Use of fibre dressings in children with severe epidermolysis bullosa

Jacqueline Denyer and Elaine Gibson

Abstract

This non-comparative study explored the benefits of a natural gelling fibre dressing in 10 children with epidermolysis bullosa (EB). The clinical challenge in managing these children is that they often present with recalcitrant wounds that are perpetuated by critical colonisation, presence of biofilms and infection. KytoCel® (Aspen Medical) is a highly absorbent dressing composed of natural, biodegradable acylated chitosan. These fibres bond with wound exudate to form a clear gel that locks in fluid absorbs pathogens and is conformable to the wound bed. It also has haemostatic properties. (Dutta PK et al, 2004; Lee et al, 2009; Stephen Haynes et al, 2014). Factors considered were whether the dressing could aid healing, reduce bleeding, reduce bioburden, be atraumatic and comfortable during wear time and removal.

Key words: Epidermolysis bullosa ■ Wound care ■ Multifunctional dressings ■ Paediatric

Epidermolysis bullosa (EB) is an umbrella term for a large group of genetically determined skin fragility disorders (Denyer, 2006). Reduced or absent vital proteins lead to a lack of tensile strength within the skin and mucous membranes, resulting in blisters or skin stripping following minor friction and trauma. Severe EB leads to early development of recalcitrant wounds that are perpetuated by critical colonisation, presence of biofilms and infection. In line with current recommendation and to avoid further antibiotic resistance in children with EB, if local colonisation of wounds is observed the use of topical antimicrobial agents are advised. Antibiotic use should be reserved for severe systemic infections caused by Group A *streptococcus*.

Studies on silver dressings in young adults and children have demonstrated an uptake of silver levels in the plasma, urine and the liver (Trop et al, 2006). This caused great concern and debate between wound care specialists throughout the UK. (Hipler and Elsner, 2006; Leaper, 2011; White et al 2011). As a result of these findings EB best practice guidelines state that:

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'Silver products should be used with caution in infants under one year. Also potential risk of raised plasma silver levels/argyria. Restrict use to 14 days and apply to a small area for short-term use only.' (Denyer and Pillay, 2012)

All children that present with EB undergo a skin biopsy to determine the severity of the disease. This causes bleeding and trauma in what is already very delicate skin. Kytocel® (Aspen Medical), a new natural gelling fibre dressing with antimicrobial properties that does not contain silver, that can also be used as a haemostat (to control bleeding), was evaluated in 10 children with EB ranging from simplex to severe dystrophic EB between April and August 2014. Factors considered were whether the dressing could:

■ Aid healing
■ Reduce bleeding
■ Reduce bioburden
■ Be atraumatic
■ Be comfortable during wear time.

Product selection

The natural gelling fibre dressing used for this study is highly absorbent. It is composed of natural, biodegradable acylated chitosan These fibres bond with wound exudate to form a clear gel that locks in fluid, absorbs pathogens and is conformable to the wound bed (Lee et al, 2009; Stephen-Haynes et al, 2014). Chitosan is a naturally occurring starch (polymer) derived from the shells of crustaceans. The absorbent properties enable it to bind and lock away commonly encountered wound pathogens such as *Escherichia coli*, *Staphylococcus aureus*, *Candida Albicans* and methicillin-resistant *Staphylococcus aureus* (Edward-Jones, 2014). The positive charge of chitosan fibres facilitates haemostasis by binding to negatively charged red blood cells, resulting in faster coagulation. (Khor and Lim, 2003; Dutta et al, 2004; Foda et al, 2007). This ability to reduce bioburden, absorb exudate and encourage coagulation is an advantage in children with EB where skin breakdown, bleeding and resulting infection remain a challenge.

EB simplex

There are three main categories of EB simplex: EBS localised, EBS generalised-severe and EBS generalised-other (Denyer, 2010; Fine et al, 2014)

Almost all forms of EB simplex are generally inherited autosomal dominantly (from one parent). Inheriting a disease such as EB depends on the type of chromosome

affected. It also depends on whether the trait is dominant or recessive. A single abnormal gene on one of the first 22 non-sex (autosomal) chromosomes from either parent can cause an autosomal EB-dominant inheritance, meaning an abnormal gene from one parent can cause disease, even though the matching gene from the other parent is normal. The abnormal gene dominates (Lupsik, 2011). Most EB simplex is a disorder of keratin proteins with the primary defects lying within proteins encoding for keratin 5 and keratin 14. These proteins form the major keratin scaffolding within the basal epidermal cells. Dysfunction of the keratin proteins in EB simplex leads to mechanical weakness of these cells. Beakdown occurs because of minor friction or rubbing resulting in blistering of the hands and feet that can be present even in the neonatal period. There is a significant risk of death in the more severe forms of simplex EB, resulting from sepis and laryngeal blistering (Fine and Hintner, 2008).

