Aktiv Druck & Verlag GmbH | ISSN 0170 - 5334 I 02330

www.ai-online.info

61. Jahrgang | Oktober 2020

A&I

ANÄSTHESIOLOGIE & INTENSIVMEDIZIN

Offizielles Organ: Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin e.V. (DGAI)
Berufsverband Deutscher Anästhesisten e.V. (BDA)
Deutsche Akademie für Anästhesiologische Fortbildung e.V. (DAAF)
Organ: Deutsche Interdisziplinäre Vereinigung für Intensiv- und Notfallmedizin e.V. (DIVI)

Kleefstra Syndrome

Leprosy

orphanaesthesia

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

SUPPLEMENT NR. 20 | 2020

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:

www.ai-online.info/Orphsuppl
www.orphananesthesia.eu

Projektleitung
Prof. Dr. Tino Münster, MHBA
Chefarzt
Klinik für Anästhesie und operative Intensivmedizin
Krankenhaus Barmherzige Brüder Regensburg
Prüfeninger Straße 86
93049 Regensburg,
Deutschland
Tel.: 0941 369-2350
E-Mail: Tino.Muenster@barmherzige-regensburg.de

DGAI
Deutsche Gesellschaft für Anästhesiologie & Intensivmedizin
www.dgai.de

A&I
ANÄSTHESIOLOGIE & INTENSIVMEDIZIN
www.ai-online.info

orphananesthesia
a project of the German Society of Anaesthesiology and Intensive Care Medicine
www.orphananesthesia.eu

orphananesthesia

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 the 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 behaviour or communication disorders affecting social interaction. Apathy and catatonia have 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% of the patients and can include tonic-clonic seizures, absence seizures, and complex partial epilepsy. Epigastric hernia, tracheo-/bronchomalacia with respiratory insufficiency, and gastro-oesophageal reflux have been also observed with a tendency to develop severe respiratory infections.

▶ **Citation:** Abdallah C: Kleefstra Syndrome. Anästh Intensivmed 2020;61:S358–S364.
DOI: 10.19224/ai2020.S358

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

© Anästh Intensivmed 2020;61:S358–S364 Aktiv Druck & Verlag GmbH

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 behaviour 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 have 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 anaesthetic 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 anaesthesia with maintenance of spontaneous ventilation and tracheal intubation under safe conditions is highly recommended. Epigastric hernia, gastro-oesophageal 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 anaesthesia 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 anaesthetic 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 the 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 the seizure threshold, and seizure precautions in the peri-operative area should be applied.

Necessary additional pre-operative testing (beside standard care)

The pre-operative 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 pre-operatively. 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. Pre-operative evaluation should include the evaluation of possible associated urinary abnormalities.

Type, frequency and severity of seizures should be documented and the treatment should be optimised pre-operatively.

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 anaesthetic medications.

Anaesthetic procedure

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

© Anästh Intensivmed 2020;61:S358–S364 Aktiv Druck & Verlag GmbH

Particular or additional monitoring

Monitoring depends 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 should be given to the following points: Potential difficult airway/injury from agitation/cardiac and neurological abnormalities, seizures. Possible pulmonary infections, and gastro-oesophageal 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 have 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. Anaesthesia and surgery is to be performed in a medical facility with capacity of taking care of potential challenges and complications.

© Anästh Intensivmed 2020;61:S358–S364 Aktiv Druck & Verlag GmbH

References

1. Cormier-Daire V, Molinari F, Rio M, Raoul O, de Blois MC, Romana S, et al. Cryptic terminal deletion of chromosome 9q34: a novel cause of syndromic obesity in childhood? J Med Genet 2003;40:300–303
2. Dawson AJ, Putnam S, Schultz J, Riordan D, Prasad C, Greenberg CR, et al. Cryptic chromosome rearrangements detected by subtelomere assay in patients with mental retardation and dysmorphic features. Clin Genet 2002; 62:488–494
3. Kleefstra T, Brunner HG, Amiel J, Oudakker AR, Nillesen WM, Magee A, et al. Loss-of-function mutations in euchromatin histone methyl transferase 1 (EHMT1) cause the 9q34 subtelomeric deletion syndrome. Am J Hum Genet 2006a;79:370–377
4. Stewart DR, Kleefstra T. The chromosome 9q subtelomere deletion syndrome. Am J Med Genet C Semin Med Genet 2007;145C:383–392
5. Willemsen MH, Vulto-van Silfhout AT, Nillesen WM, Wissink-Lindhout WM, van Bokhoven H, Philip N, et al. Kleefstra: Update on Kleefstra Syndrome. Mol Syndromol 2012;2:202–2012
6. Kleefstra T, Nillesen WM, Yntema HG. Kleefstra Syndrome. October 5, 2010; Last Update: May 7, 2015. (Eds): GeneReviews® Pagon RA, Adam MP, Ardinger HH, Wallace SE, Amemiya A, Bean L, et al. Seattle (WA): University of Washington, Seattle:1993–2017.

© Anästh Intensivmed 2020;61:S358–S364 Aktiv Druck & Verlag GmbH

Date last modified: March 2019

This recommendation was prepared by:

Author

Claude Abdallah, MD, MSc, Associate Professor, George Washington University, Children's National Health System, Washington DC, USA
cabdalla@cnmc.org

Disclosure The author has no financial or other competing interest to disclose. This recommendation was unfunded.

