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Allgrove syndrome

Freeman-Burian syndrome

orphananesthesia

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

SUPPLEMENT NR. 1 | 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 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:

www.ai-online.info/Orphsuppl
www.orphananesthesia.eu

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 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.

A survey of until now in A&I published guidelines can be found on:

www.ai-online.info/Orphsuppl
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Anaesthesia recommendations for

Allgrove syndrome

Disease name: Allgrove Syndrome

ICD 10: E27.4

Synonyms: Triple A syndrome, 4 A Syndrome, Achalasia-Addisonianism-Alacrima syndrome

Disease summary: Allgrove Syndrome (AS) is rare autosomal recessive disorder characterised by achalasia cardia, alacrimia and adrenal insufficiency, which is generally adrenocorticotropic hormone (ACTH) resistant, and neurological abnormalities. Mutations have been identified in the AAAS gene, located on chromosome 12q13 (type-2 keratin gene), that codes for the ALADIN protein. IVS14 and EVS9 are the most common mutations. Alacrimia is an early and pathognomic symptom, but achalasia (50 -100 %) and adrenal insufficiency (20 -54%) are the more common presenting features. Autonomic disturbances and other neurological symptoms (10- 23%) are rare. Patients may develop a variable combination of sensory-motor polyneuropathy amyotrophy, dysarthria, hyperreflexia, muscle weakness, dementia, abnormal autonomic function, erectile dysfunction (adult) and intellectual impairment. Diagnosis is generally made in the first decade of life when they present with dysphagia, vomiting and failure to thrive due to achalasia, hyperpigmentation of skin, shock due to adrenal insufficiency or seizures and coma due to severe hypoglycaemia. Typical dysmorphic faces including long thin face, long philthrum, narrow upper lip, down-turned mouth and sparse eyelashes may also be seen. Keratitis punctata is the most common complication of alacrimia. Patients with adrenal insufficiency are generally on a maintenance dose of a glucocorticoid like hydrocortisone. Most patients with achalasia require frequent pneumatic dilatations or surgical interventions like Heller's myotomy.

Medicine in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

Find more information on the disease, its centres of reference and patient organisations on Orphanet: www.orpha.net

▶ **Citation:** Dhar M: Allgrove syndrome. Anästh Intensivmed 2019;60:S1–S7.
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Typical surgery

Heller's myotomy for achalasia cardia (open or laparoscopic), balloon dilatation of oesophagus under endoscopic control.

Type of anaesthesia

General anaesthesia with controlled airway in the form of an endotracheal tube is the standard practice.

Necessary additional diagnostic procedures (preoperative)

Barium swallow, oesophageal manometry and upper GI endoscopy for achalasia cardia.
Cortisol levels and ACTH stimulation tests, serum electrolytes and serum glucose for adrenal insufficiency.
Schirmer's test for alacrimia.
Tests of autonomic dysfunction like heart rate and blood pressure response to standing, pilocarpine eye test and sweat test.
Motor or sensory impairment should be documented in consultation with a neurologist for medicolegal precautions.

Particular preparation for airway management

Patients are prone to recurrent respiratory tract infections due to regurgitation. Upper and lower respiratory tract symptoms must be ruled out. Active infections must be optimised. Surgery should be postponed, if required.
Cuffed or micro-cuffed endotracheal tubes should ideally be used for airway protection and to prevent micro-aspirations.
H_2 receptor blockers or proton-pump inhibitors may be given for aspiration prophylaxis and for the prevention of peptic ulcers due to stress dose of steroids.
Aspiration and decompression of stomach and oesophageal contents by naso-gastric tube prior to induction.

Particular preparation for transfusion or administration of blood products

Maintenance of intravenous fluid, should be a dextrose containing fluid like 0.45% saline in 5% dextrose. Lactated ringer for intra-operative losses.
No contraindications to blood transfusion, routine cross-matching and transfusion-related precautions should be taken.

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Particular preparation for anticoagulation

No specific precautions or requirements mentioned in literature.

Particular precautions for positioning, transport or mobilisation

Patients are prone to autonomic disturbances. Positioning and transport should be slow and gradual. Laparoscopy may require a low head position. A pneumoperitoneum should be created slowly and intraabdominal pressure should be monitored properly.

