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Osteopetrosis

orphan anesthesia

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

SUPPLEMENT NR. 14 | 2017

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.

Bisher in A&I publizierte Handlungsempfehlungen finden Sie unter:

www.ai-online.info/Orphsuppl
www.orphananesthesia.eu

OrphanAnesthesia –
a common 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 recommenations 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.

A survey of until now in A&I published guidelines can be found on:

www.ai-online.info/Orphsuppl
www.orphananesthesia.eu

Projektleitung

Prof. Dr. Tino Münster, MHBA
Geschäftsführender Oberarzt
Facharzt für Anästhesie,
Spezielle Schmerztherapie,
Notfallmedizin
Anästhesiologische Klinik
Friedrich-Alexander-Universität
Erlangen-Nürnberg
Krankenhausstraße 12
91054 Erlangen, Deutschland
Tel.: 09131 8542441
Fax: 09131 8536147
E-Mail: muenster@kfa.imed.uni-erlangen.de

Deutsche Gesellschaft für Anästhesiologie & Intensivmedizin
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Anaesthesia recommendations for patients suffering from

Osteopetrosis

Disease name: Osteopetrosis

ICD 10: Q78.2

Synonyms: Marble bone disease, Albers-Schönberg disease, osteosclerosis, fragilitas generalisata, osteopetrosis generalisata

Osteopetrosis is a rare disease caused by the failure of osteoclast function and impaired bone resorption. Marrow cavities will be filled with new endochondral bone from overwhelming osteoblast activity, leading to increased bone density, but decreased stability. Loss of haematopoieticly active bone marrow leads to pancytopenia and the re-activation of extra-medullary haematopoiesis. Alterations in bone mass, function as well as inner and outer form will cause pathologic fractures, mass effects, such as tissue compression, and can lead to pathognomonic, especially facial features. Alterations to airway, cervical spine and thoracic wall are of special interest to anaesthesia. Secondary disorders comprise anaemia, bleeding disorders, immunodeficiency, hepatosplenomegaly, hypocalcaemia, hyper-phospataemia and renal acidosis.

Clinical severance is a result of different combinations of gene dysfunctions related to osteoclast physiology. Despite of rather heterogeneous genetic arrays, the classification of osteopetrosis still relies on inheritance patterns. Autosomal dominant osteopetrosis is clinically mild, and sometimes not diagnosed until adulthood. It has an incidence of 5 in every 100,000 births, usually solely presents with pathologic fractures and comes with normal life expectancy. The autosomal recessive variant of osteopetrosis is more severe, becomes symptomatic early in infancy and childhood, and has an incidence rate of 1 in every 250,000 births. In its most severe phenotype of “malignant infantile” osteopetrosis, life expectancy is reduced to adolescence, and the most common causes of death are anaemia, bleeding and septicemia.

Calcitriol, steroids and interferon-gamma may be somewhat beneficial, but haematopoietic stem-cell transplantation offers the most effective treatment option available up to date.

Medicine in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

▶ **Citation:** Ozer AB: Osteopetrosis. Anästh Intensivmed 2017;58:S611-S617. DOI: 10.19224/ai2017.S611

Disease summary

Anomalies with concern to anaesthesia in children with autosomal recessive osteopetrosis include proptosis, a high-arched palate, broad facies, hypertelorism, frontal bossing, mandibular enlargement or hypoplasia, cervico-medullary stenosis, temporomandibular joint restriction and narrowed nasal passages. A difficult airway has to be expected in these patients. Chest wall compliance may be reduced.

Neurologic abnormalities may include loss of vision or hearing due to cranial nerve entrapment, causing compression and ischemia of nerve roots. Cases of metal retardation have been described as well.

Haematologic symptoms include (pan-) cytopenia most commonly anaemia, thrombocytopenia, leukocyte dysfunction, and hepatosplenomegaly. Hepatosplenomegaly may lead to respiratory distress by cranial displacement of the diaphragm. Immunologic compromise may be found.

Electrolyte abnormalities, such as hypocalcaemia, are common, and in severe cases of osteopetrosis calcium supplementation may be indicated.

