

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 haematopoietically active bone marrow leads to pancytopenia and the re-activation of extra-medullary hematopoiesis. 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 anemia, bleeding disorders, immunodeficiency, hepatosplenomegaly, hypocalcaemia, hyperphosphataemia 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 anemia, bleeding and septicemia.

Calcitriol, steroids and interferon-gamma may be somewhat beneficial, but hematopoietic 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



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

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 mental retardation have been described as well.

Hematologic 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 as 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.

Necessary additional diagnostic procedures (preoperative)

To detect a difficult airway and compromised 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.

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 is 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. 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 anesthesia 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 hemorrhage. However, the data related to pregnancy in patients with osteopetrosis is very limited.

Literature and internet links

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