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Turner syndrome

orphan**anesthesia**

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

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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 Patientinnen und Patienten mit seltenen Erkrankungen. Damit will OrphanAnesthesia einen wichtigen Beitrag zur Erhöhung der Patientensicherheit leisten.

Patientinnen und 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 Anästhesistinnen und Anästhesisten damit keine Erfahrungen gesammelt haben, sodass 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 eine Anästhesistin bzw. ein Anästhesist sowie eine weitere Krankheitsexpertin bzw. ein weiterer Krankheitsexperte (z. B. Pädiaterin bzw. Pädiater oder Neurologin bzw. Neurologe) beteiligt sind. Das Projekt ist international ausgerichtet, sodass 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.

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 recommendations 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.

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orphan**a**nesthesia

Anesthesia recommendations for Turner syndrome

Disease name: Turner syndrome

ICD 10: Q96.0, Q96.1, Q96.2, Q96.3, Q96.4, Q96.8, Q96.9

ORPHAcode: 881

Synonyms: 45,X/46,XX syndrome; 45,XO; Bonnevie-Ullrich syndrome

Brief disease summary: Turner syndrome (TS) is an exclusively female genetic disease caused by complete or partial absence of the second X chromosome. The karyotype is generally 45,X0 (80%) and more rarely 46X,Xp- or 46X,Xq- (5%); 15% of cases are mosaicism. It is the most commonly occurring chromosomal abnormality in women with an incidence of 1 in 2,500-3,000 births [1]. It is associated with a wide variety of anatomical and physiological abnormalities, especially related to the airway and cardiovascular system, which can pose a challenge to the anesthetist [2,3].

Physical characteristics comprise short stature, webbed neck, low set ears, micrognathia and retrognathia, cubitus valgus, widely spaced nipples and hypertelorism [1,4].

Cardinal systemic manifestations include gonadal dysgenesis and congenital lymphedema of the hands and feet [1,4]. Cardiovascular anomalies are present in 40-50% of patients, most commonly bicuspid aortic valve (25%) and aortic coarctation (10%), in addition to aortic stenosis, aortic root dilatation and a significant risk of aortic dissection. More rarely it is associated with ASD, VSD, anomalous pulmonary venous return and hypoplastic left heart [5].

There is an increased prevalence of cardiovascular disease, particularly hypertension, in addition to ischemic heart disease, cardiac conduction defects and hypercholesterolemia [1,5].

Endocrine manifestations include hypothyroidism, seen in 15-30% of patients with TS, and diabetes mellitus. There is an association with multiple autoimmune diseases [6].

Renal malformations are present in 40% of patients (absence, ectopic and horseshoe kidneys and duplication of the collecting duct), and gastro-esophageal reflux and inflammatory bowel disease are common [7-10]. Liver anomalies comprising hepatic steatosis, reduction in metabolism and bleeding disorders may be present [11-13].

Osteoarticular abnormalities may feature including scoliosis, kyphosis, osteoporosis and spina bifida occulta [14-16].

Ophthalmological and hearing impairment is common and 10% of patients with TS will have learning difficulties.

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Diagnosis may be incorrect; if uncertainty exists, the diagnosis should be re-evaluated.

Every patient is unique; individual circumstances must always guide clinical care.

Medicine is in progress; new clinical knowledge may not be yet reflected in this recommendation.



Recommendations are not rules or laws; they provide a framework to support clinical decision-making. Although this recommendation has passed a structured review process, it does not meet the formal criteria of a guideline.

Translations may not always reflect the most recent updates of the English version.



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

Emergency information

A	AIRWAY / ANESTHETIC TECHNIQUE	At risk of a difficult intubation, endobronchial intubation and accidental extubation due to a short, webbed neck, a high arched palate, micrognathia and retrognathia, limited jaw subluxation, the potential severe limitation of neck movement, and an increased incidence of multiple joint contractures which may include the temporomandibular joint.
B	BLOOD PRODUCTS (COAGULATION)	Transient thrombocytopenia in the newborn period. Severe liver disease in later life can result in a complex coagulopathy state and decreased drug metabolism. Hemostasis should be evaluated pre-operatively and corrected if necessary.
C	CIRCULATION	Cardiovascular anomalies are present in 40-50% of patients, most commonly bicuspid aortic valve (25%) and aortic coarctation (10%), in addition to aortic stenosis, aortic root dilatation and a significant risk of aortic dissection. More rarely it is associated with ASD, VSD, anomalous pulmonary venous return and hypoplastic left heart. There is an increased prevalence of cardiovascular disease, particularly hypertension, in addition to ischemic heart disease, cardiac conduction defects and hypercholesterolemia.
D	DRUGS	Nothing of note.
E	EQUIPMENT	Nothing of note.

