orphananesthesia

Anaesthesia recommendations for patients suffering from

Alkaptonuria

Disease name: Alkaptonuria

ICD 10: E70.2

Synonyms: Hereditary ochronosis, homogentisate dioxygenase deficiency

Alkaptonuria (AKU) is a rare autosomal recessive disorder with an incidence of 1:250 000 to 1:1000 000 live births. AKU is caused by a deficiency of the enzyme homogentisate 1,2-dioxygenase (HGO). This enzyme converts homogentisic acid (HGA) to maleylacetoacetic acid in the tyrosine degradation pathway. Accumulated HGA is rapidly cleared in the kidney and excreted in the urine. HGA blood levels are kept very low through rapid kidney clearance, but over time HGA is deposited in cartilage throughout the body and converted to a pigment-like polymer. This occurs through an enzyme-mediated reaction in collagenous tissues like ligaments, tendons, cartilage, and sclera.

Medicine in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

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Disease summary

As a result, AKU has three major features:

- Darkening of the urine upon contact with air. HGA is oxidized to form a pigment-like polymeric material responsible for the black color of standing urine, or after exposure to an alkaline agent.

- Ochronosis (bluish-black pigmentation of connective tissue). Accumulation of HGA and its oxidation products (e.g., benzoquinone acetic acid) in connective tissue leads to ochronosis

- Brown pigmentation of the sclera which does not affect vision, blue or gray discoloration and calcification of ear cartilage, possible discoloration on the skin of the hands, corresponding to underlying tendons and gray and black discoloration of cartilages in the joints.

- Arthritis. It often begins in the spine. Degenerative changes, mainly in intervertebral disks, may be seen throughout the entirety of the vertebral column, where the lumbar spine is the most commonly affected region. With progression of the disease it may cause changes resembling those of ankylosing spondylitis. Patients may complain of stiffness in their lower back with no other symptoms or signs of lumbar spine disease. The culprit of spinal abnormalities could possibly be disk space narrowing, widespread disk calcifications and mild osteophytosis with minimal calcification of the intervertebral ligaments. Radiographs of the large joints may show joint space narrowing, subchondral cysts, and infrequent osteophyte formation. Knees, hips, and shoulders are frequently affected. Fifty percent of individuals require at least one joint replacement by age 55 years.

Pigment deposition can be also seen in heart endocardium, valves, and kidneys. Therefore, patients may have valvular disease, nephrolithiasis, and other renal complications in the advanced age.
Impaired renal function can accelerate the development of arthritis and ochronosis due to inability to excrete HGA and worsen the progression of the disease. By around age 60, 50% of individuals with alkaptonuria have a history of renal stones.

Typical surgery

Hip or knee replacement, shoulder joint replacement, lumbar laminectomy, valve replacement. Any synovial joint may require arhtroplasty. Renal stone disease may require urological procedures including nephrostomy. Repair of ruptured ligaments and tendons may require a surgical approach. Any surgery required in non-Alkaptonuric patients may also be needed in AKU patients.

Type of anaesthesia

There are controversial recommendations for either general or regional anaesthesia.

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General anaesthesia may be not appropriate in case of severe valvular regurgitations. Limitation in the range of motion of the cervical spine most likely would cause certain problems with tracheal intubation. Deep sedation can provoke respiratory insufficiency in compromised patients. For unclear reasons, hypotension during and after surgery, complicates surgery including arthroplasty.

Degenerative changes of the lumbar spine would make the regional technique unsuccessful. Calcification of interspinous ligaments makes epidural approaches to anaesthesia difficult if not impossible. Caution should be kept while performing spinal anaesthesia because of the fact that the dura and arachnoid membrane can be damaged by HGA what predisposes to post-punction headaches.

Necessary additional diagnostic procedures (preoperative)

- Assessment of the mobility of the lumbar spine (ROM: Schober test) as well as cervical spine, X-ray of the lumbar spine.

- Pulmonary function tests should be done in patients with respiratory complaints which may be impaired due to ochronotic fibrosis of the costal cartilages and correspond to restrictive pulmonary diseases.

