orphananesthesia

Anaesthesia recommendations for patients suffering from

22q11.2 deletion syndrome

Disease name: 22q11.2 deletion syndrome

ICD 10: D82.1 (DiGeorge syndrome), Q93.81 (velo-cardio-facial syndrome)

Synonyms: DiGeorge syndrome, velocardiofacial syndrome (VCFS), Shprintzen syndrome, “CATCH-22” syndrome, conotruncal anomaly face syndrome, Takao syndrome

22q11.2 deletion syndrome is a genetic defect, resulting in variable phenotypes including DiGeorge or Shprintzen syndrome. Clinical manifestations may vary, including defects in the cardiovascular system (mostly conotruncal origin), thymus hypoplasia, and velo-pharyngeal malformations. Patients may suffer from neurodevelopmental disorders, including intellectual deficiencies and psychiatric conditions.

Prevalence of 22q11.2 deletion syndrome is approximately 1 in 4,000 live births, making it the most common form of chromosomal microdeletion disorders. The various deformities are a result of prenatal abnormalities of the third and fourth pharyngeal pouches and third branchial arch. Cardiac defects are usually of conotruncal origin, such as tetralogy of fallot, aortic arch interruption, ventricular septal defect (VSD) or persistent truncus arteriosus. Developmental defects of the thymus often lead to T-cell related immunodeficiency, which may be present in 25-30 % of the patients. Affection of the parathyroid glands may lead to hypocalcaemia, presenting as tetany or seizures.

Various neurodevelopmental or psychiatric disorders may be present, ranging from mild cognitive impairment to recurrent episodes of schizophrenia, manifesting as early as childhood or puberty. Velopharyngeal anomalies are common, resulting in an increased probability of cleft lip and palate, as well as choanal atresia or various nasal breathing obstructions. Pharyngeal insufficiency may lead to reflux and feeding difficulties especially in infancy. Laryngeal webs may also be associated with the disorder.

Other features may include renal malformations, hearing loss and skeletal deformities such as scoliosis or cervical spine abnormalities.

Medicine in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

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Typical surgery

Due to the high incidence of cardiac malformations in 22q11.2 deletion syndrome, many patients have to undergo various cardio-surgical corrections, often in early infancy. Closure of atrial or ventricular septal defects and reconstruction of the right ventricular outflow tract are the most common procedures but because of the variability, a wide range of surgical treatments may be necessary.

Velopharyngeal insufficiency, cleft palate or nasal breathing obstructions may require surgical management, including palatoplasty, posterior pharyngeal flap creation, rhino- or pharyngoplasty.

Although most patients suffer only from mild cognitive deficiencies, sedation or anaesthesia may be necessary at any age to facilitate various diagnostic or invasive procedures.

Type of anaesthesia

The most commonly described procedures in 22q11.2 are general anaesthesias combining volatile inhalational agents with opioid analgesics, but total intravenous anaesthesia also seems practicable. There are no general contraindications for any common hypnotics, opioid analgesics or non-depolarizing muscle relaxants. Use of suxamethonium has been reported but potential side effects should be weighed against more rapid onset time. The individual selection of anaesthetic agents should be based on the patients pre-existing conditions with special focus on cardiac malformations as well as type and duration of the planned surgery.

Contraindications to neuroaxial blockage, such as cardiac abnormalities, anticoagulation and scoliosis may be found regularly.

Successful peripheral regional anaesthesia in patients with 22q11.2 deletion syndrome has been published in literature and can be considered whenever feasible regarding patient safety and surgical procedure. In cardiac risk patients, epinephrine admixture to local anaesthetics should be avoided, since it may cause tachycardia and arrhythmias.

Because of the broad possibility of different approaches, the anaesthetist is encouraged to take aspects of patient comfort and individual preferences into account.

Necessary additional diagnostic procedures (preoperative)

Preoperative routine diagnostics should focus on assessing cardiac malformations and previous corrective surgery. A thorough assessment including anamnesis and clinical fitness as well as clinical examination should routinely be performed in any patient, regardless of pre-existing condition or planned anaesthesia. Previous examinations, procedures or surgeries should be taken into account. An ECG is advised even in younger and otherwise asymptomatic patients to detect potential structural changes or arrhythmias.

Any clinical sign of heart disease such as cyanosis, shortness of breath or decline in physical stamina should entail a complete cardiovascular status assessment, including echocardiography as well as the expert opinion of a cardiologist familiar with congenital heart defects.

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Every patient presenting with 22q11.2 deletion syndrome should be investigated for potential thymus hypoplasia and resulting immunological, haematological or endocrine deficiencies. The anaesthetist should inquire about previous infections which might indicate potential immunodeficiency.