Junctional EB

There are three main forms of junctional EB (Nakano et al, 2002; Uitto et al, 2007; Fine et al, 2008; Denyer and Pillay, 2012).
■ Junctional EB generalised severe
■ Junctional EB intermediate
■ Junctional EB with pyloric atresia.

All forms of junctional EB arise from mutations in genes that encode structural components of the hemidesmosomes or anchoring filaments, which provide mechanical integrity across the dermis and epidermis. Targeted proteins are laminin 332, type-XVII collagen and ɑ6 ß4 integrin. Separation of the epithelium occurs within the lamina lucida between the lamina densa of the basement membrane involving basal keratinocytes. In all forms of junctional EB, There is a tendency for chronic wounds to over-granulate in patients from an early age (Nakano et al, 2002; Fine and Hinter, 2008).

This severe sub-type carries a poor prognosis with most not surviving beyond the first 2 years of life (Pillay, 2008; Fine and Hinter, 2008). Death is caused by a combination of laryngeal blistering/respiratory distress, a profound and uncorrectable failure to thrive, chronic wounds and sepsis (Laimer et al, 2010). Despite the severity of the systemic disease, good management can help reduce the severity of the wounds.

Junctional EB (JEB) intermediate

Junctional EB results from mutations in the genes encoding type-XVII collagen or laminin 332, which are expressed in skin and other parts of the body. This can affect the oral mucosa, cornea, upper oesophagus and urogenital tract (Van den Bergh and Giudice, 2003). This type of EB carries a better prognosis than junctional EB, intermediate with the majority of children surviving to adulthood (Denyer and Pillay, 2012).

Laryngoonychocutaneous (LOC) syndrome (previously known as Shabbir's syndrome) is now considered to be a new variant of JEB, since it has similar clinical features and is associated with mutations in the ɑ3 chain of laminin (Fine et al, 2014).

Dystrophic EB (DEB)

DEB can be inherited either dominantly or recessively, with the more severe forms in general, being inherited recessively (Denyer and Pillay, 2012). In all cases there is a diminished or absent protein collagen Vll, which is a crucial component of anchoring fibrils. Anchoring fibrils act rather like Velcro® hooks; attaching the epidermis to the dermis. The extent of fragility can be varied depending on whether the causative mutation predisposes to mild or severe disease. Complications can occur such as recurrent blistering and repeated skin loss as a result of trauma. The wounds may become chronic which can lead to compromised nutrition, anaemia, repeated infection and critical colonisation. These children are prone to osteoporosis, growth failure and pubertal delay (Haynes, 2010). There is an increased risk of aggressive squamous cell carcinoma in those with severe forms of EB (Fine et al, 2009).

Recessive dystrophic EB

In recessive dystrophic EB the affected child is able to express some type-VII collagen, with variable qualitative and quantitative abnormalities of the anchoring fibrils. The clinical presentation will vary with a tendency to blistering all over the body and consequent wounding, scarring and nail loss. The development of anaemia is common with this type of EB and there is often mucosal involvement. The hands will be scarred with some webbing as a result of constant remodelling of the delicate skin.

Recessive dystrophic EB severe–generalised

In this form of EB the skin is extremely fragile, often with extensive blistering and wounding. Patients with this type of EB will frequently develop hard-to-heal or never-to-heal areas, or areas that do heal but can very quickly break down. Atrophic scarring and healing leading to disabling contractures is common.

This article discusses the various sub-types of EB where Kytocel was used. More information and guidelines pertaining to EB can be found at www.debra.org.

