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Organ: Deutsche Interdisziplinäre Vereinigung für Intensiv- und Notfallmedizin e.V. (DIVI)

De Barsy syndrome

Deletion 9p syndrome

orphanaesthesia

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

SUPPLEMENT NR. 6 | 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

Deletion 9p syndrome

Disease name: Deletion 9p syndrome

ICD 10: Q93.5

Synonyms: Alfi's Syndrome, 9p minus syndrome, Chromosome 9p deletion syndrome

Disease summary: In 1973, Alfi et al. reported three infants with partial deletion of the short arm of chromosome 9 distal to band 9p22 who had several clinical features in common. In 1976, after identifying three additional patients with the same chromosomal deletion, this group described the deletion 9p syndrome.

The deletion 9p syndrome is very rare. It is estimated to occur in one in 50,000 newborns. Since its first description, well over 100 patients have been described in the literature, but there are likely many more people affected who have either not been diagnosed or not been reported. New cases have been published occasionally that describe new features associated with deletion 9p syndrome. Whether these new features are truly part of the syndrome or only accidentally occur together remains unclear.

This syndrome is defined by deletion of the short arm of the 9th chromosome. In most cases, the breakpoint is reported in the bands from 9p21 to 9p24. The majority of cases are de novo deletions, but parental translocations are also reported. The phenotype of deletion 9p is heterogeneous and no clear correlation between breakpoint and clinical features has been established. Common features of the syndrome include mental deficiency, psychomotor and speech delay, craniofacial dysmorphism, and other congenital malformations. The syndrome appears to be balanced between males and females.

Clinical features of deletion 9p syndrome:

Common features of this syndrome include trigonocephaly with prominent forehead, small upslanting palpebral fissures, flat nasal bridge, orbital hypertelorism, long philtrum, low set dysplastic ears and long phalanges with excess of whorls. In a case series of 11 patients, the mean IQ of the patients was 48. However, the intellectual disability can range from mild to severe. Additional malformations include choanal atresia, midface hypoplasia, high arched palate, small mouth, micrognathia, and short webbed neck. Obstructive sleep apnoea may complicate these midfacial malformations. Beyond the craniofacial anomalies, the most common congenital malformations are cardiac defects (ventricular septal defect, patent ductus arteriosus and pulmonary stenosis), inguinal and diaphragmatic hernias, pylorus stenosis, omphalocele, genital and/or gonadal dysgenesis, scoliosis and/or kyphosis, and pectus excavatum. EEG changes, seizure disorders, and developmental delay of speech and motor development with truncal hypotonia are also frequently reported.

Terminal deletions of the short arm of chromosome 9 have been associated with XY sex reversal, with or without additional features of the deletion 9p syndrome. The degree of the sex reversal is variable.

▶ **Citation:** Cakmakkaya OS, Kolodzie K: Deletion 9p syndrome. Anästh Intensivmed 2021;62:S106–S114. DOI: 10.19224/ai2021.S106

Recurrent ear, respiratory and urinary tract infections are reported frequently in this patient population. Recurrent aspirations can be attributed to muscular hypotonia with impaired swallowing and coughing, gastrooesophageal reflux, diaphragmatic hernias, and pylorus stenosis. Allergies and asthma are common, but specific immunological impairments are rarely identified.

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

Correction of craniosynostosis, repair of choanal atresia, inguinal hernia, diaphragmatic hernia, omphalocele, scoliosis, insertion of ear tubes, correction of anomalies of external genitalia.

Type of anaesthesia

Although no specific agents or types of anaesthesia can be recommended for all patients, general anaesthesia might be the most feasible anaesthetic regimen given the nature of the common surgical interventions and the young age at which these procedures are usually performed. However, because of craniofacial dysmorphism, anaesthesiologists must prepare to manage a difficult airway.

Neuroaxial anaesthesia or analgesia may be indicated for certain surgical procedures, but spinal deformities might limit its relevance.

In addition, as with any patient with a seizure disorder, cerebral toxicity threshold of local anaesthetics may be lower. Therefore, if neuroaxial or peripheral regional anaesthesia is proposed in patients with deletion 9p syndrome with a seizure disorder, doses of agents must be adjusted to decrease peak plasma concentrations, especially in the newborn and young infant.

