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

www.ai-online.info

64. Jahrgang | Juli / August 2023

A&I

ANÄSTHESIOLOGIE & INTENSIVMEDIZIN

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

Phelan-McDermid syndrome

Phenylketonuria and other hyperphenylalaninemias

orphanaesthesia

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

SUPPLEMENT NR. 10 | 2023

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.

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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www.orphananesthesia.eu

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orphananesthesia

Anaesthesia recommendations for

Phelan-McDermid syndrome

Disease name: Phelan-McDermid syndrome

ICD 10: Q93.5

Synonyms: 22q13.3 deletion syndrome, Chromosome 22q13.3 deletion syndrome, Deletion 22q13 syndrome. Monosomy 22q13.3.

Disease summary: Phelan-McDermid syndrome, 22q13 deletion syndrome, is a genetic condition caused by the deletion of the terminal end of chromosome 22 or mutation of the SHANK3 gene. The genetic changes that cause PMS vary from person to person and can occur from a de novo mutation or be inherited (autosomal dominant). Global developmental delay, intellectual disability of varying degrees, autism or autistic-like behaviour, hypotonia, epilepsy, absent or severely delayed speech, gastroesophageal reflux, syndactyly, genito-urinary abnormalities, brain structural abnormalities such as microcephaly and distinctive facial features with possible tracheal stenosis may occur. Chromosomal microarray is the most common method for diagnosing Phelan-McDermid syndrome. Fluorescence in situ hybridisation (FISH) may detect larger deletions. If a diagnosis of Phelan-McDermid syndrome is suspected, but no deletion of 22q13 is detected by microarray, targeted DNA sequencing may detect mutations of the SHANK3 gene.

Mitochondrial abnormalities, specifically abnormalities in complex I and IV activity, may explain some phenotypic variation in PMS individuals.

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

▶ **Citation:** Abdallah C: Phelan-McDermid syndrome. Anästh Intensivmed 2023;64:S288–S294.
DOI: 10.19224/ai2023.S288

Emergency information

A	**AIRWAY / ANAESTHETIC TECHNIQUE**	Prepare for a difficult airway due to dysmorphic features (facial / mandibular deformities) – consider (modified) RSI in case of gastrointestinal reflux / dysphagia
B	**BLOOD PRODUCTS (COAGULATION)**	No specific recommendations
C	**CIRCULATION**	Pay attention to adequate hydration (tendency to overheat secondary to decreased perspiration)
D	**DRUGS**	No risk for MH – consider drug dose adaption in case of renal impairment – antiepileptic home medication may induce metabolism of some anaesthetic medications – careful titration of pain medications recommended (secondary to decreased sensitivity to pain)
E	**EQUIPMENT**	Temperature measurement incl. prevention of thermal perturbations recommended – patient positioning / mobilisation with caution due to seizure risk / hypotonia – consider presence of a (personal) caregiver in PACU / IMC / ICU due to developmental delay, intellectual disability or autism-like behaviour

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

Each patient should be evaluated on an individual basis. The anaesthetic management of patients with Phelan-McDermid syndrome may be complicated by airway problems such as difficult laryngoscopy secondary to dysmorphic features (microcephaly, synophrys, midface hypoplasia, hypertelorism) and a possible high arched palate. Tracheal stenosis has been described. Gastroesophageal reflux and swallowing problems may be present. A careful evaluation and management of 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.

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Patients with Phelan-McDermid syndrome usually present with global developmental delay, hypotonia and possible seizures. They commonly have an autistic-like behaviour (mouthing/chewing and teeth grinding are common) with absent or severely delayed speech.

A decreased sensitivity to pain has been described in patients with Phelan-McDermid syndrome. Increased sensitivity to anaesthetics has been documented in animal studies of a Phelan-McDermid syndrome genetic model. The choice and dosages of anaesthesia medications should be adjusted accordingly.