- Evaluation of the cardiovascular system is required and assessment of heart valves is crucial. Cardiovascular abnormalities such as generalized atherosclerosis, and conduction blocks may also be associated with ochronosis. Reports exist of calcification and stenosis of the aortic annulus leading to coronary artery disease, and the risk of myocardial infarction is higher than normal in older patients with ochronosis. Therefore, electrocardiogram and echocardiogram should be done in all individuals older than age 40 years.

- Impairment of renal function can manifest with frequent urinary tract infections and nephrolithiasis. Renal ultrasound examination or helical abdominal CT to evaluate for the presence of renal calculi is recommended if renal involvement is suspected.

Particular preparation for airway management

Limitation in the range of motion of the cervical spine most likely would cause certain problems with tracheal intubation. Because of strong evidence possibility of difficult airway should be taken into account.

Particular preparation for transfusion or administration of blood products

There is no special consideration for transfusion or administration of blood products in patients with alkaptonuria. However, these patients may be on long-term aspirin or NSAID therapy which may result in platelet dysfunctions, prolonged bleeding time, and gastrointestinal bleeding. Parenteral fluid administration may be needed for hypotensive complications.

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Particular preparation for anticoagulation

There is no evidence to support the need of particular anticoagulation.

Particular precautions for positioning, transport or mobilisation

Patients with alkaptonuria may have some joint and spine deformity due to cartilage destruction and thus difficulty may be faced during positioning and pressure points should be adequately padded to prevent any undue pressure on the diseased joints.

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

Not reported.

Anaesthesiologic procedure

Dosages of intravenous anaesthetics and muscle relaxants should be modified according to the existing renal dysfunction.

Neuraxial sonography can be considered with or without a real-time ultrasound-guided approach in spinal anaesthesia.

Particular or additional monitoring

Caution should be exercised in pulse oximeter monitoring of patients with excessive pigment deposition.

The deposition of HGA products in the tissues renders them resistant to the near-infrared photons, making near-infrared spectroscopy cerebral oximetry technically unfeasible. The pigmentation of the forehead, the systemic connective tissues degeneration, the pigmentation of the periosteum, or even the possibility of dura mater involvement in AKU may explain the inability of NIR spectroscopy photons to penetrate the frontal cortex.

In case of high risk surgery especially in patients with cardiac abnormalities arterial cannulation for invasive blood pressure measurement and central line placement is recommended.

Possible complications

There is a report of a 24-year-old alkaptonuric man with severe decreased kidney function who developed fatal metabolic acidosis and intravascular hemolysis. Hemolysis may have been caused by rapid and extensive accumulation of HGA and subsequent accumulation of plasma soluble melanins. Toxic effects of plasma soluble melanins, their intermediates, and reactive oxygen side products are increased when antioxidant mechanisms are overwhelmed. A decrease in serum antioxidative activity has been reported in patients with chronic decreased kidney function. However, despite administration of large doses of an antioxidant agent and ascorbic acid and intensive kidney support, hemolysis and acidosis could not be brought under control and hemolysis led to the death of the patient.

Increased predisposition to post-puncture headaches should be taken into account because the dura and arachnoid membrane are made vulnerable by HGA and could be damaged.

Hypotensive complications during and after surgery requiring general anaesthesia is frequently seen requiring agrressive fluid therapy.

Postoperative care

Failure to wean from mechanical ventilation after general anaesthesia or dispnea can develop due to stiffness of cartillage in the chest wall.

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

Disk herniation at the lumbar level is rare but it can cause symptoms resembling those in spinal anaesthetic toxicity or other post-punctural complications.

In general disease triggered emergency-like situations are not common in alkaptonuria.

Ambulatory anaesthesia

Ambulatory anaesthesia can be performed according to common guidelines in patients without severe cardiac, respiratory and renal abnormalities.

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Obstetrical anaesthesia

Obstetrical anaesthesia can be performed according to common guidelines in patients without severe cardiac, respiratory and renal abnormalities.

Literature and internet links

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