orphananesthesia

Anaesthesia recommendations for patients suffering from

Ehlers-Danlos syndrome

Disease name: Ehlers-Danlos syndrome

ICD 10: Q79.6

Synonyms: -

Ehlers-Danlos syndrome (EDS) comprises a group of clinically and genetically heterogeneous, inherited connective tissue diseases [1]. Different defects in the synthesis of collagen lead to an increased elasticity within different types of connective tissue (skin, joints, muscles, tendons, blood vessels and visceral organs). Depending on the specific subtype and individual aspects, defects are mild to life threatening. The current Villefranche classification recognizes six major genetic subtypes (classic (type I and II according to the old “Berlin classification”), hypermobility (type III), vascular (type IV), kyphoscoliotic (type VI A), arthrochalasis (type VII A & B) and dermatosparaxis (type VII C), most of which are linked to mutations in one of the genes encoding fibrillar collagen proteins or enzymes involved in post-translational modification of these proteins. Over the last years, several new EDS variants have been characterized; both clinically and genetically, which call for a refinement of the Villefranche classification.

Medicine in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

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

© Anästh Intensivmed 2014;55:S544-S561 Aktiv Druck & Verlag GmbH

Disease summary

Subtypes are caused by autosomal-dominant or autosomal-recessive mechanisms. Approx. 50% of all patients have de novo mutations with negative family history. Each subtype has typical symptoms; however individual symptoms and severity need to be investigated for each specific patient. The classic type (type I and II) presents with severe skin hyperextensibility and fragility, delayed wound healing, easy bruisability and generalized joint hypermobility, whereas the hypermobility type (Type III) presents with less severe skin fragility, but generalized joint hypermobility, recurrent dislocations, and chronic musculoskeletal pain. Probably the most severe type is type IV, the vascular subtype with extreme fragile blood vessels and internal organs, such as the gastro-intestinal tractus, the gravid uterus, but also spleen and liver, which are prone to tearing (rupture). Nevertheless, specific symptoms must be given respect for each individual patient due to overlapping phenomena.

On an operational perspective, surgical and anaesthetic pitfalls relate to a mixture of common features shared by most subtypes and complications related to specific variants. Therefore, accurate patients' classification should be planned before any invasive procedure.

Typical surgery

- Most EDS subtypes (particularly hypermobility subtypes):

  Operative therapy of joint instability (fingers, wrist, elbow, shoulder, knee, hip): joint debridement, tendon replacement, arthroscopy, arthroplasty), corrective surgery for scoliosis, or pectus deformity

- EDS subtypes with vascular fragility:

  Vascular complications with operative / interventional therapy: valve replacements, aortic dissection, rupture of medium-sized arteries, (vessel dissections), and hematoma evacuation, carotid-cavernous fistula

- EDS with vascular subtype (IV):

  Rupture of organs: perforations of intestines, spontaneous pneumothorax, uterine rupture, liver rupture, spleen rupture

- EDS of all subtypes:

  Ceasarean section

- Miscellaneous:

  Ophthalmologic disorders: retinal detachment, corneal/scleral rupture (in EDS kyphoscoliotic type, or in the related brittle cornea syndrome) lens luxation (the latter is infrequent and not typical for EDS; it is more frequent in Marfan syndrome).

© Anästh Intensivmed 2014;55:S544-S561 Aktiv Druck & Verlag GmbH

Type of anaesthesia

There is no definite recommendation for either general or regional anaesthesia. There are several case reports and case series of spinal and epidural anaesthesia as well as peripheral nerve blocks without any complication.

However, local anaesthetics might have reduced or no effects in some patients[2,3]. Tissue scarring results in reduced spread of the local anaesthetics and block failure. This includes the use of EMLA cream (and its use e.g. in paediatric anaesthesia for pain-reduction in venous puncture). Reports of block failure are often with respect to local anaesthesia for dental surgery and peripheral nerve blocks. No reports for block failure are published with regard to neuraxial blocks. Nevertheless, meningeal involvement, in form of isolated or multiple Tarlov cysts, is a feature of specific EDS subtypes (i.e. classic, hypermobility and kyphoscoliotic). Therefore, particularly in patients with these subtypes, spinal anaesthesia should be performed with particular care in order to avoid post-dural puncture headache. However, most Tarlov cysts are primarily located in the S1 to S4 region of the spinal cord and therefore regularly no contraindication for the performance of a spinal anaesthesia or thoracal or lumbal epidural anaesthesia. Scoliosis and / or severe spondylosis might hamper epidural spread of local anaesthetics or performance of spinal anaesthesia.

