orphanaesthesia

Anaesthesia recommendations for

Donohue syndrome

Disease name: Donohue syndrome

ICD 10: E34.8

Synonyms: Leprechaunism

Disease summary: Donohue syndrome is a rare autosomal recessive disorder with an incidence of 1 in 4 million live births [1,2] caused by mutations of the insulin receptor gene on chromosome 19p13 [3]. It was initially termed 'dysendocrinism' and 'leprechaunism' (owing to elf-like features of those affected) [4]; these terms have since been discarded in favour of Donohue syndrome.

The primary pathology is insulin resistance due to defective binding of insulin to its mutant receptor. These insulin receptor mutations are often collectively termed 'loss of function' mutations. Multiple mutations have been identified and the natural history of the disease depends on the degree of insulin resistance [5]. While patients with milder forms (the most common of which is Rabson-Mendelhall syndrome) can live into adulthood, a severe disease results in death during infancy. Clinical features include growth retardation (Intrauterine growth restriction, low birth weight, marasmus, failure to thrive), organomegaly (liver, spleen, kidneys, genitals), abnormal facies (pointed chin, microcephaly, prominent low set ears), skin features (pachyderma, hypertrichosis, acanthosis nigricans), hypotonia and relatively large hands/feet. Accelerated fasting states cause muscle wasting and low subcutaneous fat. They may also have hyperplasia of the Islets of Langerhans, nephrocalcinosis, atrophic adrenal glands, bile duct cholestasis, lymphoid hypoplasia and cystic gonadal appearances. Cardiac involvement in the form of hypertrophic cardiomyopathy, which occurs early in infancy, is attributed to the effects of IGF-1 [6]. A pathognomonic biochemical triad includes hyperinsulinism, fasting hypoglycaemia and postprandial hyperglycaemia [3].

Infants with the severe variant have a poor prognosis, succumbing to sepsis due to immunodeficiency. There is no established curative treatment, but exogenous administration of IGF-1 can be used in all insulin resistance syndromes to improve glycaemic control, to reduce levels of hyperinsulinaemia and the secondary effects of hyperinsulinism.

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

Central venous access, endoscopy, MRI, gastrostomy insertion, laparotomy.

Type of anaesthesia

Considering the risks associated, it should be ensured that the benefits of surgery justify administering anaesthesia.

General anaesthesia is described in the literature and concerns revolve around the management of their difficult airway, cardiomyopathy and unstable blood glucose [7].

There are no reports of using regional anaesthesia in these patients, however, neuraxial or peripheral nerve blocks are not contraindicated in Donohue syndrome. Concerns, preparation and precautions are similar to general anaesthesia.

The benefits of sedation must be carefully weighed against the risk of a difficult airway, haemodynamic instability and hypoglycaemia while asleep. Anaesthetic backup should be immediately available if needed.

Necessary additional pre-operative testing (beside standard care)

Fasting causes severe hypoglycaemia in Donohue syndrome, hence a short preoperative fasting time and glucose-containing intravenous maintenance fluids should be considered. Frequent blood sugar monitoring is essential in the perioperative setting.

Preoperative echocardiography is indicated as cardiomyopathy, which often exists by 1-2 months of age, may not be clinically manifest [8,9].

Particular preparation for airway management

Difficult airway should be anticipated even in patients with previously normal airways. Small thoracic diameter, poor chest compliance and abdominal distension result in low functional residual capacity and oxygen reserves which cause rapid desaturations. Bag mask ventilation may require a two-person technique and intubation can be challenging due to small mouth size. Adequate preparation includes difficult airway equipment, laryngeal mask airways, an experienced second anaesthetist and available ENT assistance with the ability to insert a rigid bronchoscope or tracheostomy if necessary [7].

It must be remembered that airway management could continue to be challenging during or after extubation.

Particular preparation for transfusion or administration of blood products

Owing to their small size and low physiologic reserve, small volume blood loss in these children may result in significant haemodynamic instability. It is prudent to ensure swift availability of blood products for transfusion.

Particular preparation for anticoagulation

No theoretical concerns with coagulation, but where organomegaly is a feature, liver functions and coagulation should be assessed preoperatively.

Particular precautions for positioning, transportation and mobilisation

The patient may need special care with movement and positioning due to abnormal body habitus and small restrictive chest.

