

Epidermolysis bullosa in children: pathophysiology, anaesthesia and analgesia

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Introduction

"Few conditions are more devastating to the physical, emotional, and social health of an infant or child than epidermolysis bullosa. The disease is actually a group of congenital abnormalities of the skin, and it encompasses a variety of genetic abnormalities of proteins that mediate adhesion of the skin. These abnormalities result in fragile skin that blisters, causing pain, deformity, social and emotional disability, susceptibility to infection and cancer, and shortened life. Children with epidermolysis bullosa require lifelong support and understanding from physicians (both specialists and generalists), from clinical support personnel, and most important, from their families."¹

Epidermolysis bullosa (EB) is a rare, genetically determined mucocutaneous, mechanobullous group of disorders. Three types have been described, but all show the same tendency for the skin or mucous membranes to separate from the underlying tissue, with minimal mechanical trauma, resulting in blistering. The disease runs a very variable course from minor disability, to those patients who have a longer life-span with pain and suffering, and to death in infancy. The cycle of trauma, secondary infection, healing, scarring, and deformity forms the pattern of their lives. Over time, many physical and emotional complications arise as these patients, because of their disabilities, face social challenges, their exclusion from normal activities and, because of frequent hospital visits, time away from school.²

Many patients will have to undergo surgical procedures as part of their disease management, but they will also require operations as for any paediatric patient. The need for anaesthesia, as well as for the management of pain and anxiety, will bring them to the attention of anaesthesiologists. The peri-operative team requires special skills and awareness peculiar to this disorder

PATHOPHYSIOLOGY

There are over 20 forms of EB, with each type based on the form of inheritance, i.e. dominant or recessive, and on the skin level where the characteristic blistering occurs. The three major categories are:

- EB simplex (EBS);
- Junctional EB (JEB);
- Dystrophic EB (DEB).

The disease process is thought to be due to an abnormal gene coding for collagen, and it is here that the future research for the management of this disorder rests. The same mutations that cause skin blistering also cause many of the extracutaneous complications of EB, including those within the eyes, gastrointestinal (GI) and genitourinary (GU) tracts, and upper respiratory tract. Secondary abnormalities, including increased expression of tissue collagenase, contribute to abnormal wound healing. Anaemia and growth retardation are at least partially the result of chronic blood, protein and nutrient loss from the skin and GI tract. It is still unknown what the underlying basis of carcinogenesis in recessive DEB is, although it has been suggested that the site of mutation within the type VII collagen gene may play an important role.

GENERAL MANAGEMENT OF CHILDREN WITH EB

Pain and pruritis

Pain

EB is a painful condition:

Individualise treatment: the same tissue damage may cause different levels of pain in different people, at different times of their disease; On different occasions, the same procedure may cause different levels of pain in the same individual

Assessment and measurement of pain:

- Difficult: Children in their own right are difficult, and EB is a painful disorder;
- Initial assessment is vital to further treatment;
- Measure and monitor the effect of therapy;
- Recognised, validated tools should be used, e.g. visual analogue scale (VAS) and FACES Pain Rating Scale;
- Beware pain vs. anxiety, as pain and anticipatory anxiety go hand in hand;
- Language, age and psychological development all impact on assessment;
- Different cultures have varying attitudes to acknowledging and treating pain;

Previous experiences and drug requirements should be documented; Neonates and infants may present with restlessness, persistent shrill cry, increased heart rate, increased respiratory rate, increased blood pressure, drawn up limbs, and/or a trembling chin.

Pain management options

General measures:

- Assess all types of pain being experienced by an individual;
- Several different therapeutic approaches may be required simultaneously;
- Pain management must be individualised, and plans may need to be changed;
- The type of dressing is important, and should be a non-stick, lubricated dressing, e.g. Mepitel®;
- Where possible, give control back to the child;
- Pre-empt pain and anxiety, and give medications timeously.

Non-pharmacological methods:

- Good explanation to and education of both patient and parents;
- Distraction of any type, e.g. virtual reality pain distraction (scarred, deformed hands may preclude this option);
- Simple coping strategies (e.g. blowing bubbles, deep breathing);
- Relaxation techniques;
- Massage, reflexology, aromatherapy;
- Music, art, play therapies ;
- Involve the parent(s);
- Comfort positions during dressing changes and venesection;
- Acupuncture, acupressure, hypnosis, transcutaneous electrical nerve stimulation (TENS);
- Non-nutritive sucking: especially in neonates and infants, 25% glucose 2 minutes prior to procedure is very successful. Breast feeding during procedures provides similiar analgesia.