Assessment and diagnosis

Within each of the four categories of EB there are subtypes that display individual clinical effects Definitive diagnosis is most commonly made from analysis of a skin biopsy using positive immunofluorescence (IF), antigenic mapping and transmission electron microscopy (EM). These key diagnostic tools help to confirm diagnosis and indicate the particular sub-type of EB. Identification of the different causative genes responsible for EB enables the recognition of the precise location and type of mutation. Owing to the rarity of expertise and facilities, however, diagnosis is generally made using IF and antigen mapping. (Denyer and Pillay, 2012)

Method

A total of 10 children with a varying range of EB from simplex to severe dystrophic disease were selected for the study. Criteria included those with chronic wounds which were critically colonised or where presence of a biofilm was suspected, or following skin biopsy for EB diagnosis.

A retrospective analysis was completed over a 4-week period. Data included gender, age, type of EB, cause of skin damage (for example skin biopsy, trauma), exudate management, visible improvement of the wounds in both critical colonisation or erythema. The paediatric team were asked to rate the dressing in terms of performance, ease of application and removal, comfort for the child, fluid handling, odour control, pain, bioburden and condition of the surrounding skin. There was a free-text section for staff to include any comments. Children were able to withdraw at any time depending on clinical assessment by the author.

Results

Seven girls and three boys were recruited with ages ranging from 10 months to 16 years, with a mean age of 7 years 2 months. The breakdown was six patients with severe generalised recessive dystrophic EB, two with junctional EB, one with LOC syndrome and one with simplex EB.

Exudate levels were measured between week 1–4, observations were made regarding the ability of the dressing to absorb fluid and reduce bioburden (case studies 1, 2, and 3). The cause of injury was noted as it was felt that the new dressing had the potential to improve outcomes, particularly when taking skin biopsy for diagnosis in new born infants (*Figure 1*). The most common cause of injury was friction and sheer (as shown in case study 3) caused by the flange of a tracheostomy. The patient in case study 1 had multi-resistant *Pseudomonas aeruginosa* (*P. aeruginosa*) blisters on her hands and feet. Children with EB are commonly referred to as 'butterfly children' (Atherton and Denyer, 2003; Fine et al, 2008; Laimer et al, 2010) because the skin is so fragile, and this has been well documented in the literature.

Exudate levels were recorded as low, medium-heavy or very heavy. This was documented and rated by both clinicians and parents. Exudate levels varied depending on the severity of the EB and the amount of blistered skin or tissue loss. The dressing proved effective in managing moderate to high exudate levels. In one patient the wound adhered to the wound margins, and a silicone primary layer was required to
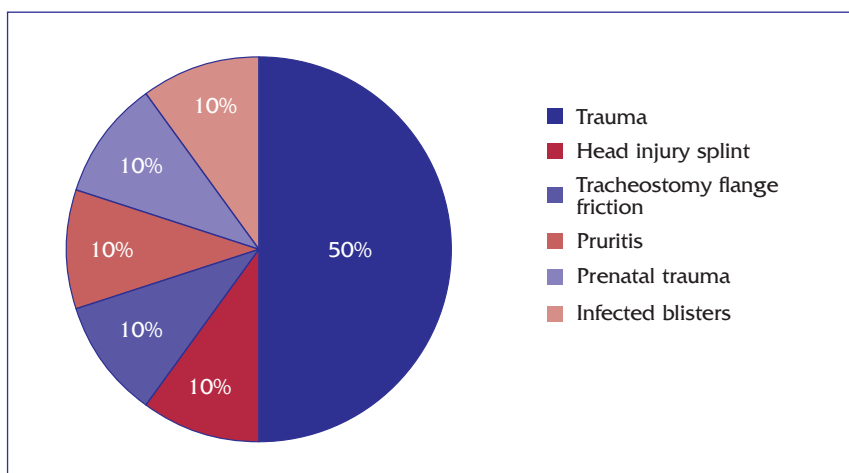

Figure 1. Cause of skin damage

prevent further trauma (*Figure 2*).

Final dressing evaluation

Staff were asked to rate the dressing performance in terms of ease of application and removal, comfort for the child, fluid handling, odour control, pain, bioburden and surrounding skin. Ease of application, comfort pain and fluid handling was rated well by staff in 9 patients. One child had a problem with adherence and stopped using the dressing.