This recommendation was reviewed by:

Reviewers

Johannes Prottengeier, Anaesthesiologist, Priv.-Doz. Dr. DESA, MHBA, Department of anaesthesiology and intensive care medicine, University Hospital Erlangen, Germany
Johannes.Prottengeier@kfa.imed.uni-erlangen.de

Usha Krishnan, MD, FAHA, Professor, Pediatrics (Cardiology), CUMC, Associate Director Pulmonary Hypertension Center, Columbia University Medical Center, New York, USA
usk1@cumc.columbia.edu

Disclosures The reviewers have no financial or other competing interest to disclose.

© Anästh Intensivmed 2020;61:S358–S364 Aktiv Druck & Verlag GmbH

Herausgeber

DGAI
Deutsche Gesellschaft für Anästhesiologie und Intensivmedizin e.V.
Präsident: Prof. Dr. R. Rossaint, Aachen

BDA
Berufsverband Deutscher Anästhesisten e.V.
Präsident: Prof. Dr. G. Geldner, Ludwigsburg

DAAF
Deutsche Akademie für Anästhesiologische Fortbildung e.V.
Präsident: Prof. Dr. H. Bürkle, Freiburg

Schriftleitung

Präsident/in der Herausgeberverbände

Gesamtschriftleiter/Editor-in-Chief:
Prof. Dr. Dr. Kai Zacharowski, Frankfurt

Stellvertretender Gesamtschriftleiter/Deputy Editor:
Prof. Dr. T. Volk, Homburg/Saar

CME-Schriftleiter/CME-Editor:
Prof. Dr. W. Zink, Ludwigshafen

Redaktionskomitee/Editorial Board

Redaktion/Editorial Staff

Carolin Sofia Kopp B.A.
Korrespondenzadresse: Roritzerstraße 27 | 90419 Nürnberg | Deutschland
Tel.: 0911 9337812 | Fax: 0911 3938195
E-Mail: anaesth.intensivmed@dgai-ev.de

Verlag & Druckerei

Aktiv Druck & Verlag GmbH
An der Lohwiese 36 |
97500 Ebelsbach | Deutschland
www.aktiv-druck.de

Geschäftsführung
Wolfgang Schröder | Jan Schröder | Nadja Schwarz
Tel.: 09522 943560 | Fax: 09522 943567
E-Mail: info@aktiv-druck.de

Anzeigen | Vertrieb
Pia Müller | Robert Kux
Tel.: 09522 943570 | Fax: 09522 943577
E-Mail: anzeigen@aktiv-druck.de

Verlagsrepräsentanz
Jürgen Distler
Roritzerstraße 27, 90419 Nürnberg
Tel.: 0171 9432534 | Fax: 0911 3938195
E-Mail: jdistler@bda-ev.de

Herstellung | Gestaltung
Pia Müller | Robert Kux |
Stefanie Triebert
Tel.: 09522 943570 | Fax: 09522 943577
E-Mail: ai@aktiv-druck.de

Titelbild
Gestaltung: Klaus Steigner
Paumgartnerstraße 28 | 90429 Nürnberg
E-Mail: mazyblue@klaus-steigner.de
www.klaus-steigner.de

Erscheinungsweise 2020
Der 61. Jahrgang erscheint jeweils zum Monatsanfang, Heft 7/8 als Doppelausgabe.

Bezugspreise (inkl. Versandkosten):

- **Einzelhefte** 30,- €
- **Jahresabonnement:**

Europa (ohne Schweiz) (inkl. 7 % MwSt.)	258,- €
Schweiz	266,- €
Rest der Welt	241,- €

Mitarbeiter aus Pflege, Labor, Studenten und Auszubildende (bei Vorlage eines entsprechenden Nachweises)

Europa (ohne Schweiz) (inkl. 7 % MwSt.)	94,- €
Schweiz	90,- €
Rest der Welt	94,- €

Für Mitglieder der DGAI und/oder des BDA ist der Bezug der Zeitschrift im Mitgliedsbeitrag enthalten.

Die Beiträge aus der A&I finden Sie online unter: **www.ai-online.info**

Allgemeine Geschäfts- und Lieferbedingungen

Die allgemeinen Geschäfts- und Lieferbedingungen entnehmen Sie bitte dem Impressum auf www.ai-online.info

Indexed in **Current Contents®/Clinical Medicine, EMBASE/Excerpta Medica; Medical Documentation Service; Research Alert; Sci Search; SUBIS Current Awareness in Biomedicine; VINITI: Russian Academy of Science.**

Nachdruck | Urheberrecht

Wichtiger Hinweis

Für Angaben über Dosierungsanweisungen und Applikationsformen kann vom Verlag und den Herausgebern keine Gewähr übernommen werden. Derartige Angaben müssen vom jeweiligen Anwender im Einzelfall anhand anderer Literaturstellen auf ihre Richtigkeit überprüft werden. Gleiches gilt für berufs- und verbandspolitische Stellungnahmen und Empfehlungen.

Allein aus Gründen der besseren Lesbarkeit wird auf die gleichzeitige Verwendung männlicher, weiblicher und weiterer Sprachformen verzichtet. Sämtliche Personenbezeichnungen gelten für alle Geschlechterformen. Dies impliziert keinesfalls eine Benachteiligung der jeweils anderen Geschlechter, sondern ist als geschlechtsneutral zu verstehen.

CONTACT US

Please do not hesitate to contact us. We will be glad to answer and provide further information to you at any time.

.....
Name

.....
First Name

.....
Department / Hospital

.....
Place

.....
Telephone

.....
E-Mail

.....
Date / Signature

Please contact me for further information ○

I would like to participate in the project ○

ADDRESS

German Society of Anaesthesiology and
Intensive Care Medicine
Ursula Homberg
Roritzerstrasse 27 | 90419 Nuremberg | Germany
Tel.: +49-911-9337828 | Fax: +49-911-3938195
Email: uhomberg@orphananesthesia.eu