Necessary additional pre-operative testing (beside standard care)

Since deletion 9p is a syndromic disorder and congenital anomalies should be expected, the past medical history must be investigated carefully.

Because ventricular septal defect, patent ductus arteriosus and pulmonary stenosis frequently accompany this disorder, a cardiac evaluation is usually performed when the diagnosis of the deletion 9p syndrome is confirmed. These records as well as recent cardiac evaluations and current status should be reviewed pre-operatively.

If cardiac defects are present, the need for pre-procedural antibiotic endocarditis prophylaxis must be assessed and prescribed in accordance with society guidelines.

Because of the frequent pulmonary infections in these patients, the respiratory system should be evaluated closely. In most cases, a meticulous physical examination and history is sufficient for a pre-operative evaluation. In the setting of new or significant findings, a chest X-ray or other imaging might be indicated. Close communication with the child's paediatrician, primary care physician, or pulmonologist may provide critical insight into the patient’s current status.

If asthma, pulmonary malformations and/or severe scoliosis further impair respiratory function, pre-operative pulmonary function tests may provide important data to define anaesthetic management.

Gastrooesophageal reflux and pyloric stenosis increase the risk for aspiration during induction of general anaesthesia. Administering a proton pump inhibitor and/or citric acid/sodium citrate pre-operatively might be indicated. The need for a rapid sequence induction should be carefully assessed.

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Patients with deletion 9p syndrome who also have EEG abnormalities and/or seizure disorders may have an increased risk for peri-operative seizures. Antiepileptic drug levels should be reviewed. If levels have not been measured recently, obtaining a pre-operative value should be considered. In addition, in consultation with the neurologist, an IV regimen should be established, especially in the setting of vomiting, strict fasting, or anticipated NPO status post-operatively.

Radiologic evaluation for rib and vertebral anomalies is recommended if a neuroaxial anaesthetic or analgesic technique is considered.

Particular preparation for airway management

Because the common features of the deletion 9p syndrome include craniofacial anomalies such as craniostenosis, midfacial hypoplasia, cleft palate/high arched palate, micrognathia, small mouth, short neck and choanal atresia, these patients incur a risk for a compromised airway, especially during induction of general anaesthesia. The risk of a difficult airway situation must be carefully weighed against the need for a rapid sequence induction (e.g., due to pylorus stenosis, gastrooesophageal reflux).

In the only case report focused on the anaesthetic management of a patient with deletion 9p syndrome, Cakmakkaya et al. described a 5-year-old girl with micrognathia and a short neck as well as gastrooesophageal reflux who underwent laparoscopic Nissen fundoplication under general anaesthesia. The critical aspect of this case was a difficult intubation. Laryngoscopy revealed a Cormack and Lehane grade III view. In addition, inserting the endotracheal tube (ET) placement was complicated by a trachea much narrower than expected for age.

In patients with craniofacial dysmorphism, reviewing the anaesthetic history followed by a meticulous pre-operative airway examination are critical. This process should be considered to anticipate and plan for a difficult mask ventilation, laryngoscopy and/or intubation. The difficult airway algorithm should be communicated to all participating providers.

Difficult airway equipment including supraglottic devices, differently sized ET tubes and a size-appropriate fibre-optic device should be readily available. A video laryngoscope has been proven to be useful in some cases of difficult airway management. Equipment and expertise to secure the airway surgically should be in place.

Particular preparation for transfusion or administration of blood products

No special considerations.

Particular preparation for anticoagulation

As appropriate for physical condition and comorbidities.

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Particular precautions for positioning, transportation and mobilisation

As appropriate for physical condition and comorbidities.

Interactions of chronic disease and anaesthesia medications

Antiepileptic medications often either induce or inhibit cytochrome P450 isoenzymes in hepatic metabolism and, therefore, can decrease or increase plasma concentrations of several drugs used peri-operatively, such as beta-blockers, calcium channel antagonists, antibiotics, or warfarin.

Anaesthetic procedure

The intraoperative anaesthetic management should be based on the patient's cardiac, pulmonary, renal and neurologic comorbidities.

Asthma, recurrent pulmonary infections and chronic aspiration may lead to a hyper-reactive airway and difficult ventilation during induction and intraoperatively. Sevoflurane is an appropriate anaesthetic agent for induction as well as maintenance of anaesthesia.

