orphanaesthesia

Anaesthesia recommendations for

Aromatic L-amino acid decarboxylase deficiency

Disease name: Aromatic L-amino acid decarboxylase deficiency

ICD 10: G24.8/ E70.9

Synonyms: AADC deficiency, DDC deficiency, DOPA decarboxylase deficiency, ALADD, AAD

Disease summary: Aromatic L-amino acid decarboxylase deficiency (AADCD) is a rare, autosomal recessive neurometabolic disorder that has been identified in approximately 120 patients worldwide. AADC converts 5-HT and L-Dopa to serotonin and dopamine respectively, dopamine being the precursor of norepinephrine and epinephrine. AADCD results in a combined deficiency of serotonin, dopamine, norepinephrine and epinephrine. AADC deficiency commonly presents in the first year of life with hypotonia, movement disorders (including oculogyric crises), developmental delay and autonomic dysfunction. Diagnostic tests include neurotransmitter metabolites in CSF, decreased AADC activity in plasma and genetic confirmation. Treatment is predominantly symptomatic with selective dopamine agonists, monoamine oxidase inhibitors (MAOIs) and pyridoxine. The main anaesthetic challenge in patients with AADCD is managing cardiovascular instability, which can develop due to a combination of low levels or circulating catecholamines and decreased sympathetic activity in the context of an intact parasympathetic system. Patients may also be extremely sensitive to exogenous catecholamines due to possible upregulation of cardiac adrenergic receptors secondary to low endogenous plasma catecholamine levels.

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Perhaps new knowledge

Every patient is unique

Perhaps the diagnosis is wrong

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Typical surgery

MRI, gastrostomy, orthopaedic procedures, gastrostomy, microlaryngoscopy and bronchoscopy.

Type of anaesthesia

There are reports of children with AADCD having undergone procedures under sedation, general anaesthesia and a combined general and regional anaesthesia technique.

There is no recommendation of one type of anaesthesia. With whichever technique is chosen the anaesthetist should plan for and be prepared for haemodynamic instability and hypoglycaemia, both during and after the procedure.

Necessary additional pre-operative testing (beside standard care)

Cardiac instability can result from catecholamine deficiency and autonomic dysfunction. Patients on bromocriptine are also at risk of developing cardiac fibrosis. Patients with AADCD should be reviewed by a paediatric cardiologist preoperatively and undergo an ECG and echocardiogram.

A preoperative sleep study should be performed on patients who have sleep apnoea. Some patients with AADCD have stridor and require preoperative otolaryngology consultation.

A proportion of patients with AADCD have epilepsy and their antiepileptic treatment should be optimised and continued prior to elective surgery.

Particular preparation for airway management

Patients with AADCD have a higher incidence of gastro-oesophageal reflux disease and are therefore at higher risk of aspiration. Airway management can also be complicated by excessive drooling.

Particular preparation for transfusion or administration of blood products

Not reported.

Particular preparation for anticoagulation

Not reported.

Particular precautions for positioning, transportation and mobilisation

Careful positioning will be required for patients with contractures.

Body temperature must be monitored and kept within normal range. Patients with AADCD may become hypothermic, hyperthermic and diaphoretic due to autonomic instability.

Interactions of chronic disease and anaesthesia medications

Patients with AADCD are likely to be on a combination of treatment agents, and precautions must be taken depending on the exact medications the patient is on. First line treatment is with selective dopamine agonists, MAOIs and pyridoxine. Additional symptomatic treatment is with anticholinergic drugs, melatonin, benzodiazepines and alpha-adrenoreceptor blockers.

MAOIs demonstrate a wide range of interactions with anaesthetic drugs. MAOIs exaggerate the cardiovascular depressant effects of volatile agents, prolong the effects of drugs metabolised by oxidation (pethidine, fentanyl, morphine and barbiturates) and inhibit plasma cholinesterase, prolonging the duration of action of suxamethonium. Pethidine in particular should not be given with MAOIs, as this can lead to profound hyperpyrexia due to serotonin release. MAOIs may potentiate the effects of antihypertensives, hypoglycaemic agents and local anaesthetics.

Anticholinergic side effects can be exacerbated if anticholinergics are given intraoperatively to those on a regular dose.

Caution must be taken when giving sedation to patients already on a benzodiazepine or alpha agonist (e.g. clonidine).

Anaesthetic procedure

Preoperatively, the need for a sedative premedication should be balanced with the risk of the cardiorespiratory depression. Prolonged fasting should be avoided due to the risk of hypoglycaemia. Blood glucose level should be carefully monitored during the perioperative period and, if required, glucose should be given intravenously.

Preparations should be made to maintain cardiovascular stability during induction, maintenance and emergence from anaesthesia. Avoid high end tidal concentrations of sevoflurane because of the risk of bradycardia. Atropine can be given to blunt vagal tone.

Neuromuscular blockers are safe to use in AADCD.

Opioids caused severe hypotension in one case and we have certainly observed profound hypotension and bradycardias on their administration and therefore recommend titrating opioids such as fentanyl and morphine very cautiously. There is no published data on the use of remifentanil and we would advise against its use as it may perpetuate profound bradycardias.

There is no association with malignant hyperthermia. Patients with AADCD can become both hyperthermic and hypothermic secondary to autonomic dysfunction.

