orphanaesthesia

Anaesthesia recommendations for

Epidermolysis bullosa

Disease name: Epidermolysis bullosa

ICD 10: Q81

Synonyms:

Disease summary: Epidermolysis bullosa (EB) is a heterogeneous group of inherited rare diseases, which are characterised by extremely fragile skin and minimal shear force-induced blister formation of the skin and mucosa. The cause of the diseases are mutations in the genes for structural proteins of the skin basement membrane zone. At least 18 different gene mutations result in more than 30 clinical subtypes of EB with a wide spectrum of clinical presentations. The incidence including all types is estimated to 1:50 000 births.

Milder forms present with localized blistering mostly at hands and feet after minor trauma, healing without scarring. In severe diseases generalised blistering with consecutive multi-systemic involvement occur at birth or shortly after. Blisters can form within the oral cavity, on the external surface of the eye, within the mucosa of the respiratory, gastrointestinal or genitourinary tract. Besides painful blister formations, patients often present with secondary problems like scarifications and contractures. Severe microstomia, ankyloglossia, oesophageal stenosis as well as significant dental decay may occur. Anaemia, recurrent infections, cardiomyopathy, malnutrition, amyloidosis, renal failure and squamous cell carcinoma are concomitant morbidities reducing life expectancy.

Since causal therapies are not yet available, strict prevention of friction and trauma is essential to avoid new blister formation.

Depending on the skin level of the blister formation, there are four major types of EB, all of them include many subtypes:

1) Epidermolysis bullosa simplex (EBS)
Blistering occurs within the epidermis. Lack of adhesion of the skin directly above the basement layer. Localized or generalized blistering may develop, usually no scarification. Generally milder than other types of EB. Most common type of EB, accounting for 70% of cases. EBS usually is inherited in an autosomal dominant manner.

2) Junctional epidermolysis bullosa (JEB)
Development of blisters within the lamina lucida (mid portion of the skin basement membrane zone). Localised or generalized forms may develop, in many cases involvement of the mucosa. Patients often present with laryngeal and tracheal lesions leading to glottic and tracheal stenosis. Blisters tend to heal with scarring. Most severe type of EB, accounting for about 5% of cases, inherited in an autosomal recessive manner.

3) Dystrophic epidermolysis bullosa (DEB)
Autosomal dominant or recessive inherited gene mutations coding for the type VII collagen. These defects lead to blister formation beyond the basal membrane zone, always healing with scarring. Joint contractures, fusion of the fingers and toes, severe mucous membrane involvement and narrowing of the oesophagus are common in severe types of DEB. Milder and more severe types of the disease are described.

4) Kindler syndrome
Autosomal recessive inherited gene mutations coding KIND1, a component of adhesion contacts in basal keratinocytes. Blistering may occur at multiple levels within the basement membrane zone or in skin layers beneath it. Generalized blistering present at birth, development of characteristic poikilodermatous pigmentation and photosensitivity later, healing with atrophic scarring. Rare subtype of EB.

Medicine is in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong

Find more information on the disease, its centres of reference and patient organisations on Orphanet: www.orpha.net

Typical surgery

- change of dressings, skin biopsy
- dental surgery (dental extraction and conservation)
- ophthalmic surgery
- plastic surgery (repair of pseudosyndactyly, surgery to contractures, excision of squamous cell carcinoma, skin grafting)
- general surgery, oesophagoscopy and -dilatation, gastrostomy, fundoplication, circumcision

Type of anaesthesia

The subtype and the severity of disease and comorbidities require an individual approach to anaesthesia management. Patients with severe disease presenting for elective procedures should be managed in a specialist centre with multidisciplinary experience concerning EB. Development of institutional protocols is advisable to care for these patients (wound dressings, pain management, airway management etc.)

Meticulous planning of every single anaesthesia management is essential to prevent formation of new blisters.

If possible, prefer deep analgosedation and/or regional anaesthesia techniques due to the possibility of severe airway complications in case of new blister formation or due to pre-existing difficult airway due to scarring. Maintaining spontaneous ventilation without touching the airway is a preferable option for short interventions.

All types of general anaesthesia (balanced techniques/total-intravenous anaesthesia, ketamine) have been described.

Peripheral regional and neuroaxial anaesthesia techniques can be performed safely, if there is no infection at the puncture site. However, local skin infiltration should be avoided.

