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Dyskeratosis congenita

Goldenhar syndrome

orphan**a**nesthesia

a project of the German Society
of Anaesthesiology and Intensive Care Medicine

SUPPLEMENT NR. 2 | 2023

OrphanAnesthesia –

ein krankheitsübergreifendes Projekt des Wissenschaftlichen Arbeitskreises Kinderanästhesie der Deutschen Gesellschaft für Anästhesiologie und Intensivmedizin e.V.

Ziel des Projektes ist die Veröffentlichung von Handlungsempfehlungen zur anästhesiologischen Betreuung von Patienten mit seltenen Erkrankungen. Damit will Orphan Anesthesia einen wichtigen Beitrag zur Erhöhung der Patientensicherheit leisten.

Patienten mit seltenen Erkrankungen benötigen für verschiedene diagnostische oder therapeutische Prozeduren eine anästhesiologische Betreuung, die mit einem erhöhten Risiko für anästhesieassoziierte Komplikationen einhergehen. Weil diese Erkrankungen selten auftreten, können Anästhesisten damit keine Erfahrungen gesammelt haben, so dass für die Planung der Narkose die Einholung weiterer Information unerlässlich ist. Durch vorhandene spezifische Informationen kann die Inzidenz von mit der Narkose assoziierten Komplikationen gesenkt werden. Zur Verfügung stehendes Wissen schafft Sicherheit im Prozess der Patientenversorgung.

Die Handlungsempfehlungen von OrphanAnesthesia sind standardisiert und durchlaufen nach ihrer Erstellung einen Peer-Review-Prozess, an dem ein Anästhesist sowie ein weiterer Krankheitsexperte (z.B. Pädiater oder Neurologe) beteiligt sind. Das Projekt ist international ausgerichtet, so dass die Handlungsempfehlungen grundsätzlich in englischer Sprache veröffentlicht werden.

Ab Heft 5/2014 werden im monatlichen Rhythmus je zwei Handlungsempfehlungen als Supplement der A&I unter www.ai-online.info veröffentlicht. Als Bestandteil der A&I sind die Handlungsempfehlungen damit auch zitierfähig. Sonderdrucke können gegen Entgelt bestellt werden.

OrphanAnesthesia –

a project of the Scientific Working Group of Paediatric Anaesthesia of the German Society of Anaesthesiology and Intensive Care Medicine

The target of OrphanAnesthesia is the publication of anaesthesia recommendations for patients suffering from rare diseases in order to improve patients' safety. When it comes to the management of patients with rare diseases, there are only sparse evidence-based facts and even far less knowledge in the anaesthetic outcome. OrphanAnesthesia would like to merge this knowledge based on scientific publications and proven experience of specialists making it available for physicians worldwide free of charge.

All OrphanAnesthesia recommendations are standardized and need to pass a peer review process. They are being reviewed by at least one anaesthesiologist and another disease expert (e.g. paediatrician or neurologist) involved in the treatment of this group of patients.

The project OrphanAnesthesia is internationally oriented. Thus all recommendations will be published in English.

Starting with issue 5/2014, we'll publish the OrphanAnesthesia recommendations as a monthly supplement of A&I (Anästhesiologie & Intensivmedizin). Thus they can be accessed and downloaded via www.ai-online.info. As being part of the journal, the recommendations will be quotable. Reprints can be ordered for payment.

Bisher in A&I publizierte Handlungsempfehlungen finden Sie unter:

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orphananesthesia

Anaesthesia recommendations for Dyskeratosis congenita

Disease name: Dyskeratosis congenita

ICD 10: Q82.8

Synonyms: Zinsser-Engman-Cole syndrome, Hoyeraal-Hreidarsson syndrome, Revesz syndrome, DC, DKC

Disease summary: Dyskeratosis congenita (DC) is a rare disease of abnormal telomere biology, leading to haematopoietic failure among other heterogeneous multisystem manifestations.

There are multiple forms of the condition with varying patterns of inheritance. There is a 3:1 male:female predilection and an incidence of approximately 1:1,000,000. The most common gene mutation (*DKC1*) in the X-linked form of DC results in impaired telomere maintenance. Other disease genes have been implicated with both autosomal dominant and recessive inheritance, including: *TERC*, *TINF2*, *ACD*, *RTEL1*, *TERT*, *CTC1*, *NHP2*, *NOP10*, *PARN*, *WRAP53*, *NAF1*, *SNT1*, *POT1* and *ZCCHC8* [1–5]. As all of these genes are important in telomere maintenance, DC is now regarded as principally a disorder of defective telomere maintenance.

