Anaesthetic management of epidermolysis bullosa

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Epidermolysis bullosa is the name given to a group of rare, genetically determined diseases characterized by cutaneous blistering and subsequent scarring. It presents a challenge to the anaesthetist managing patients who often require multiple operations. This review article includes a retrospective audit of cases treated at St Thomas’ Hospital between 1993 and 1998. We studied the case notes and anaesthetic records of patients with dystrophic epidermolysis bullosa requiring anaesthesia and recorded the anaesthetic management and complications that occurred.

Methods

Patients

From January 1993 to January 1998, 51 patients with dystrophic epidermolysis bullosa had a total of 306 anaesthetics. The ratio of males to females was 3:2, with an age range of 1–51 yr; 44% were from the UK, while the remainder were from Italy, Serbia, Croatia, Greece and Portugal. Only 12% of the foreign patients spoke English.

Surgical procedures

A total of 344 surgical procedures were performed, 38 of which were combined. Several procedures were often performed under the same anaesthetic to minimize the number of anaesthetic episodes. Most of the surgery was for the release of syndactyly and the subsequent weekly dressing changes. An impression of the hand is taken at the final dressing change so that an accurate splint can be made. Other elective procedures included excision of squamous cell carcinoma with split skin grafting, oesophageal dilatation and dental surgery.

Preoperative preparation

Of those patients who underwent venesection, more than 50% had a haemoglobin concentration of less than 10 g dl⁻¹, which is caused in part by frequent trauma and poor nutrition leading to iron deficiency anaemias. Blood transfusion is often necessary. Only 15% of patients were premedicated, but almost all of those were given an antialalgogue. Premedication was administered orally or i.m., with no reports of trauma after the latter route. Two patients had EMLA (eutectic mixture of local anaesthetic) cream for venous access with no recorded adverse effects.

Anaesthesia

I.v. access was secured in all but 41 anaesthetics; the latter were either short procedures (such as dressing changes) or when access could not be attained. Peripheral access was established in 74% of anaesthetics and cannulae were secured by wrapping Vaseline gauze over and around the cannula followed by a light crepe bandage. Minimal manual venous occlusion to aid cannulation was applied by support staff. Femoral and jugular cannulae were used in 11% of cases, and were sutured in place.

Methods of induction are shown in Table 1. Of the anaesthetics given, 61% used inhalation induction, and isoflurane and sevoflurane were the most commonly used agents. Of the i.v. inductions, propofol was the agent of choice. Maintenance of anaesthesia was usually with isoflurane, although sevoflurane and halothane were also used. Total i.v. anaesthesia with propofol was used on 31 occasions.

Neuromuscular block with succinylcholine was required for tracheal intubation and there were no problems associated with its use. Vecuronium and atracurium were used infrequently because tracheal intubation was not often performed. No problems with antagonism of block were recorded.

Two spinal anaesthetics were performed for lower limb squamous cell carcinoma excision and grafting. Most patients were placed supine, two in the prone position and one was placed in the left lateral position. Pressure points were protected with Vaseline or soft gauze.
Table 1 Agents used for induction and maintenance of anaesthesia

<table>
<thead>
<tr>
<th></th>
<th>No. of patients</th>
<th>% of all operations</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Induction</td>
<td>Maintenance</td>
</tr>
<tr>
<td>Isoflurane</td>
<td>104</td>
<td>34.0 220</td>
</tr>
<tr>
<td>Sevoflurane</td>
<td>64</td>
<td>20.9 41</td>
</tr>
<tr>
<td>Halothane</td>
<td>18</td>
<td>5.8 13</td>
</tr>
<tr>
<td>Enflurane</td>
<td>1</td>
<td>0.3 0</td>
</tr>
<tr>
<td>Desflurane</td>
<td>0</td>
<td>0.3 0</td>
</tr>
<tr>
<td>Propofol</td>
<td>90</td>
<td>29.4 31</td>
</tr>
<tr>
<td>Thiopental</td>
<td>8</td>
<td>2.4 0</td>
</tr>
<tr>
<td>Ketamine</td>
<td>2</td>
<td>0.6 0</td>
</tr>
</tbody>
</table>

