to evaluate the pain associated with dressing changes (16). This study demonstrated that patients are most likely to experience pain during dressing changes and wound cleansing and that the dressings most likely to cause pain are dried-out dressings and those that adhere to wounds. The report from the EWCA emphasizes that the pain associated with wound care should be considered an endpoint of equal importance to wound healing in the evaluation of wound care products.

Pain is an important contributor to quality of life in individuals with EB. In one of the only EB-specific quality-of-life instruments (Quality of Life Evaluation in Epidermolysis Bullosa [QOLEB]), pain is a crucial aspect of the quality-of-life measurement (17). Although the QOLEB does not specifically mention pain associated with dressing changes, it is clear that pain significantly decreases quality of life. Therefore any intervention that decreases pain, such as the use of wound care products that decrease pain with dressing changes, is likely to improve quality of life in patients with severe generalized RDEB.

Additional considerations contributing to the cost of wound care in this population include the need for daily dressing changes to evaluate for infection and to check for new blisters, especially in infants, who cannot verbalize complaints. Also, thicker, padded dressings over bony prominences are especially important to minimize the risk of creating new blisters and erosions with physical activity and to encourage independence in activities of daily living. These considerations were emphasized in a recent consensus paper on wound care in EB (18).

Advanced nonadherent wound care products that reduce pain and promote wound healing are expected to lead to better quality of life in this vulnerable patient population. Prospective studies may be possible only through multicenter collaboration for this rare disease. EB registries including the multicenter EB clinical characterization and outcomes database and the patient-driven registry at DebRA.org have been established in an effort to advance research in this life-altering condition. Patient-driven registries are especially important in rare dermatologic disorders such as EB because patients and caregivers are highly motivated to participate in the search for treatments and can provide information about rare conditions that may not be otherwise available (19).

We found a wide range in costs associated with different wound care options in patients with RDEB. The limitations of our study include the extrapolation

of wound percentage from a national EB patient registry rather than data drawn from specific patients; the assumption that all wound sites will be completely covered, including sites such as the face, where this is unlikely; and the assumption of a patient without access to insurance, whereas most patients will have access to wholesale wound care supplies through their insurance provider.

Although RCTs evaluating wound care products in patients with RDEB are lacking, small studies and expert opinion support the use of specialized nonadherent dressings that minimize skin trauma and promote wound healing. Until there is a cure, wound care for EB will remain the cornerstone of treatment and a costly necessity.

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