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Urea cycle disorders

Waardenburg syndromes

orphanaesthesia

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

SUPPLEMENT NR. 14 | 2021

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 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

Waardenburg syndromes

Disease name: Waardenburg syndromes

ICD 10: Q87.8

Synonyms: Waardenburg syndrome type I, type II, type III and type IV

Disease summary: Waardenburg syndrome (WS) is an uncommon autosomal inherited and genetically heterogeneous disorder of neural crest cell development named after the Dutch ophthalmologist P. J. Waardenburg in 1951. Based on the clinical presentations, four subtypes are described. According to the diagnostic criteria proposed by the Waardenburg consortium, a person must have two major or one major plus two minor criteria in order to be diagnosed as WS type I [Table 1]. WS type II lacks dystopia canthorum of WS type I. Type III, also called Klein–Waardenburg syndrome, has associated limb abnormalities. Type III is the rarest form of WS. Shah–Waardenburg syndrome, type IV, is an unusual variant of WS associated with Hirschsprung's disease (long-segment, short-segment or even limited to persistent constipation). It is named after Krishnakumar N. Shah who described 12 newborns with Waardenburg syndrome associated with long segment Hirschsprung's disease in 1981. WS belongs to the neurocristopathies, disorders caused by an alteration in the migration of the neural crest cells during the embryonic phase. These neural crest cells are important for the formation of several parts of the body, i.e. melanocytes, inner ear and enteric nervous system. Other features very rarely associated with WS include vestibular symptoms, urinary system abnormalities, neural tube defects, Sprengel anomaly, cleft-lip or palate, facial nerve palsy and plicated tongue, laryngomalacia, and severe cyanotic cardiopathy.

Heterozygous mutations in the PAX3 gene on chromosome 2 are seen in WS I (dominant trait). WS type III is also ascribed to PAX3 mutation, either to very specific heterozygous mutations or to bi-allelic mutants (most cases are therefore recessive). WS type II is usually transmitted as dominant trait and has been related either to MITF (mapped on chromosome 3) or SOX10 (chromosome 22) heterozygous mutations. Two cases of WS type II have been described with homozygous mutation of SNAI2 (chromosome 8). WS type IV is heterogeneous, ascribed either to SOX10 (dominant trait), EDN3 (recessive trait) or EDNRB (dominant or recessive trait) mutations.

It is noteworthy that the expressivity is variable among affected family members, i.e. some may have only white skin patches and others having also deafness and Hirschsprung's disease.

Few patients with WS type IV have in addition neurological symptoms (neuropathy, central dysmyelinating leukodystrophy with ataxia, spasticity, intellectual deficiency, and autonomic dysregulation). This dominant disorder named PCWH is caused by some specific SOX10 mutations.

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The differential diagnosis of white forelock and skin patches are vitiligo, piebaldism (rarely associated with deafness), Rozycki syndrome (leukoderma, congenital deafness, muscle wasting, and achalasia), Vogt–Koyanagi–Harada syndrome (uveitis, greying of hair, meningitis, and vitiligo of auto-immune origin), Tietz syndrome (deaf-mutism, blue eyes, and hypomelanosis, related to MITF heterozygous mutations and therefore allelic to WS type II), and tuberous sclerosis (autosomal dominant disorder with other skin manifestations, often seizures and intellectual deficiency, brain, kidney, cardiac, ocular and pulmonary lesions, but without deafness).

Table 1: Diagnostic criteria for Waardenburg syndrome type I

Major criteria	**Minor criteria**
White forelock	Broad/high nasal root
Pigmentary disturbances of the iris	Hypoplasia of alae nasi
Congenital sensorineural hearing loss	Synophrys or medial eyebrow flaring
Affected first-degree relative	Skin hypopigmentation
Dystopia canthorum or laterally Displaced medial canthi	Prematurely greying of hair

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

Neonatal surgeries, paediatric surgeries, ophthalmic surgeries, orthopaedic surgeries, cochlear implantation.