Table 2 Airway management

<table>
<thead>
<tr>
<th>Technique of airway control</th>
<th>No. of occasions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Face mask only</td>
<td>179</td>
</tr>
<tr>
<td>Laryngeal mask airway</td>
<td>57</td>
</tr>
<tr>
<td>Oral intubation</td>
<td>27</td>
</tr>
<tr>
<td>Goldman nasal mask</td>
<td>26</td>
</tr>
<tr>
<td>Blind nasal intubation</td>
<td>10</td>
</tr>
<tr>
<td>Nasal intubation</td>
<td>7</td>
</tr>
<tr>
<td>Fibreoptic intubation</td>
<td>2</td>
</tr>
</tbody>
</table>

Monitoring

All but 5% of patients were monitored using a pulse oximeter, placed either on a digit or on the ear lobe. Electrocardiograms were used in 11 cases and on each occasion care was taken to use Vaseline gauze laid over the lead ends in contact with the patient, thereby avoiding the use of adhesive electrode pads. Non-invasive arterial pressure cuffs were used, with the underlying skin wrapped in gauze, and no new bullae were reported.

Airway management

Methods of airway control are shown in Table 2. Face masks with the cushion covered with Vaseline gauze were used in 63% of the anaesthetics, while a padded Goldman nasal mask was used for anaesthesia during oesophageal dilatation. Tracheal intubation for dental procedures, some oesophageal dilatations and lengthy surgical procedures was usually performed orally with a cuffed tube using a laryngoscope with a lubricated blade. There were 16 nasal intubations, 10 of which were performed blind. Pharyngeal packs were used on each occasion and no mucosal damage was reported. At laryngoscopy, 66% were found to be grade II or better (Cormack and Lehane) while two patients had a grade IV laryngoscopy. A fibrescope was used on these occasions, and intubation was successful. Cricoid pressure was required in two cases to improve ease of intubation.

Laryngeal mask airways (LMA) were used in 57 anaesthetics (20% of cases) with only one reported complication (a new lingual bulla that caused no airway compromise after operation).

Fig 1 Blistering following handling of a patient with epidermolysis bullosa in recovery.

Table 3 Complications related to anaesthesia

<table>
<thead>
<tr>
<th>Complication</th>
<th>No. of occasions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Postoperative nausea/vomiting</td>
<td>8</td>
</tr>
<tr>
<td>New bullae</td>
<td></td>
</tr>
<tr>
<td>Facial</td>
<td>4</td>
</tr>
<tr>
<td>Lingual</td>
<td>1</td>
</tr>
<tr>
<td>Trunk</td>
<td>2</td>
</tr>
<tr>
<td>Regurgitation</td>
<td>2</td>
</tr>
<tr>
<td>Corneal ulcers</td>
<td>1</td>
</tr>
</tbody>
</table>

Analgesia

I.v. and i.m. opioids (morphine, fentanyl and pethidine) and rectal non-steroidal anti-inflammatory drugs (diclofenac) were most commonly prescribed. Local anaesthetic was applied to the donor site after split skin grafting on six occasions. Regional techniques, namely axillary block, were used in only 4.5% of all anaesthetics.

Complications

Complications associated with anaesthesia were rare (Table 3). There were four new facial blisters, three of which were caused by the face mask. The fourth involved a patient who was placed prone for excision of a squamous cell carcinoma from the posterior chest wall. The anaesthetist concerned inadvertently placed adhesive eye tapes (micropore), which predictably led to new bullae on both eyelids. Conversely, a new corneal abrasion occurred in another patient after inadequate eye protection. One lingual bulla was associated with insertion of a laryngeal mask airway but there were no reports of injury sustained after laryngoscopy. Finally, two patients suffered significant injury after poor handling. The first found new lesions over his flanks, possibly caused by positioning while anaesthetized. The other was an infant who was lifted beneath the arms by a member of the recovery team in an attempt to comfort the child. A hand was also placed against the back to support it (Fig. 1).
Discussion

Epidermolysis bullosa is the name given to a group of genetic disorders causing blistering and shearing of the skin after trivial trauma. More than 20 different subtypes of epidermolysis bullosa have been identified and are broadly grouped into three main categories: epidermolysis bullosa simplex, dystrophic epidermolysis bullosa and junctional epidermolysis bullosa (Debra International. http.debra.org.uk/debra/debrahtm). It has an incidence of approximately 1:17 000 and 46.5% are of the dystrophic type (Debra International. http.debra.org.uk/debra/debrahtm). This is the most common variety presenting for surgery related to the condition, and the only type in our study.