Lab work should include total blood count and differential. A low number of lymphocytes or hint to any pre-existing immunodeficiency may justify an absolute T-cell count. Mild thrombocytopenia may be present but is usually not of clinical relevance. Ionized calcium levels should be routinely checked to detect patients with hypocalcaemia.

Particular preparation for airway management

Literature is still inconclusive as to whether 22q11.2 deletion syndrome per se is associated with an increased likelihood of a difficult airway. However, in the presence of above-mentioned anatomical abnormalities to the airway in certain individuals, management will be predictably difficult.

Choanal atresia, if not corrected, may complicate bag and mask ventilation and render naso-tracheal intubation impossible. Especially in new-borns and infants such complications should be taken into account before inducing general anaesthesia.

Smaller intubation equipment than usually necessary should be available, since findings of a narrower airway and short trachea have been reported.

An increased rate of dysphagia and gastro-oesophageal reflux may lead to an increased risk of aspiration during induction of general anaesthesia.

Particular preparation for transfusion or administration of blood products

Intraoperative calcium levels should be closely monitored. In case of transfusion, calcium should be reassessed and meticulously substituted to avoid hypocalcaemic crisis.

If the patient shows signs of immunodeficiency or if the immunologic status is unknown, irradiated blood products should be preferred, especially in infants younger than 12 months of age.

Particular preparation for anticoagulation

The general rules for perioperative anticoagulation needs apply. In the presence of cardiac defects and resulting corrective surgery, patients may already receive anticoagulants, and any changes to this regime require expert cardiological or cardiosurgical expertise.

Particular precautions for positioning, transport or mobilisation

Not reported. Potential spine malformation such as scoliosis and cervical spine anomalies may require extra care when positioning patients for surgery.

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

Several psychiatric drugs may prolong QT intervals. Possible interactions should be considered, especially when applying antibiotics and antiemetics that are also known to increase QT prolongation. Hypocalcaemia, even if clinically unapparent, may worsen this interaction.

Anaesthesiologic procedure

Depending on the complexity of preexisting cardiac conditions, cardiac output, blood pressure, and heart rate should be kept within normal ranges using all means necessary.

Perioperative sympathonergic stress should be avoided to prevent acute decompensation of underlying cardiac conditions. Especially in new-borns and infants with uncorrected tetralogy of Fallot where cyanotic 'tet spells' must be avoided to prevent hypoxia and acute cardiac failure.

In patients with known obstructive sleep apnoea or those undergoing correction of nasal or pharyngeal malformations, sedative premedication such as benzodiazepines or long acting opioids should not be administered to avoid respiratory complications.

Particular or additional monitoring

Depending on the individual cardiac status and previous corrective surgery, additional haemodynamic monitoring may be indicated. Regular blood gases should be conducted in every patient with known hypo-parathyroidism to avoid hypocalcaemia.

Continuous invasive blood pressure measurement should be considered in patients that show any signs of cyanosis or shortness of breath as well as in major surgery.

Additional cardiac monitoring, such as transoesophageal echocardiography, central venous and pulmonary artery cannulation or other methods for haemodynamic measurement may be necessary in some patients.

Possible complications

Hypocalcaemia may lead to paraesthesias, generalized tetany and seizures, which may be difficult to diagnose in new-borns and infants.

QT prolongations are known to cause malignant arrhythmias such as Torsade de pointes, which require immediate treatment.

An increased rate of postoperative infections is to be expected in patients showing T-cell immunodeficiency. In case of non-irradiated blood transfusion those individuals are at potential risk to develop transfusion-associated graft-versus-host disease (TA-GvHD), which is often difficult to manage and presents with mortality rates of up to 90%.

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Aspiration pneumonia due to increased reflux has been reported and may be confused with cardiogenic pulmonary oedema.

Postoperative care

Patients with 22q11.2 deletion are at an increased risk of obstructive sleep apnoea due to general muscular hypotonia and velopharyngeal abnormalities. Especially after correction of pharyngeal insufficiency, some patients develop significant pharyngeal obstruction, requiring prolonged surveillance in a recovery or intensive care unit. Postoperative CPAP ventilation may reduce surveillance time, and respiratory complications.

Information about emergency-like situations / Differential diagnostics

Seizures are quite common in patients suffering from 22q11.2 deletion syndrome, but the underlying cause is often difficult to identify. Seizures may be of hypocalcemic origin, but various forms of epilepsy may also be present. Magnesium and calcium levels should be checked and substituted if necessary.

Ambulatory anaesthesia

Not described in literature. Seems not advisable due to the extent of pre-, intra- and post-operative special needs – as mentioned above. May be practicable in certain combinations of very minor surgery in mildly affected individuals.