Thorough bleeding anamnesis and individual decision making with the patient are pivotal, especially for neuraxial blocks like spinal or epidural anaesthesia.

General anaesthesia can be performed as balanced anaesthesia with volatile anaesthetics, nitrous oxide or as total intravenous anaesthesia (TIVA). Monitoring of neuromuscular blockade is advised before emergence of the anaesthesia (some patients present with muscular weakness). However, depolarising (succhinylcholine) as well as non-depolarising agents can be used in patients with EDS with regard to concomitant disease or disability.

Postural tachycardia syndrome is described as a feature in some patients with EDS subgroups with hypermobility [4].

Avoidance of central venous access and arterial puncturing is recommended in Type IV (and some patients of other subtypes) due to high risk for vascular dissection whenever possible. If those lines are needed (high risk surgery, emergencies), ultrasound guidance is strictly recommended including visualisation of correct wire localisation within the blood vessel [5].

Intraoperative patient positioning should focus on optimal padding of the patient, reduction of shear forces, protection of the eye with respect to the risk for retinal detachment due to direct force (e.g. by the surgeon's elbow). Adhesive tapes for fixation of cannulas, tubes etc. should be easily removable or avoided when possible because of the risk of severe skin damages in many patients.

Necessary additional diagnostic procedures (preoperative)

Thorough history is required including complete bleeding anamnesis. Conventional coagulation tests are usually within normal range, bleeding time might be prolonged in affected patients, patient history and bleeding anamnesis is usually quite helpful in estimating the degree of bleeding risk [1,6,7]. Physical examination of difficult airway, muscular weakness and signs of aortal and mitral insufficiency are important. Actual echocardiography results might be helpful for estimating the patient's individual risk.

Particular preparation for airway management

Careful mask ventilation is advised to avoid high risk of temporomandibular joint luxation. Tissue fragility can cause bleeding in repeated intubation attempts. Smaller endotracheal tube than in healthy patients might reduce mucosal damage in the trachea. Check cuff pressure thoroughly. Laryngeal mask airway is feasible. Reduce airway pressure whenever possible due to the risk for spontaneous pneumothorax.

Many adult patients with various forms of EDS develop temporomandibular dysfunction and block, as well as premature spondylosis or occipitalatlantoaxial instability of the cervical spine. This may lead to difficult intubation to difficult airway management [8]. Subclinical cervical spine instability should be taken into account also in patients with preserved neck flexibility and temporomandibular joint mobility in order to prevent post-operative complications, such as neck pain and compression neurologic symptoms, related to temporomandibular joint luxation and occipitoatlantoaxial instability.

Particular preparation for transfusion or administration of blood products

Prematching of RBCs is advised for patients with high risk for bleeding (Type IV EDS as well as patients with unknown or positive bleeding history). Inform your local transfusion specialist in advance for storage of sufficient numbers of blood products. In acute bleeding Type IV EDS patients, aggressive hemostatic therapy is advisable. Use of desmopressin (DDAVP) might be helpful in reducing transfusions [9-12], also in other EDS subtypes with positive history of bleeding. In high-risk surgery as well as high-risk patients, cell saving strategies might be advisable. Anecdotal reports discuss the use of tranexamic acid to prevent re-bleeding and recombinant factor VIIa for patients with massive haemorrhagia and coagulopathy [13,14].

Particular preparation for anticoagulation

Not reported.

Particular precautions for positioning, transport or mobilisation

Careful transport is needed for patients with EDS. Mobilisation should be done with respect to the danger of easy skin damage, haematoma formation and luxation of joints [1]. Shear forces should be reduced due to tissue fragility whenever possible.

Fracture and wound healing is often compromised in EDS patients again with moderate to severe extent.

