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Von Willebrand disease
Walker-Warburg syndrome

orphan**a**nesthesia

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

SUPPLEMENT NR. 6 | 2019

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 OrphanAnesthesia 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 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 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.

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orphan^aesthesia

Anaesthesia recommendations for Walker-Warburg syndrome

Disease name: Walker-Warburg syndrome

ICD 10: Q04.3

Synonyms: Warburg syndrome, HARD (hydrocephalus, agyria, retinal dysplasia) or HARDE (E for encephalocele) syndrome, Chemke syndrome, Cerebro-ocular dysplasia-muscular dystrophy syndrome, cerebro-ocular dysgenesis, Pagon syndrome.

Muscle Eye Brain disease shares many characteristics with Walker-Warburg syndrome and has sometimes been used as synonym. However, most authors consider the two entities as different syndromes. Lissencephaly type II is also sometimes used as synonym, but is actually a broader term applying also to other similar syndromes with cobblestone lissencephaly.

Disease summary: Walker-Warburg syndrome (WWS) is a rare autosomal recessive disorder, with an estimated incidence of around 1–2/100,000 live births. In about one third of the cases, Walker-Warburg syndrome is due to defects in genes encoding the protein O-mannosyltransferases (POMT 1 or 2), or mutations in fukutin or fukutin-related protein (FKRP), which all have a role in regulating the interaction between the cytoskeleton and the extracellular matrix in neurons and muscle cells. The syndrome is characterised by the triad of muscular dystrophy, brain anomalies and eye anomalies. In fact, WWS is considered to be the most severe form of congenital muscular dystrophy (CMD). Brain abnormalities typically include cobblestone lissencephaly and cerebellar malformations, but hydrocephalus, Dandy-Walker malformation and encephaloceles are also regularly described. Eye abnormalities are commonly retinal and anterior chamber malformations, and glaucoma, cataract, microphthalmia and colobomas are occasionally reported. Facial and oropharyngeal malformations, including micrognathia, small mouth opening, cleft lip and cleft palate, have regularly been reported and may lead to difficulties in airway management. Other features such as urogenital malformations (e.g., hydronephrosis, cystic kidneys, genital anomalies), ventricular septal defect, cardiomyopathy, microtia, absent auditory canals, imperforate anus or hypothyroidism have incidentally been described. Patients may be at increased risk for central and obstructive apnoea, seizures and delayed gastric emptying.

A specific therapy is not available. Surgical interventions are commonly required for the treatment of hydrocephalus or to restore malformations. Affected patients typically die before the age of 3 years of respiratory failure and pneumonia.

Medicine 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

Ventriculoperitoneal shunt, encephalocele repair, ventriculostomy, cleft lip repair, cleft palate repair.

Type of anaesthesia

The typical surgical procedures usually require general anaesthesia. The recommended procedure including requirements for premedication and preoperative fasting, induction and maintenance of anaesthesia as well as postoperative considerations are described below.

No reports of regional or local anaesthesia have been described in literature. Based on the available information on WWS, there is no reason to assume that such techniques are generally contraindicated. Neuraxial anaesthesia should be avoided in patients with untreated hydrocephalus. Since the pain is difficult to measure because of the severe mental retardation, and opioids should be avoided, regional anaesthesia – especially peripheral blocks – may be an attractive option for postoperative pain therapy.

Necessary additional preoperative testing (beside standard care)

Patients with typical WWS present with a triad of muscle-, brain- and eye abnormalities as described above. However, the clinical presentation is heterogeneous and facultative features can pose unique challenges in the perioperative period. Preoperative assessment should be aimed at identifying such pathology to allow for meticulous planning of the anaesthesia procedure. In particular, patients should be carefully assessed for facial and oropharyngeal malformations which may impede with mask ventilation and tracheal intubation. Cardiac features such as cardiomyopathy or ventricular septal defects should not be overlooked during preoperative assessment. While there is limited evidence for routine laboratory or radiologic tests, they may be considered in order to identify additional pathology, such as renal impairment. Serum creatine kinase levels are typically elevated in patients with Walker-Warburg syndrome due to muscular dystrophy. In case of an undiagnosed but suspected myopathy, a preoperative lactate and creatine kinase measurement may be crucial.

Particular preparation for airway management

Patients with WWS are at risk for difficult airway management when facial or oropharyngeal malformations are present. Specialised equipment, experienced personnel (e.g., paediatric anaesthesiologist; paediatric ENT surgeon) and back-up plans should be available and prepared according to local protocols and well-established difficult airway algorithms. Specialised equipment should include alternative airway devices, such as different blade types and sizes, supraglottic airway devices, videolaryngoscopy and equipment for fiberoptic intubation. An induction technique that preserves spontaneous ventilation until adequacy of mask ventilation is assured may be advantageous. Fiberoptic intubation via face mask or laryngeal mask may be considered. However, in cases of untreated hydrocephalus, hypercapnia during induction and airway management should be avoided.

Particular preparation for transfusion or administration of blood products

There is no evidence for a higher requirement for blood products in patients with WWS. Common surgical procedures in these patients are usually not associated with an excessive blood loss. However, the pathomechanism of the muscular dystrophy involves the inhibited integration of dystrophin in the cell membrane as in Duchenne muscular dystrophy, and patients with Duchenne muscular dystrophy are known to have increased intraoperative blood losses. Therefore, especially before major surgery, one should be prepared for greater blood losses than in healthy children.