Pharmacological options:

The choices will be determined by what is required: management of acute pain for procedures, neuropathic pain, intermittent episodes of acute pain after trauma on top of baseline discomfort, anxiety (accompanies most procedures), and depression.

Each child requires individual assessment and treatment. Multimodal analgesia is recommended. Simple analgesics include paracetamol in therapeutic doses, and non-steroidal anti-inflammatories. Opiates are used for acute episodes but are not commonly used for baseline medication. Steroids are used as part of EB treatment, and these also provide analgesia. Ketamine is excellent for change of dressings. Alpha-2 agonists (e.g. Clonidine) are very useful for both baseline and procedure-related pain and anxiety. Gabapentin provides good analgesia for neuropathic discomfort but is also used for acute pain. The tricyclic antidepressants, especially amitriptyline, are useful for this neuropathic, long term discomfort, and will also, when given as a nocte dose, improve sleep.

Local anaesthetic use should be considered for many indications, but infiltration is not recommended as this may precipitate blistering.

Successful control of pain and discomfort is a multidisciplinary challenge, and requirements change all the time. Neonates: glucose dummies, breast feeding, paracetamol and oral morphine in reduced doses with an increased interval between doses.

Blister care and dressing techniques:

- Give analgesia timeously before dressing application;
- Prepare the environment;
- Puncture tense blisters with a tiny sterile needle;
- Ethyl chloride spray administered immediately beforehand is helpful;
- Have dressings ready to apply immediately;
- Distraction is very useful in long-term management;
- Atraumatic dressings should be applied, i.e. those which do not pull skin off when removed;
- Restraint is very difficult in these children, as their skin is likely to be traumatised in the process.

Sources of pain:

These may be multiple, acute and chronic episodes, neuropathic pain, and physical, and emotional components.

Acute	Chronic
Blisters Wounds Oesophageal: blister and reflux Dental Corneal erosions Anal fissures	Inflammation of skin and mucosae Neuropathic pain Constipation Contractures Osteoporosis Procedural pain, e.g. dressings, bathing, venepuncture

Avoid:

- Sticky plasters and adhesive tapes;
- Self-adhesive plates, pads and ECG electrodes;
- Face masks with sharp edges;
- Rigid tubes, e.g. nasogastric tubes, nasal cannulae;
- Non-invasive blood pressure monitor: beware shear effect;
- Use of the Patslide® may cause damage and blistering with transfer onto the operating table;
- Do not pick EB children up under their arms.

Pruritus

Pruritus is a classical symptom of EB. It is very common and distressing and affects all aspects of life, including sleep. Pruritus is very resistant to treatment. EB pruriginosa is a feature of DEB.

Treatment options include in following:

- Emollients (e.g. Aloe Propolis Creme®, Dermol®, menthol-containing emollients);
- Antihistamines: disappointing, but sedation may be useful;

- Topical steroids: disappointing, and there are limits to its use;
- Psychological approaches, e.g. distraction, full explanation of what is to be done
- Gabapentin and pregabalin show considerable promise.

ANAESTHESIA

Children with EB may suffer from many medical problems, but the anaesthetic challenges that may be faced will be due to oral, pharyngeal, mucosal and skin involvement. Airway management and maintenance of skin integrity are problematic. Avoiding damage to skin and mucosae are basic considerations in caring for these patients. Shearing forces are much more damaging than pressure forces.

Surgical procedures may include the need for oesophageal dilation, insertion of gastrostomy dental procedures, release of contractures, skin procedures, and cancer surgery. These children may also present with other non-EB-related reasons for operations, e.g. acute appendicitis.

EMLA application is not a problem, as long as occlusive dressings are avoided.

Pre-operative assessment should include a critical, insightful assessment of the airway, both upper and lower. Over time, damage to the lips and mouth results in scarring and contractures of the mouth, and difficult laryngoscopy is to be anticipated. The teeth should be examined for caries, broken teeth, gingivitis, and overall hygiene. Many of the children are chronically undernourished, and may be small for their age, hypo-albuminaemic, and anaemic. The presence of gastro-oesophageal reflux and co-existing infections should be documented. Vascular access options may be limited, and discussion with the child and parent should include a preference for the type of induction. Only absolutely essential blood tests should be requested. Post-operative pain relief and the options for the use of regional techniques, as well as the possibility of the use of rectal suppositories, should be mentioned, and consent acquired if necessary. Suppositories should be well lubricated before insertion and this procedure performed gently, as damage to the rectal mucosa may have long-term consequences.

