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Lujan-Fryns syndrome

McArdle Disease

orphanaesthesia

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

SUPPLEMENT NR. 21 | 2020

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:

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OrphanAnesthesia –

a 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.

Find a survey of the recommendations published until now on:

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Anaesthesia recommendations for

McArdle Disease

Disease name: McArdle Disease

ICD 10: E74.04

Synonyms: Glycogen storage disease type 5, GSD type 5, GSDV, glycogenosis type V, myophosphorylase deficiency, McArdle disease, muscle glycogen phosphorylase deficiency

Disease summary: McArdle disease (GSD V) is a rare skeletal myopathy secondary to a disorder of carbohydrate metabolism. It is an autosomal recessive condition with an incidence of approximately 1 in 100,000 and is caused by the absence of muscle glycogen phosphorylase (myophosphorylase). Clinical features include exercise intolerance which consists of acute crisis of early fatigue and muscle stiffness and contractures, especially at the start of the exercise, that usually disappear if exercise is stopped or the intensity is reduced. These episodes are sometimes accompanied by rhabdomyolysis and myoglobinuria (dark urine).

GSD V was described in 1951 by Brian McArdle.

GSD V is caused by pathogenic mutations in the *Pygm* gene (chromosome 11q13) which encodes the muscle glycogen phosphorylase enzyme (GP-M) (myophosphorylase). It is an autosomal recessive disorder with an estimated prevalence of 1/100,000 with both sexes similarly affected. GP-M catalyses and regulates the breakdown of glycogen into glucose-1-phosphate in muscle fibres [1]. Almost all patients have no detectable myophosphorylase activity, thus they are unable to obtain energy from their muscle glycogen stores and, as a result, commonly experience exercise intolerance [2]. A positive family history can be identified in 50% of patients [3], and the most common mutation in the *Pygm* gene in Caucasians is the p.R50X [4].

The majority of patients (50%) are identified between the ages of 10-30 years with less than 4% of cases diagnosed before 10 years. The true incidence of the disease is unknown due to the benign character of the disease and the resulting missed or late diagnosis.

The diagnosis is based on clinical findings, and supportive laboratory findings of a low or absent myophosphorylase activity on histochemical or biochemical examination of a muscle biopsy and subsequent genetic testing. The absence of increased lactate during exercise and a raised creatine kinase are also features [5].

Although no specific treatment for the enzyme deficiency is available, affected individuals benefit from a number of therapeutic options which have been shown to reduce symptoms or to enhance the ability for physical activity, moderate aerobic training to increase cardiorespiratory fitness and muscle oxidative capacity [5]. Pre-exercise ingestion of sports drinks containing simple carbohydrates improves exercise tolerance and may protect against exercise-induced rhabdomyolysis [6]. There are a number of case reports suggesting a benefit with beta-2-sympathomimetics, vitamin B6 and coenzyme Q10 [7-8]. However,

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Phoenix et al. reported no significant beneficial effects with Vitamin B6 [9]. The best intervention to do for McArdle patients is appropriate exercise habits. For example, after gradual, supervised training, a 38-year-old patient (with no myophosphorylase activity) could run regularly and cover 10 km in 60 minutes with no rhabdomyolysis. The average time for recreational runners to complete a 10 km race generally falls between 75–80 minutes.

The prognosis is good. Fixed muscle weakness occurs in approximately 25% of affected individuals, is more likely to involve proximal muscles, and is more common in individuals of advanced age [8]. There are a small number of case reports of generalised weakness after birth with death occurring in childhood [8]. There are no reports of limitations of life due to cardio-circulatory disease. About 50% of affected individuals have recurrent episodes of myoglobinuria, and 27% of patients have acute renal failure after strenuous exercise [2]. Patients do need to learn how to cope with the disease and how to avoid major muscle damage, which can result in acute rhabdomyolysis and renal failure.

Medicine is 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

There is no typical surgery, unlike in patients suffering from other glycogen storage disorders.

Type of anaesthesia

Anaesthesia for individuals with GSD V should be undertaken with care and precaution. There is weak support in the scientific literature for a connection between GSD V and MH. Until it has been proven that a positive in-vitro contracture test in GSD V is nonspecific and there is no risk of MH, all patients with GSD V may be at risk of developing MH or MH-like syndromes. It remains wise to avoid MH trigger substances as much as possible [10].

In principle, all types of anaesthesia can be used (i.e. regional and general anaesthesia as well as a combination of both). Preference is given to local or regional techniques but if general anaesthesia is performed, all MH trigger substances must be strictly avoided.

- Depolarising muscle relaxants of the succinylcholine type
- All volatile anaesthetics including halothane, enflurane, isoflurane, sevoflurane and desflurane

Necessary additional pre-operative testing (beside standard care)

Prior to planned surgery, creatine kinase, lactate dehydrogenase, transaminases, and creatinine should be taken and monitored post-operatively for 24 hours.

Routine bloods such as a full blood count, coagulation studies, blood chemistry and blood crossmatch should be taken when indicated and according to the standard requirements of the surgical procedure.