Particular preparation for anticoagulation

There is no evidence for an increased incidence of coagulation disorders or a particular need for anticoagulation in patients with WWS. However, since enhanced coagulation and fibrinolysis have been demonstrated in other muscular dystrophies secondary to muscle degeneration, this may be considered in patients with WWS undergoing major surgery.

Particular precautions for positioning, transportation and mobilisation

Literature reports no particular precautions for positioning, transportation or mobilisation. However, due to muscle dystrophy, muscle weakness and hypotonia, extra cautious care is important. As patients may have skull defects and encephaloceles, particular care should be taken to avoid accidental pressure to brain tissue.

Interactions between of chronic disease and anaesthesia medications

Typical long-term medication has not been reported for patients with WWS.

Anaesthetic procedure

Due to an increased risk for central and obstructive apnoea, as well as diminished lung function secondary to muscular dystrophy, it may be safest to avoid sedative premedication.

It is unclear whether standard approaches to preoperative fasting need to be modified for patients with WWS. Generally, patients with severe mental retardation and hydrocephalus have an increased risk of delayed gastric emptying and an increased risk for pulmonary aspiration of gastric contents. On the other hand, prolonged fasting times are associated with a risk of hypoglycaemia and hypovolaemia in neonates. Patients should be monitored for signs of gastric retention and gastroesophageal reflux, and fasting requirements and risk for aspiration should be individually determined. A preoperative ultrasound of the gastric antrum provides useful information to determine the preoperative gastric content. If a prolonged fasting time is deemed necessary, it may be appropriate to supplement intravenous fluids and glucose.

An association between congenital muscular dystrophy (CMD) and malignant hyperthermia (MH) has only been proven for central core disease and King-Denborough syndrome.

However, patients with muscular dystrophy who are exposed to volatile anaesthetics may develop disease-related cardiac complications or – very rarely – massive rhabdomyolysis resembling malignant hyperthermia. Therefore, volatile anaesthetics should be used with caution and after individual risk-benefit analysis. In contrast, succinylcholine administration in patients with muscular dystrophy is associated with life-threatening hyperkalaemia and must be avoided in patients with WWS. Opiates and non-depolarising muscular blocking agents should be used cautiously, because the patients are at increased risk of postoperative respiratory depression and complications. Therefore, neuromuscular monitoring (train-of-four) should be used in all patients receiving non-depolarising neuromuscular blocking agents.

A difficult airway should be anticipated at induction of anaesthesia, see above for more details.

Intraoperative management should aim to maintain adequate oxygenation and haemodynamic stability, particularly to preserve cerebral perfusion and oxygenation in patients with hydrocephalus who are at risk for increased intracranial pressures (ICP). To avoid any further increases in ICP by coughing on the endotracheal tube, it may be necessary to use neuromuscular blocking agents. Ventilation should target at normocapnia to avoid increases in ICP by hypercapnic cerebral vasodilation. Adequate haemodynamics and volume status might also aid to avoid postoperative renal complications.

Particular or additional monitoring

Standard perioperative monitoring, including pulse oximetry, ECG, non-invasive blood pressure, capnography, temperature and TOF monitoring, is usually sufficient. Additional invasive monitoring may be considered when cardiac comorbidity (e.g., cardiomyopathy) is present, when excessive surgery is planned, or for the management of perioperative complications (e.g., rhabdomyolysis).

Possible complications

Difficulties in airway management may cause severe hypoxia. An increased risk for aspiration of gastric contents has been suggested, however, there is only very limited evidence for this.

Succinylcholine should never be used in patients with diagnosed or suspected WWS due to the risk of life-threatening hyperkalaemia. Volatile anaesthetics should only be used after careful consideration of the risk-benefit ratio.

Increases in intracranial pressure may compromise cerebral perfusion and oxygenation. Patients with encephalocele under anaesthesia should be positioned very carefully in order to avoid pressure on the encephalocele and thereby further increasing intracerebral pressure.

Patients may be at increased risk for seizures, especially if their anti-epileptic medication cannot be continued perioperatively.

Patients are at increased risk for respiratory complications due to muscle weakness as well as central or obstructive apnoea, especially in the postoperative period or when sedative drugs or opioids are administered.

An increased risk of renal failure in the postoperative period has been described and should especially be anticipated in patients with urogenital malformations or pre-existent renal impairment.

Post-operative care

It is crucial to ensure that the effects of neuromuscular blocking agents are completely abolished before extubation. Patients with WWS should be transferred to a postoperative care unit capable of providing advanced paediatric life support. Postoperative pain therapy should use opioids restrictively in order to avoid respiratory depression or respiratory complications. Therefore, a multimodal pain therapy including regional anaesthesia and avoiding opioids is desirable. Patients are at risk of developing postoperative respiratory or renal complications and should be monitored accordingly.

Disease-related acute problems and effect on anaesthesia and recovery

Acute emergencies may arise from “cannot-ventilate cannot-intubate situations”. See <https://www.das.uk.com/guidelines/paediatric-difficult-airway-guidelines>

Acute life-threatening hyperkalaemia and rhabdomyolysis have been described after the use of succinylcholine.

When volatile anaesthetics are used over a long time in patients with severe myopathy a high grade of suspicion of rhabdomyolysis is warranted.

Ambulatory anaesthesia

There are no reports of ambulatory anaesthesia in literature. Given potential problems that may occur in the postoperative period, we suggest that children with WWS should be admitted for inpatient care.

Obstetrical anaesthesia

Patients with Walker-Warburg syndrome typically die before the age of 3 years, hence, there have been no reports about pregnant patients.

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