DC classically presents with the clinical triad of dysplastic nails, lacy reticular pigmentation of the upper chest/neck and oral leukoplakia (white plaques) [2]. Bone marrow failure is common (80 %). DC is also associated with pulmonary fibrosis, pulmonary arteriovenous malformations, poor dentition, oesophageal stenosis, cirrhosis, hepatopulmonary syndrome, vascular ectasias, urethral stenosis, peripheral neuropathy, immunodeficiency and accelerated aging. Patients with DC have an elevated risk for leukemia as well as squamous cell cancers of the head and neck, skin or anogenital regions [6]. The treatment for DC is individualised according to symptoms. Haematopoietic stem cell transplantation (HSCT) is considered in cases of bone marrow failure or leukemia [7].

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

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Typical surgery

Dental procedures, ophthalmologic procedures, bone marrow aspirate, liver biopsy, gastroscopy, colonoscopy, head and neck tumour resection. There are also case reports of organ transplants in this patient population (i.e., liver, lung) [8–10].

Type of anaesthesia

There are very few published case reports of anaesthetic management in DC [10–14]. General anaesthesia has been described for patients with DC. Balanced anaesthetic maintenance with volatiles, opioids and/or propofol is effective.

Given the high propensity for bone marrow failure in this patient population, thrombocytopenia and coagulopathy must be ruled out prior to providing neuraxial anaesthesia or performing regional anaesthesia techniques with high risk for bleeding. Furthermore, due to the telomere defect, wound healing and tissue repair are not completely normal. Careful surgical technique is important for DC patients undergoing any operative procedure and they often require a longer recovery time compared to non-DC patients.

Necessary additional preoperative testing (beside standard care)

Neurologic examination and documentation of pre-existing peripheral neuropathies is recommended. A careful airway examination is also essential.

Full blood count (including platelet count), coagulation profile, type and screen should be obtained as should standard liver and renal function tests.

Patients with poor exercise tolerance, known pulmonary fibrosis or pulmonary arteriovenous malformations may warrant pulmonary function testing, room air arterial blood gas, and/or an echocardiographic study.

A preoperative haematology consultation will guide perioperative medication and blood product management.

Particular preparation for airway management

Patients with DC may be at risk for difficult intubation. The underlying telomere defect commonly results in poor dentition and friable oral tissue. Oropharyngeal tumours may distort the airway anatomy. Mandibular hypoplasia has also been reported in DC.

Pulmonary disease is a common (20 %) complication of DC [15]. With pulmonary fibrosis, poor lung compliance and gas exchange may further complicate airway management and ventilation, as may concomitant pulmonary hypertension, shunting and right heart failure. Pulmonary arteriovenous malformations also lead to hypoxaemia in patients with DC. Liver dysfunction resulting in ascites may further limit safe apnoea time.

A thorough airway examination is indicated. Adjuncts should be immediately available for safe tracheal intubation (e.g., supraglottic devices, video laryngoscope, flexible broncho-

scope). Apnoeic oxygen may be advisable for patients with pulmonary complications and apnoea intolerance. Efforts should be made to avoid traumatising the oral mucosa, which may be prone to bleeding.

Particular preparation for transfusion or administration of blood products

Neutropenia, anaemia, thrombocytopenia and pancytopenia are commonly seen in DC. Pre-operative evaluation of full blood count is essential, with transfusion thresholds individualised since chronically anaemic patients may be adapted to lower haemoglobin levels. The immunomodulatory effects of blood product transfusion should be carefully considered in these immunocompromised patients.

Blood products should be leukodepleted, irradiated (if patient is lymphopenic) and CMV-negative. Avoid blood donations by relatives if stem cell transplant is being considered, as this may increase the risk of future graft rejection. Indeed, stem cell transplant candidates should have the minimal necessary exposure to red cells or platelets [2,16].

Blood conservation strategies are likely beneficial for this patient population. Consider administering tranexamic acid to avoid fibrinolysis [17]. The use of topical haemostatic agents has not been described but may be useful.