Necessary additional pre-operative testing (beside standard care)

- History taking (records of previous anaesthesia, presence of gastroesophageal reflux, muscular dystrophy, difficult airway, steroid therapy, renal dysfunction, infections)
- Blood values (blood cell count, renal parameters)
- Echocardiogram and electrocardiogram (if cardiomyopathy is assumed)
- Consultation of specialists: (paediatric) dermatologist, wound care specialist, pain service, ophthalmologist, dentist, nutritionist, physiotherapist, occupational therapist.

Particular preparation for airway management

Recurrent blister formation and scarring can lead to microstomia, poor mouth opening, immobile tongue and oesophageal webs, scarification in the nostrils, nasopharyngeal fibrosis, neck contractures. There is a considerable risk of blister formation at the level of the oropharyngeal airway in case of airway management. Laryngeal and tracheal involvement in EB is rare.

Thorough lubrication of face mask, laryngeal mask airway (LMA), endotracheal tube (ETT), laryngoscope is essential.

In severely affected patients, preventive coverage of certain areas of the face (e.g. nose, cheeks, chin) with special non-adhesive dressings (e.g. Mepilex® transfer) is recommended.

The cuffed endotracheal tube (ETT) should be chosen half to one size smaller than predicted by standard formulas. Some authors prefer uncuffed tubes.

Equipment for predicted difficult airway should be available: e.g. video laryngoscope, fibre-optic bronchoscope.

LMA should be used one size smaller than predicted by standard formulas.

Particular preparation for transfusion or administration of blood products

Some severe forms of epidermolysis bullosa can result in a transfusion dependent anaemia. Causative are blood and iron loss from wounds, chronic infection, malnutrition and problems absorbing iron due to the effects EB has on the gastrointestinal tract. Oral and intravenous iron can be given often paired with erythropoetin shots. If necessary, a blood transfusion is another option. Common risks and contraindications of each blood transfusion have to be considered.

Particular preparation for anticoagulation

Not reported.

Particular precautions for positioning, transportation and mobilisation

The most important task for transport or mobilisation of the patient is to maintain the integrity of the skin, avoiding friction, secondary pressure and traumata.

The operating table needs to be extensively padded, and the patient has to be transferred very carefully. Any pulling of the patient over surfaces during transfer in an out of the operating room has to be avoided.

The operation theatre needs to be warmed in order to prevent heat loss of the patient due to the extent of skin lesions and malnutrition.

Interactions of chronic disease and anaesthesia medications

General medication should be taken as usual. Be aware that many patients with EB take an opioid medication for chronic pain. Attention should be paid to infection prophylaxis.

Anaesthetic procedure

Agitation and uncontrolled movement during induction can lead to new skin damage.

A preoperative sedative medication could be appropriate.

As the intravenous access can be difficult, consider the use of ultrasound technique for establishment of intravenous access.

A rapid and non-traumatic intravenous induction is advantageous, but an inhalational induction is also possible. Mask ventilation usually is not difficult as the tongue often is tethered and does not tend to fall back, but prolonged facial manipulation can lead to new blisters. The skin area should be protected by a silicon based foam dressing.

To avoid new blisters use vaseline or any lubricant for face masks, laryngoscope, endotracheal tubes, laryngeal masks and stomach tube.

If the patient has reflux, a rapid sequence induction is indicated. Due to a smaller mouth opening, ankyloglossia (little tongue movement), adhered epiglottis, less reclination and possible tracheal stenosis, be prepared for a difficult airway.

The endotracheal tube should be chosen one size smaller than anticipated to age and be minimally blocked. Nasal fibreoptic intubation seems to be a preferred option in severe cases, as the nasal mucosa is composed of respiratory epithelium, which is less subject to blister formation. Many patients, however, can be intubated safely as well orally via direct laryngoscopy or videolaryngoscopy. Oropharyngeal tubes should be avoided. The endotracheal tube should be fixed with non-adhesive technique. Well lubricated laryngeal masks have been used safely but may initiate new enoral blisters especially in case of microstomia.

With appropriate precautions, safe endoscopic laryngeal surgery in patients with JEB has been reported in a case series.

For eye protection, use a moisturizing ophtalmic gel, preferably free of preservatives or lanolin. After application of the gel, cover the eyes with moistened gauze to protect them from mechanical trauma. Take care that the patient will not wake up with blurred vision and rub at his eyes after extubation. Risk of corneal abrasion.