Additional disease information

Not applicable.

Typical surgery and procedures

Orthopedic procedures, cardiac valve surgery, coronary artery bypass grafts, repair of aortic aneurysms and aortic dilatation, gynecology procedures, assisted fertility techniques, and endoscopy.

Type of anesthesia

Both general and regional anesthesia have been described in patients with TS.

Given the concerns of difficult airway management, alternatives to endotracheal anesthesia should be considered where appropriate. A supraglottic airway may be beneficial in patients without reflux disorder.

Regional anesthesia, both in the form of central neuraxial and regional blocks, is an excellent option, but one should consider the patient's potential coagulation and spinal abnormalities (mainly scoliosis and spina bifida occulta). The dose of local anesthetic administered should be individualized given the patient's height.

Necessary additional preoperative testing (beside standard care)

The patient should be thoroughly worked up from a cardiovascular perspective pre-operatively. Ensure blood pressure control is optimized and a routine ECG obtained. A recent echocardiography should be obtained even if the patient has no history of congenital heart disease. If there is a history of possible ischemic cardiomyopathy, a stress test should be performed [17,18].

TS patients have smaller pharyngeal airway dimensions; hence they are at increased risk of obstructive sleep apnea [19]. This should be specifically enquired about pre-operatively.

Pre-operative evaluation of kidney, liver and thyroid function, glucose control in patients with diabetes, and clotting function should be verified.

Cognitive and otologic compromise should be elicited if present, to allow for an individualized explanation of the procedure and discussion of anesthetic plan with the family and/or health proxy.

Particular preparation for airway management

TS patients are at risk of a difficult intubation, endobronchial intubation and accidental extubation [17,18,20-22].

Increased risk of a difficult intubation is conferred by:

- A short, webbed neck
- High arched palate
- Micrognathia and retrognathia
- Limited jaw subluxation
- Potential severe limitation in neck movement
- Increased incidence of multiple joint contractures which may include the temporomandibular joint

Furthermore, patients with TS have a short tracheal length, and higher location of its bifurcation, noted in one case report to be at the level of the sternoclavicular joint (instead of opposite the T2 vertebra as is normal) with an adult tracheal tube length of 13.5 cm [20]. This predisposes to both endobronchial intubation and accidental endotracheal extubation.

Similarly, inadvertent left endobronchial intubation has been described in a case report, occurring at the time of pericardial drainage, highlighting the difficulty of maintaining the endotracheal tube in the proper position [21].

Past anesthetic records should be reviewed prior to undertaking airway manipulation. A premedication to reduce gastric contents and pH may be prescribed. Where a difficult airway is anticipated fiberoptic intubation should be performed either awake or under sedation with spontaneous breathing (e.g., propofol and remifentanyl or dexmedetomidine). Alternative airway management plans should be discussed in advance, including a supraglottic and a surgical airway, with the appropriate equipment and personnel available.

Particular preparation for transfusion or administration of blood products

Severe liver disease can result in a complex coagulopathy state and decreased drug metabolism. Hemostasis should be evaluated pre-operatively and corrected if necessary [17,18]. In the event of bleeding, thromboelastography tests are useful to guide the administration of hemostatic agents [23].

In the newborn period, there is an association with a transient thrombocytopenia (31% of patients). Due to a single functional X chromosome, girls can inherit X-linked conditions such as hemophilia but this has only rarely been described [24].

Refer to a hematologist if there is concern regarding prolonged bleeding events, a platelet count <100,000/uL, or between 100-150,000/uL in patients that need surgery [24].

Particular preparation for anticoagulation

Not reported.

Particular precautions for positioning, transportation and mobilization

Exercise caution regarding displacement of endotracheal tube intra-operatively.

Potential spinal deformities, such as scoliosis and kyphosis, may require additional care and padding when positioning the patient.

Ensure normothermia is maintained, particularly if the patient presents with poorly controlled hypothyroidism.

Interactions of chronic disease and anesthesia medications

Not reported.