Type of anaesthesia

There is no definite recommendation for either general or regional anaesthesia. Literature regarding the anaesthetic management of these cases is limited. The anaesthesiologist encountering a child with a white forelock should keep in mind the differential diagnosis and variants of WS. We would recommend an individualised anaesthetic approach in managing these patients. Both intravenous and volatile inhalational anaesthetic agents should be safe. A peripheral nerve block has been described in one case.

Meticulous attention is required with pre-operative evaluation, co-existence of other system abnormalities, airway management, and peri-operative nutrition strategies (risk of malnutrition increasing with the extent of the aganglionic segment of the intestine).

Necessary additional pre-operative testing (beside standard care)

Pre-operatively, apart from routine investigations, specific investigations are recommended only to evaluate associated conditions rather than to diagnose the disease itself. Pre-operative echocardiography will rule out cardiac anomalies, however, it is not routinely advised. Impaired autonomic control of the heart has been described in a WS type IV patient with SOX10 mutation, but without clinical consequence and normal routine ECG. Fundus examination, as these children may suffer from retinopathy of prematurity due to oxygen toxicity, etc.

Particular preparation for airway management

The possibility of a difficult airway must be kept in mind and appropriate preparations made. Difficult airway management using I-gel as conduit has been described in the literature.

Particular preparation for transfusion or administration of blood products

There may be increased requirement for blood and blood products for multiple surgeries.

Particular preparation for anticoagulation

There are no reports to suggest the need for peri-operative anticoagulation. However, these patients may be bedridden because of the secondary musculoskeletal deformities (rarely except mainly for WS type III and PCWH disease) necessitating anticoagulation following major surgery.

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Particular precautions for positioning, transportation and mobilisation

None reported.

Interactions of chronic disease and anaesthesia medications

None reported.

Anaesthetic procedure

WS patients have involvement of multiple system abnormalities. A thorough pre-operative evaluation should be done. Due precautions with anaesthetic implications pertaining to paediatric anaesthesia should be practiced. One may encounter communication difficulties due to congenital deafness.

Multiple system abnormalities may pose different challenges depending on the age of presentation and the extent of musculoskeletal system involvement. These patients may present technical difficulties both during regional as well as during general anaesthesia.

Anticipation of difficult mask ventilation due to facial dysmorphism, hypoplastic alae nasi, muscle contractures and difficult intubation due to cleft lip-palate should be borne in mind.

Electrolyte imbalances should be kept in mind in patients presenting for intestinal obstruction and repeated surgeries.

Careful consideration of the dosage of the drugs is essential because of the possible alteration in pharmacodynamics and kinetics due to associated malnutrition.

Partial albinism may pose a difficulty in assessing pallor and capillary refilling time.

Positioning of the patient may be difficult, especially in case of older patients with PCWH disease, due to spasticity and muscle contractures.

Particular or additional monitoring

None reported.

Possible complications

Difficult airway management, electrolyte imbalances, malnutrition, autonomic dysfunction, colostomy complications.

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Post-operative care

These patients may need to be carefully monitored for respiratory depression, apnoeic spells because of the altered pharmacokinetics and dynamics due to severe malnutrition making them susceptible to an overdose of anaesthetics, opioids and neuromuscular blocking agents. The possibility of reduced tear and saliva production in some patients should be kept in mind.

Colostomy care is important. Temperature regulation is important as one of our patients died of sclerema neonatorum, which was considerably due to hypothermia.

Disease-related acute problems and effect on anaesthesia and recovery

The possible emergency scenario is a neonate for emergency laparotomy for intestinal obstruction. An anaesthesiologist who is experienced in airway management should be in charge of the case.

Ambulatory anaesthesia

Procedures of short to moderate duration may be undertaken and managed according to the standard guidelines for ambulatory anaesthesia.

Obstetrical anaesthesia

A patient with WS presenting for obstetrical anesthesia has not been reported in the literature. We want to emphasise that numerous cases of WS type I and II are familial, with dominant inheritance, and include affected female subjects who gave birth to children. It is very likely that there is no increased risk of obstetrical complication.

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

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