Preoperative administration of granulocyte colony-stimulating factor (GCSF) for the treatment of leukopenia has been described [14]. However, in patients taking androgen therapy for DC, concurrent GCSF administration has been implicated in life-threatening splenic rupture [18].

Particular preparation for anticoagulation

The need for perioperative anticoagulation must be weighed against bleeding risks and should be addressed in a multidisciplinary fashion.

Particular precautions for positioning, transportation and mobilisation

Not reported.

Interactions of chronic disease and anaesthesia medications

Not reported. Liver failure may be associated with the prolonged elimination of anaesthetic medications, such as opioids, benzodiazepines and neuromuscular blocking agents. In such instances, choosing medications that are eliminated independently of liver function may result in a more predictable offset of medication effects.

Commonly used anaesthetic agents may be administered to patients with pulmonary complications of dyskeratosis congenita. Most halogenated volatile anaesthetics have bronchodilatory properties, although desflurane may cause bronchial irritation. At higher concentrations, volatile anaesthetics reverse hypoxic pulmonary vasoconstriction and may worsen intrapulmonary shunting. Nitrous oxide may increase pulmonary vascular resistance and worsen pulmonary hypertension; additionally, it may confer risk of air trapping and

pneumothorax in patients with pulmonary honeycomb cysts or bullae. Avoidance of excessive sedation and respiratory depression is advisable.

Anaesthetic procedure

General anaesthesia has been performed successfully in DC. There are no specific restrictions on the types of medications for induction or maintenance, though the presence of significant liver dysfunction may support the selection of agents that do not depend on hepatic clearance. Careful planning is necessary to ensure safe airway management. For patients with pulmonary fibrosis, a restrictive approach to fluid management is preferred and prolonged hyperoxygenation should be avoided in order to avoid exacerbating alveolar dysfunction [19]. Any decision to pursue elective surgery under general anaesthesia should be carefully weighed against the risk of pulmonary exacerbation.

There is no reported literature on regional anaesthesia in patients with DC. Given the risk of pulmonary complications, regional anaesthesia may often be preferable to general anaesthesia [19]. Neuraxial anaesthesia may be unsafe in the context of severe thrombocytopenia. However, regional techniques with a low risk of bleeding may be considered. Continuous regional anaesthesia catheters may be helpful for postoperative analgesia, but this must be weighed against the risk of infection in immunocompromised patients.

Dental procedures using local anaesthesia have been described [20].

Overall, there are very few reports describing anaesthetic management of patients with DC [10,13,14,20].

Particular or additional monitoring

Standard monitors should be used as appropriate (e.g., electrocardiogram, non-invasive blood pressure, pulse oximetry, capnography, gas analyser).

Intraoperative transoesophageal echocardiography may be indicated for patients with pulmonary hypertension and right heart failure, but oesophageal probe placement may be difficult or prone to complications if there are oesophageal strictures or varices. Invasive arterial blood pressure transduction and stroke volume variation may also guide fluid management.

Urethral stenosis may hinder insertion of urinary catheters.

The intraoperative use of thromboelastography has not been described but is likely helpful for managing acute haemorrhage.

Possible complications

Difficult airway management is a significant concern as are postoperative pulmonary complications. Patients with poor pulmonary function may require postoperative ventilatory support.

Haemorrhage and opportunistic infection are complications relating to bone marrow failure.

Meticulous attention to aseptic technique and administration of surgical antibiotic prophylaxis are essential given immunocompromise.

Postoperative care

Patients with pulmonary dysfunction may require prolonged postoperative ventilatory support in the intensive care unit and may benefit from non-invasive positive pressure ventilation after extubation.

Continued dosing of tranexamic acid and antibiotic prophylaxis until 48 hours post-operatively has been reported [17].

Disease-related acute problems and effect on anaesthesia and recovery

Cf. airway management and ventilation considerations as mentioned previously.

Ambulatory anaesthesia

Minor procedures can be considered as day cases, particularly in patients with limited systemic manifestations of DC. Local and regional anaesthetic techniques are preferred in patients with pulmonary compromise [19].

Obstetrical anaesthesia

There is no reported literature on obstetrical anaesthesia in patients with DC. Pregnancy may be associated with new pancytopenia or worsening of existing cytopenias [1].

There must be careful consideration of risks associated with neuraxial anaesthesia (bleeding disorder) versus general anaesthesia (difficult airway).

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Please note that in this recommendation, the reviews are both by non-anaesthesiologists.

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