Dystrophic epidermolysis bullosa has two distinct genotypes: an autosomal dominant form and a commoner recessive form. The gene responsible for dystrophic epidermolysis bullosa is known as COL7A1 (Debra International. http.debra.org.uk/debra/debrahtm) which codes for VII collagen, a protein that anchors the lamina densa within the superficial dermis. Recessive dystrophic epidermolysis bullosa fibroblasts synthesize very low amounts of type VII collagen.20

There is little in the way of drug therapy to reduce the incidence or severity of the bullae21 and surgery is important in the prevention of serious debilitating sequelae. Often multiple surgical procedures are required.

Surgical intervention

The presenting problems of an epidermolysis bullosa patient are widespread. Scarring of the skin and soft tissues leads to contractures and fusion of fingers and toes causing syndactyly. Surgery is required to prevent contracture and preserve limb function. This is performed in one procedure, unlike other workers who prefer a two- or three-stage operative plan.4 The surgery is examined at two subsequent dressing changes. Hand splints and physiotherapy are also invaluable in retaining useful function. Figure 2 shows the effect of correction of syndactyly.

These patients also suffer blistering to mucosal membranes, in particular the oesophagus, which leads to strictures and failure of oral feeding.21 This is thought to occur twice as often in woman as in men.2 There is a risk of regurgitation or reflux and therefore pulmonary aspiration.23 Fatal oesophageal perforation has been noted twice in previous case series49 and oesophageal dilatation is obviously dangerous. Malnutrition and anaemia may require special preoperative care.

Facial trauma and scarring classically result in microstomia, narrowed nasal apertures and poor eyelid retraction (so that corneal damage is not uncommon and may occur during operation). Surgical correction may be necessary to improve mouth opening and permit eyelid closure. Dental condition is often poor because of severe dental caries. Early dental intervention is required to salvage teeth and gums, and to permit oral nutrition. In later life, malignant degeneration of stratified squamous epithelium may occur. Wide excision and split skin grafting in some patients is required.

Infection, especially with common commensals such as staphylococci and beta haemolytic streptococci,22 are not unusual as patients often have both poor cellular and humoral immunity9 and may also have had long-term steroid treatment.9 Prolonged admission to hospital is often needed and this increases the risk of acquiring resistant nosocomial infection.9

Anaesthetic management

We prefer general anaesthesia as the sole anaesthetic, despite several studies published on the use of regional techniques.47 Our series of 306 anaesthetics given over a 5-yr period included only two regional cases (both subarachnoid). This preference is supported by a relatively low incidence of complications. Regional techniques have very precise indications and are not applicable to all surgical procedures.

Management in general is one of a ‘no touch’ principle. However, direct pressure to the skin is not as damaging as frictional or shearing forces.4 Therefore, adhesive dressings should never be used. Even positioning requires the utmost care to avoid moving the sheets beneath the patient and ideally patients should place themselves on the operating table.9

Care must be taken to protect the eyes.22 A previous audit9 detailed the high incidence of corneal damage in patients reviewed after anaesthesia. The incidence of such injury has decreased to only one reported case in the present series. Simple eye ointments are used abundantly as soon as the patient is anaesthetized. An episode of inadvertent taping of the eyelids, in a patient placed in the prone position, led to blistering.

Premedication

During the preoperative assessment, a full history should be obtained and patient’s previous anaesthetic experiences
reviewed. Co-existing problems should be assessed, in particular signs of anaemia, infection and malnutrition.

Sedative premedication is useful in younger patients to avoid restlessness and injury, particularly during inhalation induction. However, adults are often best brought to the theatre fully awake so as to assist in positioning. Excessive salivation may occur and an antiallagogue such as atropine or glycopyrrolate may be administered. Antacid prophylaxis may be required if there is a history of reflux, regurgitation or a confirmed oesophageal stricture. EMLA can be applied before operation but no adhesive dressing can be used and great care must be taken in wiping away any residue. Older patients may present for surgery on long-term steroids and with adrenal suppression. Perioperative treatment with hydrocortisone may be required.

Monitoring

Minimal monitoring, as advocated by the Association of Anaesthetists, is not always possible, and these patients are often poorly monitored. Digital pulse oximetry probes are often difficult to place as much of the surgery is reconstruction of digits secondary to syndactyly and therefore ear probes are used instead. There are no reports of either probe having caused pressure-induced bullae.

Electrocardiogram monitoring is difficult because the adhesive pads can cause trauma at application or removal. The adhesive part can be removed and the electrode laid beneath the patient or wrapped in mummified thoracic dressing to obtain good contact and a reasonable trace. A further adaption is to place the adhesive dots on the underside of a chest radiograph over suitably placed holes. The patient is then placed on the film and the authors describe satisfactory recordings.