Patients may receive macrophage colony stimulating factor (M-CSF), erythropoietin (EPO) and blood transfusions as supportive measures in addition to the disease altering drugs mentioned above.

Typical surgery

The most common procedure, which requires anaesthesia, is a bone marrow biopsy. Other indications for surgeries can include pathological bone fractures, submandibular abscesses, osteomyelitis, dental interventions, oral and maxillofacial surgery. Surgery for aspergilloma has also been described.

Type of anaesthesia

There is no data available to favour any particular anaesthetic technique in this disease. However, since a difficult airway is an expected state in these patients, awake fiberoptic intubation may be necessary on a regular basis. Sufficient equipment for the management of a difficult airway such as supraglottic devices and an emergency surgical airway set must be available before induction of anaesthesia.

Neuraxial or regional blocks can be an alternative in patients with a difficult airway; however, changes in bone structure, fractures (e.g. chronic compression fractures of the vertebrae) or ankylosis of the dorsal spinal column may present severe difficulties for these techniques. More importantly, abnormal coagulation patterns, especially thrombocytopenia, may result in contraindications to any neuraxial block.

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Necessary additional diagnostic procedures (preoperative)

To detect a difficult airway and comprised ventilation, temporo-mandibular joint mobility, the oral cavity, pharynx and cervical spine should be examined carefully. Radiographs or CT-scans of these regions of interest can be advisable. If kyphosis, scoliosis, and/or rib cage deformity are present, chest radiography and spirometry should be considered. Because dysphagia is observed in many children with osteopetrosis, patients should be examined in terms of risk for aspiration and history of aspiration pneumonia.

Liver function (coagulation profile) and kidney function (BUN and electrolytes) should also be examined. The most common electrolyte imbalance in osteopetrosis is hypocalcemia. In those patients who received a bone marrow transplantation as specific treatment for osteopetrosis, hypercalcemia may be observed owing to the engraftment of osteoclasts arising from precursor cells.

Patients suffering from osteopetrosis can be immunologically compromised! If an infection is present, diagnosis and treatment should be planned accordingly.

Perioperative consultations of specialists from haematology or immunology may be necessary.

Particular preparation for airway management

Awake, fibre-optic intubation must be considered as the first choice. In certain cases, a laryngeal mask airway or an anaesthesia technique protecting spontaneous breathing can be considered as alternative methods. Establishment of a surgical airway must be possible in a "can't ventilate - can't intubate" condition. Nasal intubation may be followed by significant bleeding if thrombocytopenia is present. In patients with a difficult airway, awake extubation should be preferred.

Be aware of the possibility of upper airway collapse and negative pressure pulmonary oedema following extubation.

Particular preparation for transfusion or administration of blood products

Coagulation disorders (esp. thrombocytopenia) are common, should be identified early and addressed appropriately. Blood and coagulation products must be available in surgery prone to significant bleeding.

In severe cases of osteopetrosis, bone marrow transplantation is available and usually leads to a significant clinical improvement (especially haematological abnormalities).

Particular preparation for anticoagulation

In osteopetrosis, bone marrow fibrosis may lead to pancytopenia including thrombocytopenia, and an increased risk of bleeding. This has to be weighed against indications to anticoagulation.

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Particular precautions for positioning, transport or mobilisation

Skeletal stability is severely decreased. Extreme caution should be employed to prevent fractures. Contractures and deformities may be present and must be cushioned appropriately.

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

Stress dose steroids should be given to the patients who are receiving long term steroid therapy. Interferon gamma-1b can increase theophylline and digoxin levels, which should be closely monitored. Opioids suppress interferon-gamma levels!

Anaesthesiologic procedure

Certainly there are those very mildly affected patients, for which no additional steps need to be taken other than careful positioning.

However, in those more severely affected, a proper evaluation of airway and ventilation is crucial to the choice of the anaesthesiological procedure. Adherence to the difficult airway algorithm is elemental.

Blood loss rate and transfusion need should be closely monitored due to bleeding tendency.

Regional anaesthesia may not be feasible in the presence of anatomical abnormalities or bleeding disorders.