Total intravenous anaesthesia may be useful in reducing agitation and emesis in the recovery room. Succinylcholine has been used successfully. Non-depolarising muscle relaxants sometimes show prolonged duration of action due to hypoalbuminaemia and low muscle mass. Be very careful when suctioning the stomach and oropharynx under direct vision before extubating, as this easily causes new wounds. Avoid fluid and heat loss and consider a sophisticated pain treatment.

Although general anaesthesia is mostly done, regional anaesthesia is advisable as a basic principle often in combination with sedation, as airway management can be avoided. Single shot and continuous peripheral nerve blocks as well as central neuroaxial blocks have been performed successfully without additional risk. Subcutaneous infiltration with local anaesthe-

tics should be avoided, as new blisters can occur. For all these procedures, rubbing or wiping the skin for disinfection should be avoided, whereas patting the skin with a moist wipe is usually well tolerated.

Particular or additional monitoring

Standard monitoring is sufficient, adapted to the surgical intervention. Any adhesive is contraindicated because it may cause new blisters. Generally consider to minimize monitoring whenever possible to avoid further harm to the patient.

The adhesive part of ECG leads should be cut off and the electrodes fixed by silicon based tape.

Clip-on pulsoximeters can be used safely. The self-adhesive part of paediatric pulsoximeter probes must be removed, the probe itself can be fixed by silicon based tape. Alternatively, the adhesive part may be covered by the adhesive site of a Tegaderm® dressing. The non-adhesive site of the Tegaderm® thereafter may be secured on the skin by silicon based tape (Mepilex®).

Intravenous catheter and any other device should be fixed with non-adhesive technique like silicon based products (Mepilex® transfer, Mepitac®).

A layer of cotton-wool padding should underlay the blood pressure cuff or the tourniquet.

Arterial lines should be sutured in place.

Avoid invasive temperature probes if possible. A lubricated axillary probe should be preferred.

Possible complications

- New blisters, especially oropharyngeal and periglottic,
- Difficulty getting venous access due to contracted fingers and multiple scars,
- Difficult airway due to small mouth opening or tracheal stenosis,
- Dysphagia, oesophageal stenosis and reflux,
- Anaemia, hypovolaemia,
- Difficult pain therapy.

Post-operative care

Excellent analgesia is important to prevent excessive movements and new skin trauma. A multimodal approach using nonsteroidal analgesics and opioids by the intravenous route is the most convenient method. High doses of analgetics may be required. Continuous regional anaesthesia techniques are advisable if indicated. Rectal suppositories are not recommend-

ed in the first line because of the risk of rectal wounds, but successful use has been reported. If used, they should be well lubricated with a jelly.

Many patients suffer from severe chronic itch. Therapeutic options are antihistaminics, gabapentin, pregabalin, serotonin noradrenaline reuptake inhibitors and behavioral interventions.

In case of emergence delirium, immediate sedation is recommended, as uncontrolled movements easily cause new blisters.

Swallowing of oral medication/nourishing can be painful after airway manipulation and due to pre-existing significant oesophageal stenosis. Many patients are not able to swallow pills or capsules.

Oxygen masks with sharp edges should be strictly avoided. Prolonged surveillance in the recovery room should to be planned in case of performed airway management, as new enoral blisters may occur.

Disease-related acute problems and effect on anaesthesia and recovery

- Systemic inflammatory reactions,
- Septic complications,
- Formation of new blisters especially concerning the airway.

Ambulatory anaesthesia

Small procedures performed under analgosedation can be realized in an experienced ambulatory setting. If airway manipulations are considered, an ambulatory proceeding is not recommended because of the risk of new formation of enoral blisters. Generally, pain management can be challenging.

Obstetrical anaesthesia

Pregnancy itself is not affected by the disease. The severity of skin fragility, however, may change to the better as well as to the worse during pregnancy. Vaginal delivery is the preferred mode and possible for most patients, but blisters of the vaginal mucosa have been described after delivery. Many case reports also describe successful caesarean delivery without negative consequences for mother and child. Regional anaesthesia (spinal/epidural anaesthesia) can be performed safely, if there are no infected blisters at the punction site. If urinary catheters are necessary, they need to be well lubricated before insertion. Some patients with EB have strictures of the urinary tract, which might render a catheter insertion impossible.

Due to frequently difficult airway management, an early insertion of an epidural catheter should be considered to prevent general anaesthesia in case of emergency.

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