Comments from staff are as follows:

'This wound was not expected to heal despite optimal care. I think the Kytocel must have reduced the bioburden for the first time in 2 years.' (Child 2)

'The wound has virtually healed, flexion will al-ways be a challenge junctional EB.' (Child 4)

'Multidrug-resistant *Pseudomonas* was present in the sputum and wound of this child. Where Kytocel had been in contact with the wound bed *Pseudomonas* was eradicated by week 4, however, she continues to have resistant *Pseudomonas* in her sputum.' (Child 6)
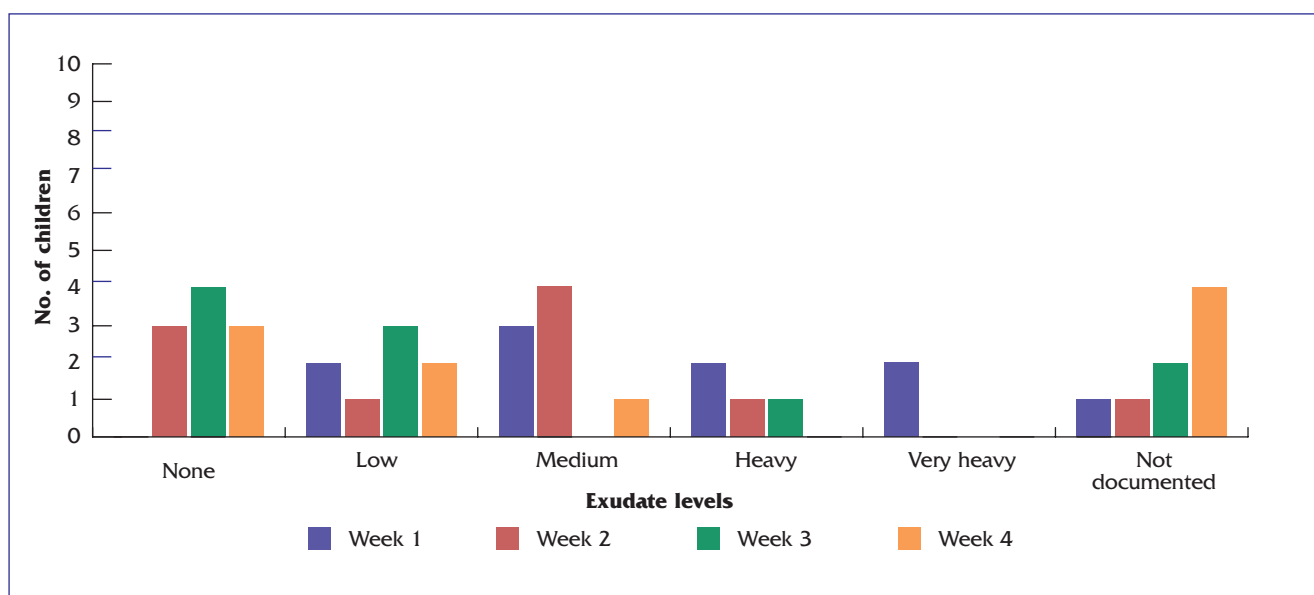

Figure 2. Wound exudate week 1–4

Figure 3. Case study 1

a) 14 May 2014
b) 25 May 2014
c) 28 May 2014

Discussion

Improvements in recalcitrant wounds where all other therapies have failed are very encouraging. The studies presented in this article found that:

- Wound healing had improved significantly in nine out of ten children, even in those with severe recessive dystrophic EB
- Where skin biopsies had been taken, the dressing provided haemostasis and was an effective haemostat
- The eradication of *P. aeruginosa* in one child was supported

by wound swabs taken before and after application

- In all but one child Kytocel proved to be easy to apply and remove.

Further studies in the use of chitosan dressings in this group of patients will be helpful. The author plans to try the products on neonates suffering wounds from prenatal activity and birth trauma to see whether the healing process is accelerated.

Case study 1

An 8-year-old girl with EB simplex localised had severe blistering on her feet which became worse in hot weather. The ulcerated area on her foot became heavily colonised and inflamed (*Figure 3a*). Kytocel was gently packed into the ulcer with KerraLite Cool Border (Crawford Healthcare) applied as a secondary dressing. The dressings were changed daily as she likes to soak her feet daily in cool water after school. The ulcer appeared cleaner at the first dressing change. By 25 May (*Figure 3b*), the wound bed was healthier, exudate levels reduced from medium to low, and no smell was detected. By 28 May (*Figure 3c*) the wound was superficial and no longer required packing with Kytocel ribbon. The wound went on to heal 2 weeks later.