Anesthetic procedure

If the patient is hypothyroid or diabetic, consider premedication to ensure reduced gastric pH in the event of aspiration. Ensure optimal perioperative medical management of blood glucose [18].

In the adult TS patient, the principal perioperative concern relates to the risk of aortic dissection, and the BP should be tightly controlled [17,18].

If general anesthesia is used, ketamine and pancuronium should be used with caution in patients with known aortic coarctation or hypertension due to the risk of severe hypertension [18].

If the patient has severe liver dysfunction, use lower doses of benzodiazepines and use hepatically metabolized neuromuscular agents with caution. Dosing of renally excreted drugs should be modified and NSAIDs should be avoided if the patient has renal insufficiency [17,18].

Opioids, propofol, local anesthetics, volatile agents and nitrous oxide have been used without any complication [17,20].

Central neuraxial blockade may be difficult due to the patient's spinal abnormalities or may be contraindicated in the case of spina bifida occulta in which case peripheral nerve blockade can be employed.

Antibiotic prophylaxis should be used in case of valvular heart disease (e.g., bicuspid aortic valve) in accordance with current guidelines.

Particular or additional monitoring

Consider placing an arterial line to facilitate tight control of BP.

Possible complications

Difficult venipuncture.

Endobronchial intubation – detected by a sudden increase in airway pressures, unilateral absence of breath sounds on auscultation and reduced peripheral oxygen saturations.

Accidental extubation.

Severe perioperative hypertension.

Postoperative care

If the patient is clinically hypothyroid, hypothermia and hypotension caused by anesthetic agents may delay recovery from anesthesia.

If the patient is euthyroid, there are no reports of any specific issues to consider post-operatively.

Disease-related acute problems and effect on anesthesia and recovery

Severe perioperative hypertension in patients with known or previous aortic coarctation can result in aortic dissection.

Ambulatory anesthesia

No specific contraindications to ambulatory anesthesia.

Obstetrical anesthesia

Natural pregnancies have been reported in 2-7% of patients with TS but increasingly assisted fertility techniques are being used with oocyte donation [25-27].

All pregnancies are considered to be high risk and TS patients have higher maternal mortality rate than the general population on account of the high proportion of patients with cardiovascular malformations. The most serious complications comprise worsening of pre-existing hypertension or aortic dissection, which although rare, occurs six times more frequently and at younger ages than the general population [25-28].

Following the death of two patients with TS in France from acute aortic dissection, the French National Authority for Health released comprehensive guidelines regarding the management of women with TS in 2010 [25]. This mandates pre-pregnancy risk counseling and a comprehensive checkup. This comprises general, gynecological and cardiovascular examination, evaluation of BP including Doppler US of the renal arteries and MRI of the heart and aorta with repeat aortic diameter evaluation, renal ultrasound, thyroid and liver function tests and blood glucose level.

Antenatal care should be multidisciplinary and occur in a tertiary center [25,26]. Hypertension should be rigorously treated with beta blockers. There is no clear evidence for prophylactic medication in women with TS who have aortic dilatation. Echocardiography should be performed at the end of the first and second trimesters, and every month during the third trimester. MRI may be used if deemed necessary. The risk of preeclampsia, severe hepatic steatosis and cholestasis is increased in patients with TS and prescription of low dose aspirin is recommended [1,25].

Delivery ideally should occur in a facility with on-site cardiologists and cardiac surgeons. Cesarean section is necessary in up to 85% of cases because of narrowing of the pelvis and to avoid the hemodynamic stress of labor [25,29]. Vaginal delivery with close BP monitoring can take place if there is no fetal-pelvic disproportion or associated disease. An arterial line can be considered for invasive monitoring.

Anesthesia for cesarean delivery can be challenging due to lumbar scoliosis and short stature. Regional anesthesia remains preferable to general anesthesia to avoid sympathetic stimulation during intubation and emergence and to avoid potential complications associated with difficult airway management.

There are several case reports of successful regional anesthesia utilizing careful combined spinal-epidural techniques to avoid hemodynamic instability [26,27,29]. In one case report [26], there was a noticeable delayed onset of motor block, but this has not been replicated in other case reports.

If regional anesthesia fails, consider awake fiberoptic intubation.

Cardiovascular risk persists after delivery. Therefore, women should receive a further ultrasound of the aortic root diameter 5-8 days after delivery [25].

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