Probable interaction between anaesthetic agents and patient's long term medication

Not reported.

Anaesthesiologic procedure

Optimal padding of the patient in the OR is an important issue. Extent of matched blood products (as well as the provision of cell saver even for small surgical procedures for patients with abnormous coagulation) should be discussed with the team.

Avoid tourniquets (this topic should be discussed with the surgeon) whenever possible - high risk for haematoma and compartment syndrome (and unstoppable diffuse bleeding especially in EDS subtypes with vascular fragility). The authors have anecdotal knowledge of lethal complications due to the use of tourniquets in elective minor surgery.

Avoid insertion of central venous catheters and arterial lines whenever possible. If needed, ultrasound guidance of each procedural part is strictly recommended to avoid vessel dissection [5].

Laryngeal mask and intubation are possible. Reduce cuff pressure whenever possible, use a smaller than usual endotracheal tube to reduce potential mucosal damage. Difficult airway status should be anticipated.

Particular or additional monitoring

Prefer non-invasive monitoring whenever possible. Some patients develop extensive haematoma even by repetitive non-invasive blood pressure measurements. On the other hand, invasive blood pressure monitoring is exposing the patient to the risk of vascular wall dissection with high morbidity and mortality (especially for EDS subtypes with vascular fragility).

Possible complications

Patient positioning: plexus neuropathy, postoperative visual loss due to direct pressure to the eye. Skin damage and haematoma formation when patient was insufficiently padded and positioned or due to shear forces to the skin.

Spontaneous pneumothorax due to mechanical ventilation and airway bleeding during repeated intubation attempts. Difficult airway status can be observed in some patients with atlantooccipital instability as well as higher risk of temporomandibular joint luxation due to mask ventilation or intubation.

Postdural puncture headache (PDPH) might occur more often in EDS patients than in normal population in neuraxial blockades and should be discussed with the patient. However, this is solely an expert opinion with regard to the fragility of (dural) tissue and a case series of patients with spontaneous CSF leaks with high rates of underlying EDS [15].

© Anästh Intensivmed 2014;55:S544-S561 Aktiv Druck & Verlag GmbH

Postoperative care

Postoperative care should focus on the development of bleeding & haematoma at the operation site. Furthermore, some patients report muscular weakness after extubation. Carefull patient positioning and mobilisation is advised to reduce the risk of joint luxation. In all EDS subtypes, but particularly in the hypermobility subtype, early mobilization is a key point in order to prevent excessive deconditioning and unexpected deterioration of the musculosceletal system and cardiovascular reactivity.

Information about emergency-like situations / Differential diagnostics

caused by the illness to give a tool to distinguish between a side effect of the anaesthetic procedure and a manifestation of the disease

Acute vascular dissection (e.g. aortal dissection, peripheral arterias & veins) may be caused spontaneous or iatrogenic (especially during angiographic interventions [16]). Compartment syndromes can be caused by vasculare puncture and resulting haematoma. High risk of pneumo (haemo-)thorax must be anticipated during ventilation as well as central venous access. Spontaneous rupture or rupture after bagatell trauma of intestines, organs or other tissues (bowel, uterus, esophagus, vagina) are reported. However, these situations are most often encountered in patients with EDS subtypes of vascular fragility and unusual in patients with other subtypes.

Ambulatory anaesthesia

Not reported. We strongly encourage to operate patients in centres with expertise for EDS and the special conditions within this syndrome. Crossmatching of RBCs is important for patients with EDS with vascular fragility and those with high bleeding risk even for minor surgery.

Obstetrical anaesthesia

There are case series with parturients for all types of delivery (vaginal, forceps, caesarean section and all common types for anaesthesia (general, epidural, spinal). Uterine rupture and delayed wound healing are complications for both vaginal delivery and caesarean sectio. Severe bleeding - especially for patients with EDS with vascular fragility must be anticipated for both vaginal delivery as well as caesarean section. In the hypermobility subtype, episiotomy is related to pelvic prolapse. Therefore, caesarean section may be considered as first delivery option in this EDS subtype.

