orphanaesthesia

Anaesthesia recommendations for

Andersen disease

Disease name: Andersen Disease (GSD IV)

ICD 10: E74.09

Synonyms: Adult polyglucosan body disease, Amylopectinosis, Andersen disease, Andersen glycogenosis, brancher deficiency, branching enzyme deficiency, glycogen branching enzyme deficiency, glycogenosis type IV, glycogen storage disease IV, glycogen storage disease type 4, glycogenosis 4, glycogenosis type IV, GSD IV, GSD type IV, GSD4, type IV glycogenosis

Disease summary: Andersen disease (GSD IV) is a rare genetic disorder of glycogen metabolism. It is caused by the deficient activity of the glycogen-branching enzyme, resulting in accumulation of abnormal glycogen in the liver, muscle, and/or other tissues. The disease is inherited as an autosomal recessive trait. Clinically, the symptoms and findings become evident in the first months of life. Such features typically include failure to thrive and hepatosplenomegaly. In such cases, the disease course is typically characterized by progressive cirrhosis and liver failure, leading to potentially life-threatening complications. In addition, several neuromuscular variants of GSD IV have been described that may be evident at birth, in late childhood, or in adulthood.

GSD IV was named after the principal investigator Dorothy Andersen who first described the disease in 1956.

GSD IV is a disorder of glycogen metabolism. Glycogen is a complex carbohydrate stored in cells of the body which is converted into glucose for use as energy. GSD IV is characterized by the deficient activity of the glycogen-branching enzyme (GBE1) which normally increases the number of branch points during the formation of glycogen. In most cases, deficient GBE1 activity leads to a generalized accumulation of the structurally abnormal glycogen. GBE1 is located at chromosome 3p14 and encodes for a 702 amino-acid protein [1-2]. Various specific mutations of the GBE gene have been identified including the classic hepatic form, those with non-progressive liver disease, and newborns with the severe neuromuscular form. GSD IV accounts for 3/1000 of all glycogen storage diseases and 1 in 760’000 live births. GSD IV is inherited as an autosomal recessive trait. All individuals carry 4-5 abnormal genes [3-4].

GSD IV may vary in age at onset, symptoms and signs, degree of abnormal glycogen accumulation and specific organs affected. The most common, classic form of the disease is typically characterized by progressive cirrhosis to liver failure. In such cases, the disease typically becomes evident during infancy or up to about 18 months of age. Symptoms and signs commonly include failure to thrive and hepatosplenomegaly. In the majority of individuals with classic GSD IV, progressive liver disease may lead to liver transplantation or

potentially life-threatening complications by roughly five years of age. However, there are rare cases reports of individuals having a non-progressive liver disease [5-7].

Several neuromuscular variants of GSD IV have also been described in the medical literature. There may be isolated muscle involvement beginning in late childhood, with myopathy and/or cardiomyopathy. Accumulation of the abnormal glycogen in a skeletal muscle may lead to muscle weakness and reduced exercise tolerance, and muscular atrophy. Those with cardiac involvement develop a dilated cardiomyopathy; symptoms may include fatigue, feeding difficulties, failure to thrive; shortness of breath with exertion and eventually at rest [2].

A fatal perinatal neuromuscular variant has been reported. This form may be characterized by hydrops, hypotonia, muscle atrophy and contractures, with neurologic involvement, leading to death usually in the neonatal period [9-11].

In addition, a rare neuromuscular variant has also been described in adults. This form of the disease, so-called adult polyglucosan body disease, may be characterized by dysfunction of the central and peripheral nervous systems. Individuals develop progressive muscle weakness, gait disturbances, mild cognitive impairment or dementia. [12]

GSD IV is usually diagnosed during infancy or childhood or, in some rare cases, in adult-hood. Biopsy may demonstrate an abnormal deposition of amylopectin-like materials. However, testing to confirm the diagnosis requires detection of deficient GBE activity via indirect enzyme assay [13-14].

The treatment of GSD IV is directed toward the specific symptoms that are apparent in each individual. Specific therapies are symptomatic and supportive and may include long-term management of cirrhosis and impaired liver function; neuromuscular disease; and/or cardiac failure. In individuals with progressive liver failure, liver transplantation has been conducted and may be effective in some cases. According to reports in the medical literature, following transplantation, some patients may develop progressive accumulation of abnormal glycogen in other organs, such as the heart, leading to potentially life-threatening complications. However, reports indicate that most patients have not had neuromuscular or heart complications, over follow-up periods of up to 13 years. In some of these patients, accumulations of glycogen in the heart and skeletal muscle have appeared to diminish following transplantation [7-8].

Genetic counselling will be of benefit for affected individuals and family members. Other treatment for this disorder is symptomatic and supportive.

