

Anaesthesia recommendations for patients suffering from **Lowe syndrome**

Disease name: Lowe syndrome

ICD 10: E72.03

Synonyms: OCRL, oculo-cerebro-renal syndrome, oculo-cerebro-renal syndrome of Lowe, Lowe-Terrey-MacLachan syndrome

Oculocerebrorenal syndrome of Lowe (OCRL) is an X-linked disorder (Xq25-q26), first described by Lowe, Terrey, and MacLachan in 1952. The estimated prevalence is 1 in 500,000 patients and caused by a defect of the enzyme phosphatidylinositol 4,5-biphosphate 5-phosphatase. This leads to accumulation of phosphatidylinositol 4,5-biphosphate in multiple subcellular compartments. Enzyme deficiency may impair membrane and endosomal trafficking, actin dynamics, cell adhesion, cell motility and cell polarization. Renal involvement of OCRL comprises tubular dysfunction characterized by proteinuria and the renal Fanconi syndrome, manifesting as renal tubular acidosis, loss of potassium, phosphate and aminoacids. The renal manifestations become apparent in the first months of life, kidney function declines progressively with end-stage renal disease mostly in the fourth decade. Bilateral cataracts are present at birth and are associated with glaucoma in approximately half of the affected males, often resulting in progressive visual loss. Global hypotonia and areflexia is also noted soon after birth, and patients exhibit mental retardation (median IQ 45), stereotypic behaviour and temper tantrums, and seizure disorder. Patients have typical faces characterized by large forehead, sunken eyes, large, poorly shaped ears, and sometimes retrognathism. These children may require anaesthesia for different operations such as ocular surgery, orthopaedic procedures, orchidopexy or gastrostomy. The main anaesthetic concerns in these patients are difficult airway, muscular weakness, electrolyte and acid base imbalance.

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

Typical surgery

Ocular surgery (cataract, glaucoma, strabismus); orthopaedic procedures; orchidopexy or gastrostomy; sedation for diagnostic procedures.

Type of anaesthesia

There is no definitive contraindication for either general or regional anaesthesia.

Total intravenous anaesthesia or inhalation anaesthesia can both be used without preference.

As most of the surgical procedures occur in childhood, general anaesthesia is more suitable in most cases, although regional or local anaesthesia can be performed without restriction.

Necessary additional diagnostic procedures (preoperative)

Assessment of renal function, electrolytes and blood gas analysis is recommended. Note that kidney function is overestimated when using serum creatinine as patients have abnormal muscle mass. Consider measuring serum cystatin C as an alternative marker of kidney function. Abnormalities in serum electrolytes or renal acidosis should be corrected before proceeding to surgery.

Neurological consultation may be planned for seizures, which are observed in ca. 50% of Lowe patients. They may have myoclonic, generalised tonic-clonic seizures, infantile spasms, and partial complex seizures. Magnetic resonance imaging may show a mild ventriculomegaly and multiple periventricular cystic lesions.

Particular preparation for airway management

Retrognathism, craniofacial abnormalities and abnormal teeth structure that occur by hypophosphatemic rickets make direct laryngoscopy and tracheal intubation difficult.

Particular preparation for transfusion or administration of blood products

There is impaired early activation of platelets, i.e. platelet adhesion and shape change caused by disturbed Rho-A dependent signalling in ORCL-1 deficiency which may manifest as a bleeding disorder. This defect is only detected using the PFA-100 platelet function analyser, while aPTT, PT and other platelet aggregation tests are normal.

Mild thrombocytopenia can be in around 20% patients. Tranexamic acid has been observed to increase platelet function in these patients. As they have metabolic acidosis erythrocyte suspensions must be used carefully.

Particular preparation for anticoagulation

There is no evidence to support anticoagulation. Heparin anticoagulation can be used for haemodialysis.

Particular precautions for positioning, transport or mobilisation

Osteopenia from chronic acidosis or hypophosphatemic rickets causes fragility of bone structures, which requires attention while positioning.

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

Not reported.

Anaesthesiologic procedure

The most important point of anaesthetic management of these patients may be metabolic acidosis. In the presence of acidosis, any agent that rapidly decreases the sympathetic tone may potentiate circulatory depression. Since most opioids are weak bases, acidosis can increase the fraction of the drug in the non-ionized form and facilitate penetration of the opioid into the brain, causing increased sedation and depression of airway reflexes, possibly predisposing to pulmonary aspiration.

Careful titration of perioperative IV fluids to prevent hyperhydration or dehydration is mandatory. Ophthalmic beta blockade may lead some systemic effects following local resorption.

Sevoflurane induction may cause hypokalaemia-induced seizures.

Be prepared for managing difficult airway situation.

Muscle relaxants should be reduced by 25-50% because of increased sensitivity.

Hyperventilation should be avoided to prevent alkalosis followed by decrease in Serum potassium levels, because it can lead to severe cardiac arrhythmias.

Because these patients have risk of glaucoma, direct pressure on the eye from face mask and poor prone positioning must be avoided.

Propofol and a non-depolarizing neuromuscular blocking agent are suitable for induction.

Particular or additional monitoring

There is no report for additional monitoring other than standard monitoring.

Possible complications

There is a potential risk for pneumonia due to muscular hypotonia.

Sedative premedication can mask hypoglycaemic symptoms.

Hypokalaemia can cause serious cardiac arrhythmia.

These patients have risk of acute glaucoma.

Postoperative care

Electrolyte abnormalities, metabolic acidosis must be optimized during hospitalization. Antiepileptic drug therapy must be regulated carefully.

These patients have a tendency to develop pneumonia due to hypotonia and poor cough reflex. Postoperative monitoring of blood sugar and supplemental glucose-containing fluids, along with potassium supplements must be used to prevent episodes of hypoglycaemia.

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 diseases, e.g.:

Not available

Ambulatory anaesthesia

Ambulatory anaesthesia should only be done in case of low-risk surgery and if the patient is in a stable condition. Physical and systemic evaluation should reveal no severe impairment.

Obstetrical anaesthesia

This syndrome exclusively affects males. Therefore there is no report about obstetrical courses.

Literature and internet-links

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4. Pandey R, Garg R, Chakravarty C, Darlong V, Punj J, Chandralekha. Lowe's syndrome with Fanconi syndrome for ocular surgery: perioperative anesthetic considerations. *J Clin Anesth* 2010 Dec;22(8):635-7. doi: 10.1016/j.jclinane.2009.09.018
5. Saricaoglu F, Demirtas F, Aypar U. Preoperative and perioperative management of a patient with Lowe syndrome diagnosed to have Fanconi's syndrome. *Paediatr Anaesth* 2004 Jun;14(6):530-2
6. <https://ghr.nlm.nih.gov/condition/lowe-syndrome>
7. <http://rarediseases.org/rare-diseases/lowe-syndrome>
8. <http://lowesyndrome.org>

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This guideline has been prepared by:

Author

Fatma Saricaoglu, Department of Anaesthesiology and Reanimation, Hacettepe University, Ankara, Turkey
fatmasaricao@yahoo.com

Peer revision 1

Arend Bökenkamp, Department of Pediatric Nephrology, VU University Medical Center Amsterdam, The Netherlands
a.bokenkamp@vumc.nl

Peer revision 2

Richard Alan Lewis, Departments of Ophthalmology, Medicine, Pediatrics, and Molecular and Human Genetics, Baylor College of Medicine, Houston, Texas, USA
rlewis@bcm.tmc.edu

Please note that this guideline has not been reviewed by two anaesthesiologists but by two disease experts.