Interactions of chronic disease and anaesthesia medications

Careful induction is warranted as hypertrophic cardiomyopathy predisposes these children to cardiovascular instability and arrest.

Anaesthetic procedure

Intravenous access and nasogastric tube should be secured before or soon after induction. Gastric contents should be aspirated before and during bag mask ventilation to minimise abdominal distension. Inhalational induction with spontaneous ventilation is recommended as it minimises gastric insufflation and the apnoeic period. Nitrous oxide should be avoided to optimise oxygenation in view of a potentially difficult airway, poor functional residual capacity and an underlying cardiomyopathy.

Intravenous induction, if done, should be titrated gradually to effect. A technique combining opiates, benzodiazepines and ketamine allows induction to proceed without sudden changes in heart rate, blood pressure and cardiac output.

These children mount a normal stress response to surgery, hence intraoperative glycaemic control should be individualised with frequent blood sugar measurements.

Hepatobiliary compromise must be factored in while assessing drug metabolism. Nephrotoxic drugs and NSAIDs must be avoided in patients with nephrocalcinosis and renal tubular dysfunction.

Particular or additional monitoring

Invasive haemodynamic monitoring with central venous pressure and invasive arterial blood pressure may be required for patients with cardiomyopathy and/or procedures involving fluid shifts or haemodynamic fluctuations.

Possible complications

1. Difficult airway including difficult mask ventilation, difficult intubation and difficult extubation,
2. Desaturation and hypoxic arrest,
3. Haemodynamic instability leading to cardiac arrest,
4. Hypoglycaemia and/or hyperglycaemia.

Post-operative care

Preparation for difficult airway (personnel, equipment, drugs) should be maintained in the immediate postoperative period.

Close glycaemic monitoring and control is essential to prevent hypo/hyperglycaemia. Combined with scrupulous antisepsis, normoglycaemia aids wound healing and avoids infections in a child with compromised immunity.

These patients must be cared for in a multidisciplinary setting where specialist input (endocrinology or cardiology for example) is readily accessible.

Disease-related acute problems and effect on anaesthesia and recovery

1. Fasting hypoglycaemia: symptoms are masked under anaesthesia and complications may occur if not detected and managed.

2. Delayed recovery from the effects of neuromuscular blockade and/or opiates: due to muscle wasting, low fat reserves and increased sensitivity in the setting of failure to thrive.

Ambulatory anaesthesia

Not feasible as these patients need intravenous fluid therapy and close monitoring of glycaemic control.

Obstetrical anaesthesia

Not reported.

References

1. Mohamed S. An infant with Leprechaunism, ambiguous genitalia and poor glycaemic control: a management challenge. Acta Endocrinologica (Buc) 2014;10:134–139
2. Martínez-Frías M, Bermejo E, Rodríguez-Pinilla E, Martínez-Fernández ML. Síndrome de Donohue (Leprechaunismo). ECEMC 2010;24: 1–2
3. Nijim Y, Awni Y, Adawi A, Bowirrat A. Classic Case Report of Donohue Syndrome (Leprechaunism; OMIM *246200): The Impact of Consanguineous Mating. Medicine (Baltimore) 2016;95: e2710
4. Online Mendelian Inheritance in Man (OMIM) Insulin Receptor -147670
5. Longo N, Wang Y, Smith SA, Langley SD, DiMeglio LA, Giannella-Neto D. Genotype–phenotype correlation in inherited severe insulin resistance. Human Molecular Genetics 2002; 1;11:1465–1475
6. Hovnik, T., Bratanič, N., Podkrajšek, K.T. et al. Severe progressive obstructive cardiomyopathy and renal tubular dysfunction in Donohue syndrome with decreased insulin receptor autophosphorylation due to a novel INSR mutation Eur J Pediatr 2013;172:1125
7. Kirkwood A, Stuart G, Harding L. Donohue syndrome: A review of literature, case series, and anesthetic considerations. Pediatr Anesth 2018;28:23–27
8. Planchenaulta D, Martin-Coignardb D, Rugemintwazac D. Le syndrome de Donohue ou leprechaunisme: a propos d'un cas. Arch Pediatr 2014;21:206–210
9. Baykan A, Cansever M, Konuskan B. Hypertrophic cardiomyopathy with leprechaunism. J Pediatr Endocrinol Metab 2008;21:317–318.

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Please note that this recommendation was not reviewed by an anaesthesiologist and a disease expert but by two anaesthesiologists instead.

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