We simply place the adhesive dots onto three jelly defibrillation pads normally used for cardioversion. These pads are not adhesive and when laid in the CM5 configuration remain in place and give excellent electrical contact. If the leads are pulled they simply glide across the pad or the pad lifts off the skin without trauma.

Despite the obvious potential for blistering beneath the cuff, non-invasive arterial pressure monitoring can be used, as we report no new bullae from their use. Automated devices have the potential for generation of high cuff pressures and for this reason previous authors have suggested sphygmomanometers to measure arterial pressure. However, we have found, along with others, that provided the arm is well wrapped with wool, cuff-induced blistering does not occur.

Intra-arterial monitoring has been recommended previously as the measurement of choice. However, scarring over the wrist may make insertion into a radial artery difficult and occlusive pressure required to stop bleeding on removal of the cannula may cause unnecessary trauma.

Anaesthesia

As these patients undergo repeated anaesthetics, they have often formed their own opinion as to the anaesthetic that best suits them. Venous access is invariably difficult and therefore inhalation induction is popular. In the audit by Griffin and Mayou, 44% of inductions were inhalation, mostly with cyclopropane. With the loss of this drug from clinical practice and the advent of agents such as sevoflurane, inhalation induction has increased to 61% of all anaesthetics given. Sevoflurane suits these patients, with rapid induction and recovery. Unlike halothane, postoperative involuntary movements and shivering are minimal with less risk of inadvertent trauma. However, sevoflurane was used to maintain anaesthesia in only 13.4% of anaesthetics, being replaced by isoflurane, presumably to reduce cost.

For i.v. induction, propofol was the agent of choice over thiopental as it provides a smoother induction and better conditions for insertion of laryngeal masks. Thiopental was once thought to be relatively contraindicated, as many believed that porphyria was closely linked with epidermolysis bullosa. This has long since been disproved and thiopental can be used without problem.

Ketamine has been advocated in the past as an induction agent but excitation on recovery could cause further trauma. Its use in this hospital as an induction agent, and similarly as an analgesic, has decreased.

The use of neuromuscular blocking agents has previously been questioned but vindicated. Concerns that succinylcholine-induced fasciculations could lead to trauma and the hyperkalaemic response in patients with dystrophic muscle are not confirmed, although this agent was used less in our present study than in the previous audit. Medium duration blockers, such as atracurium and vecuronium, were also used to a lesser degree. It has been suggested that low albumin concentration changes the pharmacokinetics of many anaesthetic drugs, particularly neuromuscular blocking agents, but we noted no alteration in drug dosing to accommodate this, and no obvious clinical sequelae.

Airway problems

The first issue beyond safely maintaining an airway is avoidance of further bullae. Traditional manipulation of the airway is difficult because a face mask cannot be applied firmly. Intubation was advocated to avoid the trauma related to the use of the face mask. Face masks can be used safety but must be prepared by several layers of Vaseline gauze. More gauze must be placed beneath the anaesthetists’ fingers while applying minimal chin lift. Head tilt can be achieved by gentle manipulation of the head with a hand beneath the occiput. The airway is not inherently difficult to maintain, because the tongue is often small and scarred and does not fall back into the pharynx. Lubricated oral airways can be used with care, but are seldom necessary.

Several reports have supported the use of the head box. Its use is complicated by poor airway control, no
be lubricated with a water-based gel. The cuff should be thought to be responsible for a new lingual bulla. We advise an LMA, with only one complication, where the LMA was patients. In our series, 57 anaesthetics involved insertion of evaluated its use in dystrophic epidermolysis bullosa and felt that the problems of tracheal intubation were overemphasized. Tracheal lesions do not appear to occur after intubation probably because the trachea is lined with columnar epithelium.

Fig 3 Typical microstomia, limited mouth opening and poor dentition in a patient with epidermolysis bullosa

We noted four cases (1.4%) in which facial bullae occurred as a direct result of airway manipulation, almost the same incidence as in the previous audit from this hospital. The mucosa is at risk but damage was only seen as one lingual bulla caused by an LMA. Previously, the laryngoscope blade was blamed for the appearance of lingual and other intra-oral bullae. James and Wark reviewed airway management in dystrophic epidermolysis bullosa and felt that the problems of tracheal intubation were overemphasized. Tracheal lesions do not appear to occur after intubation probably because the trachea is lined with columnar epithelium.