Case study 2

An 11-year-old boy presented with severe generalised recessive dystrophic EB with the added complications of anaemia and malabsorption syndrome. Nutrition was poor and he was increasingly obtaining chronic wounds. He is very particular about his choice of dressings and has refused topical antimicrobials in the past. After a lot of encouragement he agreed to try Kytocel under his usual dressing on one wound on his right shoulder that had failed to heal in 2 months (*Figure 4a*). The dressing were changed every other day. After the first dressing change there was a marked reduction in exudate (*Figure 4b*). The wound appeared clean and as the exudate level decreased the Kytocel became increasing adherent to the wound causing distress on removal. Applying an atraumatic dressing as a wound contact layer (Urgotul, Urgo Medical) prevented adherence and did not reduce the efficacy of Kytocel. The authors would recommended this dressing approach where there is a need to reduce the wound bioburden and there is any concern regarding adherence owing to low exudate levels.

The wound healed by day 10 (*Figure 4c*).

Case study 3

This 3-year-old girl presented with LOC syndrome. Blistering and development of granulomas within her trachea meant she was dependent upon a tracheostomy for her survival. It is essential that the tube does not become dislodged and the securing tapes must therefore be very tight. The flange of the tracheostomy tube rubbed against her fragile skin causing an area of ulceration. She developed a multidrug-resistant strain of *pseudomonas* in her sputum. The wound quickly became colonised, associated with bleeding friable tissue (*Figure 5a*). The wound had failed to heal for 25 days. KytoCel was applied to the wound with KerraLite Cool Border applied as a secondary dressing. The dressing was changed daily (*Figure*

5b). Within 2 weeks bleeding and exudate had reduced and the wound had reduced in size. At 19 days the wound had healed (*Figure 5c*) and wound swabs confirmed eradication of *pseudomonas*, despite the fact her sputum remains colonised.

Conclusion

Early results have indicated in this small pilot study that KytoCel dressings are helpful in treating recalcitrant wounds in patients with severe forms of EB. The authors recommend that further studies be undertaken extending to adult EB patients to see whether the same benefits can improve patients outcomes. BJN

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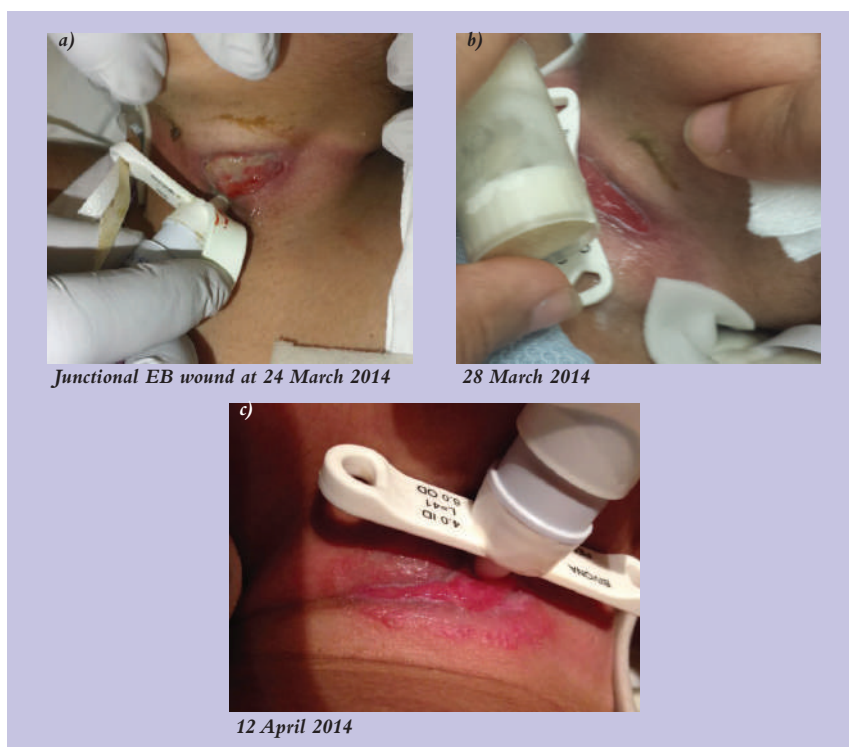
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a) *Severe dystrophic EB 14 June 2014*

b) *16 June 2014*

c) *24 June 2014*

Figure 4. Case study 2

a) *Junctional EB wound at 24 March 2014*

b) *28 March 2014*

c) *12 April 2014*

Figure 5. Case study 3