Amniotic membrane grafting in patients with epidermolysis bullosa with chronic wounds

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Background: Severe forms of epidermolysis bullosa (EB) are characterized by chronic, nonhealing wounds.

Objective: We sought to evaluate the usefulness of amniotic membranes in patients with EB.

Methods: A retrospective chart review of patients with EB who were treated with amniotic membranes (two patients, 8 applications) was conducted. The primary outcome measure was number of days to complete healing, and the secondary outcome measures were a qualitative wound score, a visual analog scale score, and potential adverse effects.

Results: The number of days to detect a significant clinical response, defined as greater than 50% improvement, was 40.3 ± 21.2 days. The median qualitative wound score was 2 (range 0-5). The mean visual analog scale score at last follow-up was 31.4 ± 26.8. No adverse events were noted.

Limitations: Retrospective design, healing assessed by comparing photographs, and partial grafting of some wounds were limitations.

Conclusion: This proof-of-concept study revealed the potential usefulness of amniotic membrane grafting in promoting healing of chronic wounds in patients with EB (J Am Acad Dermatol 2010;62:1038-44.)

Key words: amniotic membrane; biological dressing; chronic wounds; epidermolysis bullosa.

Epidermolysis bullosa (EB) refers to a group of inherited bullous disorders, characterized by fragility of the skin and mucous membranes, and blister formation in response to minor friction or trauma. Persistent skin damage adversely affects the patient's quality of life. In the absence of a cure, the current therapeutic goal is the prevention and healing of chronic wounds. In patients with EB, chronic inflammation and bacterial infection are two of the factors that interfere with proper wound healing. The characteristics of an ideal dressing for EB are to control moisture balance, be nonadherent and atraumatic, reduce pain, allow epithelialization, promote healing, be widely available, and be inexpensive.[1]

Abbreviations used:

AM:	amniotic membrane
EB:	epidermolysis bullosa
RDEB:	recessive dystrophic epidermolysis bullosa
VAS:	visual analog scale

The amniotic membrane (AM) has many natural biological properties that prevent scarring, reduce inflammation, stop the formation of blood vessels, minimize infection, and promote wound healing.[2] There are several successful reports of AMs used in patients with extensive burns and venous ulcers where it was demonstrated to be safe, easy to use, and extremely beneficial in allowing fast re-epithelialization of denuded skin.[2-10]

The objective of this study was to evaluate the usefulness of AMs in treating chronic wounds in patients with EB.

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METHODS

Patients and setting

A retrospective chart review of patients with EB, who were treated with AMs, was conducted at our hospital from November 2007 to July 2008. The study received approval from our research ethics board. The grafting was performed in chronic wounds, defined as present for more than 3 months, which failed to heal despite topical and systemic therapy. One wound has previously failed artificial grafting with Apligraf (Organogenesis Inc, Canton, MA).

CAPSULE SUMMARY

- Patients with epidermolysis bullosa have chronic, nonhealing wounds.
- Amniotic membranes are biological dressings that improve wound healing.
- In this retrospective study we proved the concept that amniotic membrane may be beneficial in patients with epidermolysis bullosa with chronic wounds.
- Further prospective studies are needed.

AM grafting

AMs were recovered from placentas that would normally get discarded from cesarean sections. The donors were extensively screened, at the time of delivery and 6 months after, for infectious organisms, such as HIV, hepatitis B and C, human T-lymphotropic virus 1 and 2, herpesvirus 1 and 2, cytomegalovirus, toxoplasma, and syphilis, and the seasonal West Nile virus. In addition, the AMs were tested for bacteria. AMs were kept at −80°C until they were clinically applied. The membranes were supplied from Comprehensive Tissue Centre Capital Health (Edmonton, Alberta, Canada).

The AM application was done in our outpatient dermatology clinic. The skin was cleansed with normal saline and the AMs (supplied in approximate 3- × 3-cm pieces) were applied on the affected areas after thawing at room temperature for 5 minutes. No suturing was required. To improve adhesiveness, we used blow by sterile air at 42°C for 5 minutes provided by a Bair Hugger Patient Warming System (Arizant Healthcare Inc, Eden Prairie, MN). A silicone dressing was applied to prevent movement and suprainfection. Patients were instructed not to remove dressings for 7 days. At the 7-day mark the dressing was replaced and topical antibiotics were prescribed to reduce the risk of suprainfection. In addition, all patients were instructed to receive oral broad-spectrum antibiotics for 2 weeks before and 2 weeks after grafting to reduce the risk of infection.

Outcome measures

Photographs of wounds were taken before and after each application and were used to compare results with baseline photographs. The scoring was done by a single investigator by comparing photographs at each follow-up visit against baseline. The primary outcome measure was number of days to complete healing, and the secondary outcome measures were a qualitative wound score, a visual analog scale (VAS) score, and potential adverse events. The qualitative wound score assessed the degree of redness (0 = none, 1 = pink, and 2 = beefy red); exudates (0 = none, 1 = mild, and 2 = moderate/severe); odor (0 = no and 1 = yes); and size (0 = smaller, 1 = same, and 2 = bigger). The extent of the wound at follow-up was compared with baseline with a 100-mm VAS where 0 represented no healing and 100 represented complete healing. For analysis purposes, scores of 0 to 24 represented no or minimal improvement, 25 to 49 represented mild improvement, 50 to 74 represented significant improvement, and 75 to 100 represented complete healing.

Statistics

Descriptive statistics were calculated. Mean, median, SD, minimum, and maximum were determined for continuous variables. Number and percentage of patients were determined for discrete variables.

RESULTS

Patient characteristics

The characteristics of the two patients, both with recessive dystrophic-type EB (RDEB), are summarized in Table I. Patient 1 was an 18-year-old man who had chronic wounds on his left buttock, right upper aspect of his chest, another chronic wound in his left buttock which extended to the back of thigh, right front aspect of his trunk, left front aspect of his trunk, and upper aspect of his back. Patient 2 was a 16-year-old girl who had chronic wounds on the front and back of her left hand, and front upper aspect of chest. In both patients, the grafted wounds were present for at least 3 months (up to 2 years). The characteristics of the AM grafts are shown in Table II. The mean total surface area of AM used was $72.00 \pm 24.05\ cm^2$. The patients were prescribed oral broad-spectrum antibiotics, such as moxifloxacin/oxofloxacin to reduce infection. Topical treatments included silver sulfadiazine or mupirocin with silicone dressings.