Griffin and Mayou described one-third of all patients who were intubated orally but there were some in whom microstomia, tongue immobility, reduced jaw movement and poor dentition rendered intubation difficult (Fig. 3). They recommended blind nasal intubation and several patients in our series were intubated via this route. However, the nasal apertures may be scarred and are often too narrow to admit a nasal tube.

Difficult intubation was significantly less in our study than reported previously, but in two cases laryngoscopy failed and these patients were intubated using a fiberoptic laryngoscope. Cricoid pressure was used twice not to prevent regurgitation but to aid intubation. Provided pressure is applied evenly and with no sideways movement, cricoid pressure is not contraindicated in dystrophic epidermolysis bullosa patients. During extubation, oropharyngeal suctioning can lead to life-threatening bullae formation.

The use of the laryngeal mask has found widespread acceptance in anaesthesia but no previous studies have evaluated its use in dystrophic epidermolysis bullosa patients. In our series, 57 anaesthetics involved insertion of an LMA, with only one complication, where the LMA was thought to be responsible for a new lingual bulla. We advise a size smaller than normal and the shaft and cuff should be lubricated with a water-based gel. The cuff should be inflated to maintain shape but not to secure within the pharynx, and therefore there should be a leak. Vaseline gauze should then be wrapped around the shaft at the mouth in order to minimize trauma to the lips and to weigh the mask down in situ. Particularly in children, removal of the laryngeal mask is strongly recommended before the patient wakes so as to minimize trauma to the airway and teeth. The LMA is a useful airway adjuvant in the management of these patients.

In a recent report on anaesthesia for children with epidermolysis bullosa, the authors presented the use of an oropharyngeal airway. This is a soft, plastic tube, larger than a tracheal tube, and resembles a laryngeal mask without the cuff. Although in their practice the device was effective, it caused a high incidence of mucosal damage.

Analgesia

Morphine has previously been contraindicated in dystrophic epidermolysis bullosa because of concern about histamine releasing properties in patients who may have porphyria. This is not true and these patients should not be denied morphine. In our audit, analgesia was given with intraoperative i.v. and postoperative i.m. opioids. Chevaleraud, Ragot and Glicenstein considered that rectal administration of analgesia should be avoided as the anus was always the seat of new or old lesions, but other investigators have used the rectal route for premedication. Several of our patients received non-steroidal anti-inflammatory drugs via this route without complaint, and we consider this practice to be safe.

Recent reports advocate regional anaesthesia alone for surgery. Such procedures are easy to perform (the landmarks in these undernourished individuals are obvious), there are less airway or recovery difficulties, and postoperative analgesia is excellent. We prefer not to use regional techniques in isolation as single-stage hand surgery requires a large amount of split skin graft tissue that cannot be obtained simply from the forearm beyond the tourniquet. Others sites such as the abdomen or thigh must be available. A language barrier and patients too young to comply appropriately for long procedures are further contraindications. Also, as sedation cannot always be avoided, airway support may become necessary.

Regional anaesthesia in combination with a general anaesthetic is useful for postoperative pain control, particularly for hand surgery. The technique is standard, but the site should be inspected for complicating lesions, and compression distal to the point of injection should be avoided. The skin should be cleaned with spray antiseptics.

Axillary blocks for hand surgery in epidermolysis bullosa have reported 98% success rates without the use of a nerve stimulator. The authors argued the positive electrode would require an adhesive dot, but on the occasions on which we used a nerve stimulator, a needle was placed in the skin. Others have described the inadequacy of the axillary block and a need for further injections to block other nerves (musculocutaneous and the thoracobrachialis) to complete
the anaesthetic, in particular to permit the use of a tourniquet. Interscalene block has also been described when the axilla is too diseased, although this block may not be ideal for hand surgery.24

Subarachnoid and epidural anaesthesia in epidermolysis bullosa has been reported.19 In our series, two spinal anaesthetics were performed for removal and grafting of squamous cell carcinomas. No skin infiltration was used, simply a 25-gauge Whitacre spinal needle to reach the subarachnoid space. Both events were successful.

Other regional blocks included an ankle block for talar amputation and two penile blocks. Local anaesthetic was applied to the dressing covering the donor site of the skin graft.

Oral medication after operation is best given in the effervescent form,4 5 as many of these patients find swallowing difficult

Conclusion

Patients with epidermolysis bullosa may need anaesthesia outside a specialist centre, for procedures often unrelated to their disorder, such as general surgery13 or obstetrics.3 Anaesthesia has few complications provided that care is taken to minimize trauma.

Acknowledgements

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