

Anaesthesia recommendations for patients suffering from

Waardenburg syndromes

Disease name: Waardenburg syndromes

ICD 10: Q87.8

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

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 to be diagnosed as WS type I [Table 1]. WS type II lacks dystopia canthrum of WS type I. Type III, also called Klein–Waardenburg syndrome, and 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.

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

Disease summary

Heterozygous mutations in 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 expressivity is variable among affected family members, i.e. some may have only white skin patches and others having also deafness and Hirschprung'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.

The differential diagnosis of white forelock and skin patches are Vitiligo, Pie baldism (rarely associated with deafness), Rozycki syndrome (leukoderma, congenital deafness, muscle wasting, and achalasia), Vogt–Koyanagi–Harada syndrome (uveitis, graying of hair, meningitis, and vitiligo of auto-immune origin), Tietz syndrome (deafmutism, 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 graying of hair

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 white forelock should keep in mind the differential diagnosis and variants of WS. We would recommend an individualized anaesthetic approach in managing

these patients. Both intravenous and volatile inhalational anaesthetic agents should be safe. Peripheral nerve block has been described in one case.

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

Necessary additional diagnostic procedures (preoperative)

Preoperatively, apart from routine investigations, specific investigations are recommended only to evaluate associated conditions rather than to diagnose the disease itself. Preoperative echocardiography will rule out cardiac anomalies, though 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

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 perioperative 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 a major surgery.

Particular precautions for positioning, transport or mobilisation

None reported.

Probable interaction between anaesthetic agents and patient's long-term medication

None reported.

Anaesthesiologic procedure

WS patients have involvement of multiple system abnormalities. Thorough preoperative 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 involvement of the musculoskeletal system. These patients may present technical difficulties both during regional as well as 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 born in mind.

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

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

The presence of partial albinism may pose difficulty in assessing pallor and capillary refilling time.

Positioning of the patient may be difficult, especially in 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.

Postoperative 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 overdose of anaesthetics, opioids and neuromuscular blocking agents. Possibility of reduced tear and saliva production in some patients should be kept in mind.

Care of colostomy is important. Temperature regulation is important as one of our patient died of sclerema neonatorum, which was considerably due to hypothermia.

Information about emergency-like situations / Differential diagnostics

caused by the illness to give a tool to distinguish between a side effect of the anaesthetic procedure and a manifestation of the disease

The possible emergency scenario is a neonate for emergency laparotomy for intestinal obstruction. An experienced anaesthesiologist who can manage airway 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

Patient with WS presenting for obstetrical anesthesia has not been reported in the literature. We want to emphasize 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.

Literature and internet links

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Please note that this guideline has not been reviewed by an anaesthesiologist but by two disease experts instead.