Particular or additional monitoring

Monitoring is implemented in a standard fashion (electrocardiography, non-invasive blood pressure, peripheral oxygen saturation). In cases of high-risk surgeries, major fluid shifts or advanced disease, arterial cannulation for invasive blood pressure measurement and central venous line placement are recommended. Blood loss and transfusion requirements should be closely monitored.

Possible complications

Hypognathism, narrowing of nasal passages and the oropharynx may result in upper airway collapse and negative pressure pulmonary oedema following extubation.

Even small trauma to the airway during intubation may lead to significant bleeding, and rapidly deteriorating intubation conditions.

Complications related to regional anaesthesia may occur due to anatomical and structural differences of bones. During regional anaesthesia, unintentional intraosseous injection of local anaesthetic solution may lead to a systemic toxic reaction.

Postoperative care

General considerations: Postoperative care may have to be provided in an ICU or HDU environment depending on
1. severity of phenotype
2. severity of procedure, and
3. specific risk for complications (e.g. bleeding, airway obstruction etc.).

Dysphagia is observed in many children with osteopetrosis. Nutritional support should be provided, and aspiration pneumonia should be monitored in these patients.

Upper airway deformation may lead to obstructive sleep apnea syndrome (OSAS). Post-OP care should be provided according to OSAS-Guidelines.

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

Apart from the above-mentioned complications, literature provides no further data on disease specific emergencies.

Ambulatory anaesthesia

The level of care necessary to provide safe anaesthesia for patients with osteopetrosis strongly depends on the extent to which they are clinically affected. In autosomal-dominant cases with only mild phenotypes and no systemic symptoms except susceptibility to fractures, outpatient anaesthesia can be considered in accordance with the surgical conditions.

Obstetrical anaesthesia

Female patients with an autosomal dominant form of osteopetrosis have a normal life span, and may become pregnant. Vaginal delivery may be complicated by pelvic deformation. Neuroaxial blocks may be impossible due to bleeding disorders and vertebral abnormalities. Bleeding disorders also can influence post-partum haemorrhage. However, the data related to pregnancy in patients with osteopetrosis is very limited.

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These guidelines have been prepared by:

Author
Ayse Belin Ozer, Anaesthesiologist, Firat University, Medical School, Elazig, Turkey
abelinozer@gmail.com

Peer revision 1
Miguel Farfán, Clinical Epidemiology specialist, Department of Orthopaedic Surgery, Fundación Santa Fe de Bogotá, Bogotá, Colombia
farfan4084@hotmail.com

Peer revision 2
Frédéric Lézot, Institut National de la Santé et de la Recherche Médicale, Equipe Ligue Nationale Contre le Cancer, Nantes, France
frederic.lezot@univ-nantes.fr

Editorial Revision
Johannes Prottengeier, Anaesthesiologist, Department of Anaesthesiology, University Hospital, Erlangen, Germany

Please note that this guideline has been reviewed by an anaesthesiologist and by two disease experts.

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Herausgeber

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Alexandra Hisom M.A. &
Dipl.-Sozw. Holger Sorgatz

Korrespondenzadresse: Roritzerstraße 27 | 90419 Nürnberg | Deutschland
Tel.: 0911 9337812 | Fax: 0911 3938195
E-Mail: anaesth.intensivmed@dgai-ev.de

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E-Mail: info@aktiv-druck.de

Anzeigen | Vertrieb
Pia Engelhardt
Tel.: 09522 943570 | Fax: 09522 943577
E-Mail: anzeigen@aktiv-druck.de

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Rosi Braun
PF 13 02 26 | 64242 Darmstadt
Tel.: 06151 54660 | Fax: 06151 595617
E-Mail: rbraunwerb@aol.com

Herstellung | Gestaltung
Manfred Wuttke | Stefanie Triebert
Tel.: 09522 943571 | Fax: 09522 943577
E-Mail: ai@aktiv-druck.de

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ADDRESS

German Society of Anaesthesiology and
Intensive Care Medicine
Nina Schnabel
Roritzerstrasse 27 | 90419 Nuremberg | Germany
Tel.: +49-911-9337822 | Fax: +49-911-3938195
Email: nschnabel@orphananesthesia.eu