Centrally acting dopamine antagonists (e.g. metoclopramide, haloperidol) must be avoided as they can worsen the symptoms of dopamine deficiency. Phenothiazines (e.g. prochlorperazine) should not be given because of their antidopaminergic, antiadrenergic and antiserotonergic properties. Serotonin antagonists (e.g. ondansetron, granisetron) should also be avoided.

Procedures should be timed so that patients can continue taking their regular medications.

Particular or additional monitoring

Temperature and glucose monitoring should be undertaken in all patients with AADCD.

In patients with known cardiac disease or in those undergoing major surgery, we recommend the use of an arterial line and to consider placing a central venous line.

Possible complications

Autonomic instability means that patients with AADCD can become both hypotensive and bradycardic under anaesthesia or hypertensive and tachycardic/develop arrhythmias. They appear to be sensitive to exogenous catecholamines and vasopressors such as phenylephrine and therefore should be titrated with caution with the aid of invasive blood pressure monitoring.

If inotropic support is required, the first line treatment is peripheral low dose dopamine (1-2mcg/kg/min) as recommend by the international consensus and which we have used successfully. There is no further published data on which inotrope to use as a second line agent, and we advise cautious titration with the agent of choice. Ephedrine will be ineffective in this group of patients due to its indirect mode of action, and there is experience of phenylephrine leading to severe bradycardia due to the baroreceptor response.

Patients with AADCD are susceptible to hypoglycaemia, temperature fluctuations and dehydration (autonomic dysfunction can result in excessive sweating and diarrhoea).

Post-operative care

Patients with AADCD should be monitored for postoperative sympathetic impairment with possible cardiac involvement.

Treat nausea and vomiting with supportive care. If an antiemetic is needed, give low dose domperidone (it does not cross the blood brain barrier).

Disease-related acute problems and effect on anaesthesia and recovery

Dystonic crises can occur in patients with AADCD and are often precipitated by a change in medication or a concurrent infection. Severe crises can lead to airway compromise and rhabdomyolysis. Management is supportive, with patients potentially requiring sedation (usually with a benzodiazepine) and organ support on intensive care.

Several patients with AADCD have died suddenly, on the background of known previous arrhythmias.

Pyrexia can be secondary to autonomic instability. A blood sugar level should always be checked as these patients are prone to hypoglycaemia.

Patients can develop profuse diarrhea secondary to the increased vagal activity on the gastrointestinal tract. Fluid balance and electrolytes should be carefully monitored.

Ambulatory anaesthesia

Patients with AADCD should remain in hospital for postoperative monitoring.

Obstetrical anaesthesia

Case reports of successful pregnancies have been published in patients with AADC. No anaesthetic considerations have been published to date.

References

1. Wassenberg T, Molero-Luis M, Jeltsch K, Hoffmann GF, Assmann B, Blau N, et al. Consensus guideline for the diagnosis and treatment of aromatic l-amino acid decarboxylase (AADC) deficiency. Orphanet J Rare Dis 2017;12:12. DOI: 10.1186/s13023-016-0522-z
2. Arnoux JB, Damaj L, Napuri S, Serre V, Hubert L, Cadoudal M, et al. Aromatic L-amino acid decarboxylase deficiency is a cause of long-fasting hypoglycemia. J Clin Endocrinol Metab 2013;98:4279–4284. DOI: 10.1210/jc.2013-2740
3. Helman G, Pappa MB, Pearl PL. Widening phenotypic spectrum of AADC deficiency, a disorder of dopamine and serotonin synthesis. JIMD Rep 2014;17:23–27. DOI:10.1007/8904_2014_327
4. Vutskits L, Menache C, Manzano S, Haenggeli CA, Habre W. Anesthesia management in a young child with aromatic l-amino acid decarboxylase deficiency. Paediatr Anaesth 2006; 16:82–84. DOI: 10.1111/j.1460-9592.2005.01605.x
5. Berkowitz DH, Ganesh A. Combined general and regional anesthetic in a child with aromatic L-amino acid decarboxylase deficiency. Anesth Analg 2006;103:1630–1631. DOI: 10.1213/01.ane.0000247197.78421.93
6. Ide S, Sasaki M, Kato M, Shiihara T, Kinoshita S, Takahashi JY, et al. Abnormal glucose metabolism in aromatic l-amino acid decarboxylase deficiency. Brain Dev 2010;32:506–510. DOI: 10.1016/j.braindev.2009.05.004
7. Pons R, Ford B, Chiriboga CA, Clayton PT, Hinton V, Hyland K, et al. Aromatic L-amino acid decarboxylase deficiency: clinical features, treatment, and prognosis. Neurology 2004;62: 1058–1065. DOI: 10.1212/WNL.62.7.1058
8. Antonini A, Poewe W. Fibrotic heart-valve reactions to dopamine-agonist treatment in Parkinson's disease. Lancet Neurol 2007;6:826–829. DOI: 10.1016/S1474-4422(07)70218-1
9. Andersohn F, Garbe E. Cardiac and noncardiac fibrotic reactions caused by ergot-and nonergot-derived dopamine agonists. Mov Disord 2009;24:129–133. DOI: 10.1002/mds.22385.

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