In patients with seizure disorders, the epileptogenic properties of anaesthetics and other medications used peri-operatively should be considered. Premedication with a benzodiazepine might be warranted. Hyperventilation should be avoided, especially in newborns/infants during an induction with sevoflurane, as this may decrease the threshold for seizures.

Literature suggests a decreased MAC of volatile anaesthetics as well as overall lower BIS values in children with intellectual disabilities. In addition, pre-existing muscular hypotonia might reduce the amount of muscle relaxants needed.

Particular or additional monitoring

As appropriate for physical status, extent of surgery and comorbidities.

Possible complications

Summary of possible peri-anaesthetic complications (for a more detailed explanation see above and chapters below):

Anaesthesia induction:

- Difficult airway management
- Regurgitation, aspiration
- Seizures.

Intraoperative:

- Ventilation difficulties.

Emergence:

- Delayed emergence
- Upper airway obstruction
- Regurgitation, aspiration
- Seizures.

Post-operative care

Due to residual effects of anaesthetic and analgesic agents, patients with craniofacial anomalies incur a higher risk of upper airway obstruction, especially in the early post-anaesthetic period. In addition, hypotonia can contribute to impaired post-anaesthetic respiratory function, and gastrooesophageal reflux increases the risk of post-operative aspiration. Therefore, prolonged post-operative monitoring may be necessary.

Patients with intellectual disability and speech delay often cannot express their needs, including the level of pain. A family member or caretaker with close relationship to the patient at the bedside may not only calm the patient but also help the post-anaesthetic care team to better understand the patient's needs.

Disease-related acute problems and effect on anaesthesia and recovery

Recurrent ear, urogenital or respiratory infections are common in patients with deletion 9p syndrome. In case of peri-operative infection signs, the possibility of infections not related to surgery should also be kept in mind.

Delayed recovery from anaesthesia can be related to an increased sensitivity to anaesthetic medications. However, pre-existing muscular hypotonia might mimic prolonged anaesthetic effects. It is important to evaluate and document the pre-operative functional status to be able to recognise the return-to-normal function in each individual patient.

Ambulatory anaesthesia

In general, procedures should be performed in a medical centre with multidisciplinary resources and experience in managing syndromic patients.

The feasibility of ambulatory anaesthesia largely depends on the individual patient's comorbidities. Since difficult airway management and/or delayed or complicated recovery are common, in general, we do not recommend ambulatory anaesthesia.

Obstetrical anaesthesia

In cases of deletion 9p syndrome described in the literature, the syndrome was diagnosed at birth or later in life. Abnormal pregnancy or delivery are rarely reported in retrospect. Although often low considering gestational age, Apgar scores seem to be within normal range.

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Table 1: Common features of the deletion 9p syndrome (with references).

Craniofacial appearance	▪ Trigonocephaly ▪ Craniosynostosis ▪ Mid-facial hypoplasia ▪ Flat nasal bridge ▪ Long philtrum ▪ Micrognathia ▪ High-arched palate ▪ Upslanting palpebral fissures ▪ Epicanthus ▪ Hypertelorism ▪ Highly arched eyebrows ▪ Low hair line ▪ Webbed neck ▪ Short neck [1–3]
Organ Systems	
Nervous System	▪ Mental retardation ▪ Motor development delay ▪ Speech delay ▪ Muscular hypotonia ▪ EEG changes/seizures [2,4,5]
Cardiovascular System	▪ Ventricular septal defect ▪ Patent ductus arteriosus ▪ Pulmonary stenosis [6–8]
Respiratory System	▪ Choanal atresia ▪ Pulmonary hypoplasia ▪ Laryngomalacia [3,9,10]
GI System	▪ Diaphragmatic hernia ▪ Gastroesophageal reflux ▪ Duodenal stenosis ▪ Umbilical/inguinal hernia ▪ Omphalocele [5,8,9]
Urinary System	
Genital System	▪ Impaired gonadal development ▪ Abnormal external genitalia development ▪ Hypospadias ▪ Ambiguous genitalia [2,8,11,12]
Musculoskeletal System Vertebrae Extremities	▪ Scoliosis [2,9] ▪ Long middle phalanges of the fingers ▪ Long fingers and toes ▪ Increased number of whorls on the fingers ▪ Foot positioning defects ▪ Simian crease [1,2]

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