Pressure points and bony prominences should be properly padded, especially in cases of sensory neuropathies and longer duration surgery. Similar precautions should be followed during transport.

Eyes should be properly lubricated and covered.

Probable interaction between anaesthetic agents and patients' long-term medication

Patients with adrenal insufficiency are on maintenance steroid doses, Cushing syndrome may be seen as a side effect. Stress doses of steroid are required peri-operatively and hydrocortisone is the drug of choice. The dose of hydocortisone and other steroids varies among different pediatric age groups and body weight [24,25].

Avoid etomidate as it is shown to depress adrenal function for 3-6 hours post administration. No direct interaction with other anaesthetic agents is mentioned in literature.

Anaesthetic procedure

General anaesthesia with the airway being secured with an endotracheal tube, preferably cuffed or microcuffed.

Induction should be done slowly, giving drug in aliquots, to prevent sudden cardiovascular collapse or autonomic instability.

Rapid sequence induction using a short-onset drug like rocuronium to minimise aspiration. Caution in use of succinyl choline, in presence of myopathies causing upregulation of extra-junctional acetylcholine receptors (hyperkalaemic response). Nondepolarising blockers also may induce a variable response in such cases. Titrate dosing according to neuromuscular monitoring.

Maintenance of euglycaemia intraoperatively by use of Insulin infusion, if required. Sometimes a steroid infusion may also be required.

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Particular or additional monitoring

Intraoperative monitoring of serum glucose, electrolytes (sodium, potassium).
Invasive blood pressure monitoring for the early detection of any autonomic or hemodynamic disturbances.
Use of neuromuscular monitoring to titrate optimal dosing of neuromuscular blocking drugs, and to optimise reversal and adequate recovery.
Intraabdominal pressure monitoring, peak airway pressure monitoring, urine output and end tidal CO_2 to detect complications of pneumoperitoneum.

Possible complications

Adrenal crisis leading to hypotension or shock, hypoglycaemia, hyponatraemia or hyperkalaemia (due to stress of surgery, infection or trauma).
Hyperglycaemia due to steroids.

Post-operative care

Head end elevation and aspiration prophylaxis. Topical lubricating ointment for eyes.
Steroids should be tapered to maintenance dosing. Pain relief with intravenous paracetamol or rectal suppository.

Information about emergency-like situations/ Differential diagnostics

Adrenal crisis, hypotension and shock should be differentiated from adverse effects or side effects of anaesthetic agents, or haemodynamic effects of autonomic dysfunction.
Hyploglycaemia coma, hyponatremia may be a cause of delayed recovery from anaesthesia.
Hyperkalaemia may lead to dangerous arrhythmias or even cardiac arrest.

Ambulatory anaesthesia

May be practiced for shorter recurrent procedures like oesophageal balloon dilatations.

Obstetrical anaesthesia

There is not much literature on anaesthesia in this group of patients. Patients are mostly encountered in the paediatric age group.