Obstetrical anaesthesia

General fertility is not affected but accompanying heart disease and psychological conditions may complicate pregnancy and delivery. Increased rates of “small for gestation age” and stillbirths are reported. Systemic anticoagulation may lead to an increased bleeding risk during pregnancy and delivery. Patients with known 22q11.2 deletion should visit obstetric facilities that are specialized in high-risk deliveries and experienced in treating patients with cardiac malformations if relevant.

Contraindications (anticoagulation, cardiac malformations, scoliosis, etc.) to neuroaxial blockade may be present. Because of the high variability of 22q11.2 deletion syndrome, the risks of general anaesthesia should be evaluated and compared with those of neuroaxial blockade in every obstetrical patient so that an individual approach entailing the lowest risks for mother and child can be made.

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Literature and internet links

1. Kobrynski LJ, Sullivan KE. Velocardiofacial syndrome, DiGeorge syndrome: the chromosome 22q11.2 deletion syndromes. Lancet 2007;370(9596):1443-1452
2. Schwinger E, Devriendt K, Rauch A, Philip N. Clinical utility gene card for: DiGeorge syndrome, velocardiofacial syndrome, Shprintzen syndrome, chromosome 22q11.2 deletion syndrome (22q11.2, TBX1). Eur J Hum Genet 2010;18(9):1-3
3. Tézenas Du Montcel S, Mendizabai H, Aymé S, Lévy A, Philip N. Prevalence of 22q11 microdeletion. J Med Genet 1996;33(8):719
4. Momma K. Cardiovascular Anomalies Associated With Chromosome 22q11.2 Deletion Syndrome. Am J Cardiol 2010;105(11):1617-1624
5. Bassett AS, McDonald-McGinn DM, Devriendt K, et al. Practical guidelines for managing patients with 22q11.2 deletion syndrome. J Pediatr 2011;159(2):332-9.e1
6. Fung WLA, Butcher NJ, Costain G, et al. Practical guidelines for managing adults with 22q11.2 deletion syndrome. Genet Med 2015;17(8):599-609
7. Twite MD, Ing RJ. Tetralogy of Fallot: perioperative anesthetic management of children and adults. Semin Cardiothorac Vasc Anesth 2012;16(2):97-105
8. Poldermans D, Bax JJ, Boersma E, et al. Guidelines for pre-operative cardiac risk assessment and perioperative cardiac management in non-cardiac surgery. Eur Heart J 2009;30(22): 2769-2812
9. McLean-Tooke A, Spickett GP, Gennery AR. Immunodeficiency and autoimmunity in 22q11.2 deletion syndrome. Scand J Immunol 2007;66(1):1-7
10. Crockett DJ, Goudy SL, Chinnadurai S, Wootten CT. Obstructive Sleep Apnea Syndrome in Children with 22q11.2 Deletion Syndrome after Operative Intervention for Velopharyngeal Insufficiency. Front Pediatr 2014;2:84
11. Schwengel D a, Sterni LM, Tunkel DE, Heitmiller ES. Perioperative management of children with obstructive sleep apnea. Anesth Analg 2009;109(1):60-75
12. Chan C, Costain G, Ogura L, Silversides CK, Chow EWC, Bassett AS. Reproductive Health Issues for Adults with a Common Genomic Disorder: 22q11.2 Deletion Syndrome. J Genet. Couns 2015;24(5):810-821
13. Passariello M, Perkins R. Unexpected postoperative tachycardia in a patient with 22q11 deletion syndrome after multiple dental extractions. Paediatr Anaesth 2005;15(12):1145-1146
14. Cohen V, Powell E, Lake C. Failure of neuraxial anaesthesia in a patient with Velocardiofacial syndrome. International Journal of Obstetric Anesthesia. Vol 20. Netherlands 2011:256-259
15. Kienle F, Muenster T, Wurm J, Prottengeier J. Anaesthesia and orphan disease: 22q11.2 Microdeletion disorder (DiGeorge syndrome). Eur J Anaesthesiol (EJA) 2015;32(12):888-889.

Online Resources:

Practical Guidelines by Society of Cardiovascular Anesthesiologists:
http://www.scahq.org/ClinicalPracticeGuidelines/Guidelines.aspx

Patients and Parents information:
http://www.22q.org/
http://www.vcfsef.org

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This guideline has been prepared by:

Authors
Florian Kienle and Johannes Prottengeier, Anaesthesiologists, University Hospital Erlangen, Germany
Florian.Kienle@kfa.imed.uni-erlangen.de
johannes.prottengeier@googlemail.com

Peer revision 1
Natalie Forshaw, Anaesthesiologist, Great Ormond Street Hospital, London, United Kingdom
natalieforshaw@doctors.org.uk

Peer revision 2
Richard Kirschner, Section of Plastic and Reconstructive Surgery, Nationwide Children's Hospital, The Ohio State University College of Medicine, Columbus OH, USA
richard.kirschner@nationwidechildrens.org

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