orphanaesthesia

Anaesthesia recommendations for

Kleefstra Syndrome

Disease name: Kleefstra Syndrome

ICD 10: Q93.5

Synonyms: 9q subtelomeric deletion syndrome, 9q- syndrome, 9q34.3 deletion syndrome, 9q34.3 microdeletion syndrome, chromosome 9q deletion syndrome

Disease summary: Kleefstra syndrome is a very rare genetic disorder with unknown prevalence that may be associated with a distinctive facial appearance, muscular hypotonia, heart defects, frequent respiratory infections, seizures and urogenetic defects. These patients may also have characteristics of autism, developmental/speech delay and other psychiatric disorders.

Kleefstra syndrome is caused by the deletion of the EHMT1 gene or by mutations that disable its function. This would lead to a perturbation in formation of an enzyme called euchromatic histone methyltransferase (EHMT). A lack of this enzyme impairs proper control of the activity of certain genes in many organs and tissues, resulting in the abnormalities of development and functions that are characteristic of Kleefstra syndrome. Kleefstra syndrome, caused by a microdeletion at 9q34.3 or an intragenic EHMT1 pathogenic variant, is inherited in an autosomal dominant manner. The majority of cases reported to date have been de novo. Males and females are affected equally. Up to date there are just 114 confirmed cases of KS documented in literature, but as many individuals with this condition are not diagnosed, the true prevalence may be much higher. The syndrome has been identified worldwide and in all ethnic groups. Kleefstra Syndrome may involve different parts of the body. This syndrome may include dysmorphic features (microcephaly, brachycephaly, synophrys, hypertelorism, anteverted nares, midface hypoplasia, prognathism, and macroglossia). Patients with Kleefstra Syndrome present usually with developmental and intellectual delay, hypotonia and absent or limited speech. They commonly exhibit an autistic-like behavior or communication disorders affecting social interaction. Apathy and catatonia has been described in adolescents with Kleefstra Syndrome. High birth weight and childhood obesity have been reported. People with Kleefstra syndrome may also have structural brain abnormalities and congenital heart defects (conotruncal heart defect, ASD/VSD, tetralogy of Fallot, aortic coarctation, bicuspid aortic valve, and pulmonic stenosis). In a number of individuals, atrial flutter has been reported. Genitourinary abnormalities (hypospadias, cryptorchidism, vesico-ureteral reflux, hydronephrosis, renal cysts and chronic renal insufficiency) may be present. Seizures have been reported in 30% and can include tonic-clonic seizures, absence seizures, and complex partial epilepsy. Epigastric hernia, tracheo-/bronchomalacia with respiratory insufficiency, and gastroesophageal reflux have been also observed with a tendency to develop severe respiratory infections.

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

Typical surgery

Patients may present at different ages, for different types of surgeries/procedures and exams: such as magnetic resonance imaging, CT scans, otorhinolaryngology or plastic surgery, brainstem auditory evoked response (BAER) study, urology and dental surgery among many others.

Type of anaesthesia

Patients with Kleefstra Syndrome with speech disorders may benefit from sign language or use of pictograms. Patients with autistic like behavior or communication disorders affecting social interaction may benefit from a consultation with child life specialists, if available; or from premedication prior to surgery. Apathy and catatonia has been described in adolescents with Kleefstra Syndrome. The presence of structural brain abnormalities should be documented.

Each patient should be evaluated on an individual basis. The anesthetic management of patients with Kleefstra Syndrome may be complicated by airway problems such as difficult laryngoscopy secondary to dysmorphic features. A careful evaluation and management of a possible difficult airway should be planned. In the presence of a difficult airway, induction of anesthesia with maintenance of spontaneous ventilation and tracheal intubation under safe conditions is highly recommended. Epigastric hernia, gastro esophageal reflux and obesity may increase the risk of aspiration in these patients. The presence of tracheo-/bronchomalacia with respiratory insufficiency, and a tendency to develop severe respiratory infections may predispose to respiratory complications. Regional anesthesia may be indicated and helpful in providing analgesia, in the absence of contraindications.