In order to minimise trauma to the skin, preoperative blood tests should be minimised to absolute essentials. Most venesections can be performed under general anaesthesia.

Premedication should be prescribed on an individual basis. The use of restraint when the child becomes agitated may cause significant damage to his or her skin. The decision for antacid prophylaxis should be made on an individual basis. Because gastro-oesophageal reflux is so common with this condition, many children are already taking H₂-receptor blocking or proton pump inhibitor drugs. Many are also on long-term corticosteroid medications, so peri-operative administration of steroids may be required. Because of scarring in the mouth and upper GI tract, some of these children cannot swallow

well, and secretions may be problematic. In these circumstances, atropine may be useful.

Because intravenous access is often very difficult, induction of anaesthesia is frequently by inhalational techniques. Rectal methods have been described.²

Airway management requires particular care not to damage the skin of the face, the eyes, the oropharynx, larynx, and trachea. To minimise friction, a lubricant (e.g. Vaseline® or liquid paraffin) may be used on the face mask as well as on the anaesthetist's hands. The hand of the anaesthetist may be used instead of a mask. Intubation must be performed carefully, with lubrication of the laryngoscope blade to minimise friction on the lips, gums, and palate. The endotracheal tube must be well lubricated and softened in warm water. In those patients in whom airway difficulties are anticipated and a bougie is required to facilitate intubation, damage to any part of the airway may occur. In an attempt to better visualize the vocal cords, damage and blistering to the forehead and scalp may also develop after manipulation of the head and neck when attempts are made to improve visualisation of the vocal cords. An endotracheal tube, uncuffed and half to one size smaller than would normally be selected, is usually required. All tubing should be padded, and Vaseline® gauze wrapped around any part which may come in contact with the patient.

As long as cricoid pressure is applied directly without any lateral movement or slipping over the larynx, rapid sequence intubation can be performed safely.

The endotracheal tube may be secured with Vaseline® gauze, held by the anaesthetist, or remain unsecured during surgery. The latter option may not be ideal during dental surgery.

Laryngeal mask airways (LMA) have been used successfully in patients with EB but, must be placed extremely carefully to avoid damaging the lips and palate. They should also be very well lubricated, with only minimal air inflated into the cuff. To minimise trauma to the airway and teeth, it is recommended that the LMA be removed prior to the child awakening.

Monitoring

Minimal monitoring, as defined by SASA guidelines, may not always be possible. For short procedures, clinical observation may be sufficient. Pulse oximetry and capnography are recommended for all cases, but non-invasive blood pressure should only be performed when precautions are taken to avoid damage to skin underlying the cuff (e.g. using Vaseline® gauze or Mepitel® around the arm before placing the cuff). The placement of ECG electrodes may also cause damage on removal. Surgical staples and crocodile clips may be preferred.

Anaesthetic technique

General anaesthesia is generally preferred. Regional anaesthesia has been proposed and, after initial concerns over causing more

bullae, more techniques are now being used. Areas where the skin is infected or likely to break down should be avoided. Care should be taken when cleaning the skin: rubbing should be avoided and antiseptic spray used instead. Infiltration of local anaesthesia should be avoided.

EB patients may have difficulty swallowing medication, so effervescent medications or sublingual drops are preferred.

Pain should be anticipated and treated pre-emptively and aggressively.

CONCLUSION

Children with epidermolysis bullosa, some more than others, pose a formidable challenge to the anaesthesiologist. This is a condition which requires multidisciplinary input, and the anaesthesiologist should be part of this team. Pain, anxiety, and itching are everyday companions to these patients, and an anaesthesiologist on the EB team contributes significantly to the successful management of these problems. Airway management, especially for difficult intubation, may require fibre-optic bronchoscopic skills, but these children may also present to any non-paediatric specialist hospital, and peri-operative morbidity can be significantly minimised with the education of theatre staff and peri-operative medical caregivers. Implementing measures to prevent damage to skin and mucosa, and assuming a “no-touch” approach, ensures that anaesthesia for children with EB may be undertaken with few untoward consequences.

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