Literature and internet links

1. Allgrove J, Clayden GS, Grant DB, Macaulay JC. Familial glucocorticoid deficiency with achalasia of the cardia and deficient tear production. Lancet 1978;1:1284–1286
2. Sarathi V, Shah NS. Triple-A syndrome. Adv Exp Med Biol 2010;685:1–8
3. Bhargavan PV, Kumar KM, Rajendran VR, Fassaludeen AS. Allgrove syndrome – A syndrome of primary adrenocortical insufficiency with achalasia of the cardia and deficient tear production. J Assoc Physicians India 2003;51:726–728
4. Kasar PA, Khadilkar VV, Tibrewala VN. Allgrove syndrome. Indian J Pediatr 2007;74:959–961
5. BG Arun, BS Deepak, Murali R Chakravarthy. Anaesthetic management of a patient with Allgrove syndrome. Indian J Anaesth 2014;58(6):736–738
6. Dhar M, Verma N, Singh RB, Pai VK. Triple A to triple S: From diagnosis, to anesthetic management of Allgrove syndrome. J Clin Anesth 2016;33:141–143
7. Ozer AB, Erhan OL, Sumer C, Yildizhan O. Administration of anesthesia in a patient with allgrove syndrome. Case Rep Anesthesiol 2012;2012:109346
8. Gazarian M, Cowell CT, Bonney M, Grigor WG. The "4A" syndrome: Adrenocortical insufficiency associated with achalasia, alacrima, autonomic and other neurological abnormalities. Eur J Pediatr 1995;154:18–23
9. Soltani A, Ameri MA, Ranjbar SH. Allgrove syndrome: A case report. Int J Endocrinol Metab 2007;4:160–163
10. Ali H A, Murali G, Mukhtar B. Respiratory failure due to achalasia cardia. Respir Med CME 2009,2;1:40–43
11. Teramoto S, Yamamoto H, Yamaguchi Y, et al. Diffuse aspiration bronchiolitis due to achalasia. Chest 2004;125,1:349–350
12. Etemadyfar M, Khodabandehlou R. Neurological manifestations of Allgrove syndrome. Arch Iran Med 2004;7,3:225–227
13. Weber A, Wienker TF, Jung M, Easton D, Dean HJ, Heinrichs C, et al. Linkage of the gene for the triple A syndrome to chromosome 12q13 near the type II keratin gene cluster. Hum Mol Genet 1996;5:2061–2066
14. Aghajanzadeh M, Safarpoor F, Hydayati MH, Kohssari MR, Mashhour MY, Soleymani AS. Allgrove syndrome: Reports of cases and literature review. Saudi J Gastroenterol 2006;12:34–35
15. Hines RL, Marschall KE. Adrenal insufficiency. In: Hines RL (editor). Stoelting's Anesthesia and Co-Existing Disease. Philadelphia: Churchill Livingstone/Elsevier 2008;436–437
16. Babu K, Murthy KR, Babu N, Ramesh S. Triple A syndrome with ophthalmic manifestations in two siblings. Indian J Ophthalmol. 2007;55:304–306
17. Salehi M, Houlden H, Sheikh A, Poretsky L. The diagnosis of adrenal insufficiency in a patient with Allgrove syndrome and a novel mutation in the ALADIN gene. Metabolism 2005;54:200–205
18. Ismail EA, Tulliot-Pelet A, Mohsen AM, Al-Saleh Q. Allgrove syndrome with features of familial dysautonomia: a novel mutation in the AAAS gene. Acta Paediatr 2006;95:1140–1143
19. Shah A, Shah A. Esophageal achalasia and alacrima in siblings. Indian Pediatr 2006;43:161–163
20. Villanueva-Mendoza C, Martínez-Guzmán O, Rivera-Parra D, Zenteno JC. Triple A or Allgrove syndrome. A case report with ophthalmic abnormalities and a novel mutation in the AAAS gene. Ophthalmic Genet 2009;30:45–49
21. Grant DB, Barnes ND, Dumic M, et al. Neurological and adrenal dysfunction in the adrenal insufficiency/alacrima/achalasia (3A) syndrome. Arch Dis Child 1993;68:779–782
22. Fernbach SK, Poznanski AK. Pediatric case of the day. Triple A syndrome: achalasia, alacrima and ACTH insensitivity. Radiographics 1989;9:563–564

23. Etemadyfar M, Khodabandehlou R. Neurological manifestations of Allgrove syndrome. Arch Iran Med 2004;7:225–227
24. Migeon C. Adrenal steroid therapy. In: Rudolph A, Barnett H, Einhorn A (eds). Pediatrics. New York: Appleton-Century-Crofts 1977;1651–1662
25. Chilren's hospital of Philadelphia. Pathway for the Child at Risk for HPA Suppression: Stress Steroid Dosing and Weaning Recommendations. http://www.chop.edu/clinical-pathway/steroid-stress-dosing-and-weaning-clinical-pathway (accessed on Dec 2018)
26. Tebaibia A, Boudjella MA, Benmediouni F, Lahcene M, Oumnia N. Familial achalasia associated or not to Allgrove syndrome: about 18 families. United European Gastroenterol J 2013;1(1S):A26
27. Tebaibia A, Boudjella MA, Benmediouni F, Lahcene M, Oumnia N. Genotypic heterogeneity and clinical features in Allgrove syndrome: about 78 cases. United European Gastroenterol J 2013;1(1S):A27.

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