People with Kleefstra syndrome should be evaluated for congenital heart disease or arrhythmia as well as for pulmonary hypertension. In the presence of pulmonary hypertension, special anesthetic precautions would include availability of inhaled Nitric Oxide (NO) in the peri-operative area and in the operating room if needed. Also, in this case, avoidance of haemodynamic perturbations, especially those increasing heart rate and/or pulmonary resistance, are recommended.

Renal function and genitourinary abnormalities should be documented, and the choice of intra- and peri-operative fluids and medications should be adjusted in the presence of chronic renal insufficiency. Difficulty in placement of a Foley catheter may be encountered in the presence of urogenital abnormalities.

Seizures have been reported in 30% of patients with Kleefstra syndrome and can include tonic-clonic seizures, absence seizures, and complex partial epilepsy. Seizure medications' administration, avoidance of drugs/agents that may lower seizure threshold, and seizure precautions in the perioperative area should be applied.

Necessary additional pre-operative testing (beside standard care)

The preoperative examination should be thoroughly conducted to take into consideration concomitant issues. Baseline neurological/mental status and facial deformities should be assessed. Considerations prior to initiation of anaesthesia care are collecting information about the best approach to deal with the behavioural and communication issues. Evaluation of the airway should be done preoperatively. Patients with Kleefstra Syndrome may have cardiac and respiratory issues, as well as structural brain abnormalities. Baseline cardiac/pulmonary and

brain examination and attention to signs and symptoms of possible problems with evaluation by a specialist may be recommended. The presence of renal problems should be determined. Preoperative evaluation should include the evaluation of possible associated urinary abnormalities.

Type, frequency and severity of seizures should be documented and treatment should be optimized preoperatively.

Particular preparation for airway management

Careful evaluation for difficult tracheal intubation secondary to dysmorphic features is recommended. The presence of facial, mandibular deformities and macroglossia may result in difficulties in mask ventilation and airway maintenance.

Particular preparation for transfusion or administration of blood products

None reported.

Particular preparation for anticoagulation

None reported.

Particular precautions for positioning, transportation and mobilisation

Developmental delay and/or autistic-like behaviour may require help with mobilisation and transport. Prevention of risk of injury from seizures and careful positioning is indicated secondary to hypotonia.

Interactions of chronic disease and anaesthesia medications

There is no known interaction between anaesthetic agents and patient's long term medication. However, special pharmacological considerations for this syndrome are related to possible involvement of vital organs/urological tract that may alter the clearance of medications. Concomitant use of antiepileptic medications may induce the metabolism of some anesthetic medications.

Anaesthetic procedure

Consideration and preparation for a possible difficult airway. Possibility of seizures.

Particular or additional monitoring

Depending on the presence of any cardiac, or structural brain abnormalities with possible increased intracranial pressure. Additional monitoring or more invasive monitoring may be needed depending on the severity and length of the procedure.

Possible complications

Special attention to the following points: Potential difficult airway/injury from agitation/cardiac and neurological abnormalities, seizures. Possible pulmonary infections, and gastroesophageal reflux. Possible renal problems. Possible agitation secondary to behavioural problems and inability to communicate secondary to cognitive and speech delay.

Post-operative care

Documentation and stabilisation: Airway patency, haemodynamic stability, intracranial pressure.
Management of seizures, management of agitation and pain as described above.
Positioning secondary to hypotonia or agitation.

Disease-related acute problems and effect on anaesthesia and recovery

Down syndrome
Smith-Magenis syndrome
Pitt-Hopkins syndrome
Rett syndrome
2q37 deletion syndrome

Ambulatory anaesthesia

Each patient must be evaluated carefully for co-morbidity and/or airway issues. Anaesthesia and surgery to be performed in a medical facility with capacity of taking care of potential complications.

Obstetrical anaesthesia

Only few individuals with Kleefstra Syndrome have been known to reproduce. Anesthesia and surgery is to be performed in a medical facility with capacity of taking care of potential challenges and complications.

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