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

Typical surgery

There are a number of published case series of paediatric liver transplantations performed for GSD IV between 1984 and 1999 with variable success. Liver transplantation for GSD IV is recognised but consideration needs to be taken of the extra-hepatic symptoms and burden of disease [5-7] No comment is made in the papers to either anaesthetic or intensive care management.

Type of anaesthesia

Anaesthesia for individuals with GSD IV should be undertaken with care and precaution. Anaesthesia should ideally be undertaken in a specialist institution that has experience in the management of these children and adequate intensive care backup.

In principle, all types of anaesthesia can be used (i.e. regional and general as well as a combination of both).

Necessary additional pre-operative testing (beside standard care)

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

Diagnostic investigation and evaluation typically includes various studies to help detect and characterize certain abnormalities associated with GSD IV and include: laboratory studies, specialized imaging e.g. abdominal ultrasound (USS), CT and MRI scanning, electro-myography studies and echocardiography to assess cardiac structure and function.

Particular preparation for airway management

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

Particular preparation for transfusion or administration of blood products

The classic form of the disease is typically characterized by progressive cirrhosis to liver failure with disease typically evident in early infancy up to about 18 months of age. They are therefore at risk of bleeding due to impaired liver function [5-7]. Careful pre-operative evaluation should be performed and planning undertaken into the preparation for transfusion and administration of blood products and consent taken from families. Discussion with haematology should be undertaken where indicated for support and advice.

Particular preparation for anticoagulation

Standard management.

Particular precautions for positioning, transportation and mobilisation

Standard management.

Interactions of chronic disease and anaesthesia medications

Standard management.

Anaesthetic procedure

There are no specific anaesthetic case reports or anaesthetic reviews of children with GSD IV. The only case report is mistitled GSD IV but is with regard to GSD IX [15].

Children with GSD IV should be anaesthetised after a thorough perioperative 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.

With limited published data on children with GSD IV undergoing anaesthesia, the anaesthetic recommendations are based upon the authors' perceived best practice.

Dependent on the degree of organ involvement found at the perioperative assessment, it may be necessary to have two anaesthetists to be present, preferably with experience of children with GSD IV. The child should be fully monitored prior to induction. The period of preoperative fasting should be minimised and peri-operative maintenance fluids commenced as soon as possible to avoid dehydration and hypoglycaemia. Blood sugars should be monitored and appropriate fluid replacement commenced.

The most common, classic form of GSD IV is characterized by progressive cirrhosis. An evaluation by a hepatologist may be warranted and a review of liver function tests should be undertaken along with coagulation studies for procedures [2].

Reports in the medical literature of patients developing progressive accumulation of abnormal glycogen in other organs such as the heart suggest that all children with GSD IV who present for anaesthesia should have a thorough cardiac assessment [2, 7-8]. This should include an electrocardiogram (ECG), a recent echocardiogram (ECHO), and where indicated a review by a paediatric cardiologist. This information will help to direct decisions to pursue regional anaesthesia over general anaesthesia and guide an open discussion about the risks of anaesthesia with the child's family.

The rare neuromuscular variant of GSD IV patients characterized by dysfunction of the central and peripheral nervous systems should be reviewed with careful pre-operative evaluation on status and documentation of neurological deficits. Discussion and counselling should include the risk of deterioration of clinical status, potential need for postoperative respiratory support, and weigh the risks and benefits of regional and general anaesthesia [12].

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

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

Post-operative care

Attentive care of the patient with GSD IV must continue into the post-operative period. Children with significant organ involvement including cardiac must be fully monitored with oxygen saturations, ECG and blood pressure in an intensive care or high dependency setting for an appropriate period of time after the surgery.

Standard ward post-operative care may be appropriate in some cases but consider 24-hour postoperative supervision in an intensive care unit if there are any concerns.

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 apply to children with GSD IV.

Ambulatory anaesthesia

Due to the complexity of GSD IV, ambulatory care is not recommended as part of routine care apart. Inpatient admission and management is suggested as best practice.

Obstetrical anaesthesia

There are no case reports or reviews in the literature of obstetric anaesthesia in patients with a diagnosis of GSD IV. In the past, many children with GSD IV may have not survived to adulthood. Case reports in the literature of adults with myopathy (central and peripheral) suggests the need for consultant obstetric review and careful planning for delivery in conjunction with anaesthesia. The myopathy should be documented and discussion had with the patient with regard to vaginal delivery and the risk of central neuroaxial blockade to the patient [2.]

Perioperative assessment should involve routine bloods including full blood count, coagulation studies, blood chemistry including liver function and crossmatch as a baseline and further investigations dependent on clinical examination and findings as in paediatrics. If

liver dysfunction is present, it may be pertinent to consider whether spinal/epidural anaesthesia is appropriate. Perioperatively, the risk of bleeding may be higher if liver dysfunction is present, and this should be planned for and discussions had with hepatologists and haematologists to ensure best care.

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Please note that this recommendations was not reviewed by an anaethesiologist and a different disease expert, but by anaesthesiologists only.