Diagnostic investigations for patients under investigation for GSD V include: routine biochemistry including serum CK (creatine kinase), urate, carnitine and acyl carnitine; screening DNA blood test to look for hot spot mutations; electromyography (EMG) for patients for whom the diagnosis is not confirmed to rule out other disorders, and muscle and skin biopsy.

Particular preparation for airway management

A difficult airway is not a classic feature of GSD V.

Particular preparation for transfusion or administration of blood products

Standard management.

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Particular preparation for anticoagulation

Standard management.

Particular precautions for positioning, transportation and mobilisation

Tourniquets should be avoided in GSD V as they can cause muscle damage [12].

Interactions of chronic disease and anaesthesia medications

Standard management.

Anaesthetic procedure

Children with GSD V should be anaesthetised after a thorough peri-operative assessment, careful consideration as to the necessity of the surgical procedure and a frank discussion with the family regarding the risks of anaesthesia and the options available to them.

In general, patients with GSD V are at risk of developing specific peri-operative complications; hypoglycaemia, rhabdomyolysis, myoglobinuria, acute renal failure, post-operative fatigue and possibly malignant hyperthermia (MH). Identification of patients at risk for malignant hyperthermia is the first step for safe peri-operative management. Patients reporting an MH event or complications during anaesthesia should be referred to an MH Investigation Centre for further diagnosis, if possible. For safety reasons, patients who decline MH testing should be treated as though at risk.

Management of the glycogen storage diseases involves maintaining an adequate blood glucose level and supplementing the muscle with alternate energy sources. In infants, this usually involves regular daytime snacking and nocturnal intragastric glucose feeds or uncooked cornstarch in older children.

The anaesthesia machine must be flushed free of volatile anaesthetics prior to anaesthesia, as recommended in the guidelines from the European MH Group (EMHG) and the MH Association of the United States (MHAUS). All parts of the anaesthesia machine that might have been in contact with volatile anaesthetics must be exchanged and the gas circuit washed with a fresh gas flow of 10l/min for at least 10 minutes. Newer anaesthetic workstations may require significantly more time for purging the machine. The use of an inline charcoal filter apparatus will also reduce volatile gas concentrations to very low levels.

The vaporiser should be removed from the anaesthetic machine in order to avoid an accidental administration of volatile anaesthetics. Nitrous oxide is safe in patients who are thought to be susceptible to MH. In susceptible pigs, administration of xenon did not trigger MH, however, studies in humans are lacking.

Premedication can be administered as usual (i.e. benzodiazepines), but prophylactic administration of dantrolene is obsolete. Intravenous anaesthetic agents, such as barbiturates, propofol, etomidate are safe to use both for induction and maintenance of anaesthesia. All opioids are safe for use including morphine, remifentanil, alfentanil, fentanyl.

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Avoid suxamethonium in all patients with myopathy due to the risk of hyperkalaemia and MH.

Dantrolene must be immediately available in the unlikely event of MH.

Termination of anaesthesia should be carried out in a routine environment. Administration of antagonists such as neostigmine or naloxone is possible, if required.

Particular or additional monitoring

Standard monitoring of vital signs should be performed in all types of anaesthesia including sedation. Monitoring should follow the usual standard and at least comprise ECG, blood pressure, pulse oximetry and continuous measurement of body temperature as well as capnography in ventilated patients.

Possible complications

Patients will be at risk of MH if trigger substances are administered. Therefore, all trigger substances must be strictly avoided.

MH is characterised by hypermetabolism due to overflooding of the myoplasm with calcium. Clinical signs include: Tachycardia, hypercapnia, hypoxaemia, muscle rigidity and masseter muscle spasm, hyperthermia, rhabdomyolysis and metabolic as well as respiratory acidosis.

Hypermetabolism-induced disturbances of permeability in skeletal muscle cells may cause elevated Ca^{2+} levels and K^{+} levels, which may lead to severe cardiac arrhythmias. Blood analyses might reveal elevated concentrations of creatine phosphokinase (CK) although CK levels only start to increase 2–4 hours after the onset of MH, reaching a maximum after 24–36 hours. In case of severe injury of skeletal muscle cells, myoglobin can be detected in blood and urine. Delayed therapeutic intervention may be lethal resulting in bradycardia or cardiac arrest.

Rhabdomyolysis and myoglobinuria may lead to acute renal failure.

Post-operative care

Standard ward post-operative care, but consider 24-hour post-operative supervision in an intensive care unit if there are any concerns [10].

Disease-related acute problems and effect on anaesthesia and recovery

In the event of cardiac and/or respiratory compromise or arrest, standard national paediatric resuscitation guidelines should be applied to children with GSD V.

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Ambulatory anaesthesia

Standard guidelines.

Obstetrical anaesthesia

As patients with GSD V have a normal fertility, pregnancies are possible and have been described. A prenatal diagnosis is possible. For delivery, Caesarean sections and vaginal delivery are possible. Regional anaesthesia is recommended [13-15].

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Please note that this recommendation has been reviewed not by an anaesthesiologist and a disease expert but by two disease experts instead.

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