Literature and internet links

1. Parapia LA, Jackson C. Ehlers-Danlos syndrome - a historical review. Br. J. Haematol. 2008 Apr;141(1):32–5
2. Hakim AJ, Grahame R, Norris P, Hopper C. Local anaesthetic failure in joint hypermobility syndrome. J R Soc Med. 2005 Feb;98(2):84–5
3. Arendt-Nielsen L, Kaalund S, Bjerring P, Høgsaa B. Insufficient effect of local analgesics in Ehlers Danlos type III patients (connective tissue disorder). Acta Anaesthesiol Scand. 1990 Jul;34(5):358–61
4. Mathias CJ, Low DA, Iodice V, Owens AP, Kirbis M, Grahame R. Postural tachycardia syndrome - current experience and concepts. Nat Rev Neurol. 2012 Jan;8(1):22–34
5. Solan K, Davies P. Anaesthetic and intensive care management of a patient with Ehlers–Danlos Type IV syndrome after laparotomy. Anaesthesia. 2004
6. Jackson SC, Odiaman L, Card RT, van der Bom JG, Poon M-C. Suspected collagen disorders in the bleeding disorder clinic: A case-control study. Haemophilia. 2012 Oct 3
7. Lane D. Anaesthetic implications of vascular type Ehlers-Danlos syndrome. Anaesth Intensive Care. 2006 Aug;34(4):501–5
8. Halko GJ, Cobb R, Abeles M. Patients with type IV Ehlers-Danlos syndrome may be predisposed to atlantoaxial subluxation. J. Rheumatol. 1995 Nov;22(11):2152–5
9. Stine KC, Becton DL. DDAVP therapy controls bleeding in Ehlers-Danlos syndrome. J. Pediatr. Hematol. Oncol. 1997 Mar;19(2):156–8
10. Yasui H, Adachi Y, Minami T, Ishida T, Kato Y, Imai K. Combination therapy of DDAVP and conjugated estrogens for a recurrent large subcutaneous hematoma in Ehlers-Danlos syndrome. Am. J. Hematol. 2003 Jan;72(1):71–2
11. Balduini CL, Noris P, Belletti S, Spedini P, Gamba G. In vitro and in vivo effects of desmopressin on platelet function. Haematologica. 1999 Oct;84(10):891–6
12. Mast KJ, Nunes ME, Ruymann FB, Kerlin BA. Desmopressin responsiveness in children with Ehlers-Danlos syndrome associated bleeding symptoms. Br. J. Haematol. 2009 Jan;144(2):230–3
13. Bolton-Maggs PHB, Perry DJ, Chalmers EA, Parapia LA, Wilde JT, Williams MD, et al. The rare coagulation disorders - review with guidelines for management from the United Kingdom Haemophilia Centre Doctors' Organisation. Haemophilia. 2004 Sep;10(5):593–628
14. Faber P, Craig WL, Duncan JL, Holliday K. The successful use of recombinant factor VIIa in a patient with vascular-type Ehlers-Danlos syndrome. Acta Anaesthesiol Scand. 2007 Oct;51(9):1277–9
15. Schievink WI, Gordon OK, Tourje J. Connective tissue disorders with spontaneous spinal cerebrospinal fluid leaks and intracranial hypotension: a prospective study. Neurosurgery. 2004 Jan;54(1):65–70, discussion70–1
16. Burcharth J, Rosenberg J. Gastrointestinal surgery and related complications in patients with ehlers-danlos syndrome: a systematic review. Dig Surg. 2012;29(4):349–57.

Last date of modification: October 2013

These guidelines have been prepared by:

Author
Thomas Wiesmann, Anaesthesiologist, University Hospital Marburg, Germany
wiesmann@med.uni-marburg.de

Peer revision 1
Franziska Malfait, Anaesthesiologist, Elect Ghent University, Belgium
fransiska.malfait@ugent.be

Peer revision 2
Marco Castori, Division of Medical Genetics, Department of Molecular Medicine, Sapienza University, San Camillo-Forlanini Hospital, Rome, Italy
MCastori@scamilloforlanini.rm.it

© Anästh Intensivmed 2014;55:S544-S561 Aktiv Druck & Verlag GmbH