Patients with Phelan-McDermid syndrome may be predisposed to increased body temperature secondary to decreased perspiration. Special caution should be exerted in maintaining adequate hydration and normothermia. Careful positioning secondary to seizure risk should be applied.

A recent study suggests that mitochondrial dysfunction, as measured by abnormal electron transport chain complex activity, may affect a significant portion of individuals with PMS.

Necessary additional preoperative 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 and the presence of gastroesophageal reflux should be done preoperatively. Patients with Phelan-McDermid syndrome may have cardiac and respiratory issues as well as immunological problems. Baseline brain imaging for the presence of arachnoid cysts and attention to symptoms of possible increased intracranial pressure with evaluation by a neurologist may be recommended. Lymphoedema may appear in adolescence or adulthood. The presence of renal problems should be determined. Preoperative evaluation should include the evaluation of possible associated kidney/urinary abnormalities.

Type, frequency and severity of seizures should be documented and treatment should be optimised preoperatively. The tolerance to pain should be assessed as much as possible by interviewing the family or by reviewing previous medical records. Tendency to overheat and decreased perspiration should also be documented as much as possible by interviewing the family.

Patients with PMS may be affected by mitochondrial dysfunction and anaesthesia should be planned accordingly.

Particular preparation for airway management

Careful evaluation for difficult tracheal intubation secondary to dysmorphic features. The presence of facial, mandibular deformities and possible tracheal stenosis may result in difficulty in mask ventilation and airway maintenance.

Particular preparation for transfusion or administration of blood products

Not reported.

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Particular preparation for anticoagulation

Not reported.

Particular precautions for positioning, transportation and mobilisation

Developmental delay, autistic-like behaviour may require help with mobilisation and transport. Risk prevention of injury from seizures and careful positioning is indicated secondary to hypotonia.

Interactions of chronic disease and anaesthesia medications

There are no known interaction between anaesthetic agents and patients´ 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. Decreased perspiration and overheating may also affect cardiac output and hydration status. Concomitant use of antiepileptic medications may induce the metabolism of some anaesthetic medications. Decreased sensitivity to pain/increased sensitivity to anaesthetics has been documented in animal studies of Phelan-McDermid syndrome genetic model. Careful titration of pain medications is recommended secondary to decreased sensitivity to pain.

Anaesthetic procedure

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

Particular or additional monitoring

Special precautions to be taken in titrating administration of medications, especially pain medications in view of coexistence of decreased sensitivity to pain with possible agitation secondary to behavioural problems.

Possible complications

Special attention to the following points: Potential difficult airway/injury from agitation/ hyperthermia from overheating. CNS (seizures); urinary problems. Over- or under-estimation of pain secondary to decreased sensitivity to pain with possible agitation secondary to behavioural problems and inability to communicate secondary to cognitive/speech delay. Possible mitochondrial dysfunction.

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Postoperative care

Documentation and stabilisation: Airway patency, haemodynamic stability.

Management of seizures, management of agitation and pain as described above.

Positioning secondary to hypotonia or agitation.

Prevention of thermal perturbations and hydration status secondary to decreased perspiration.

Disease-related acute problems and effect on anaesthesia and recovery

Differential diagnosis includes syndromes associated with hypotonia, developmental delay, speech delay and/or autistic-like behaviour (Prader-Willi, Angelman, Williams, Smith-Magenis, Fragile X, Sotos, FG syndrome, trichorhinophalangeal and velocardiofacial syndromes, autism spectrum disorders and cerebral palsy).

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

No fertility studies that would exclude the possibility of reproduction have been performed. Females with Phelan-McDermid syndrome go through puberty and begin menstruation at the normal age. Anaesthesia and surgery have to be performed in a medical facility with capacity of taking care of potential challenges and complications.

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Further information

- https://omim.org/entry/606232
- https://www.orpha.net/consor/cgibin/Disease_Search.php?lng=EN&data_id=10630&Disease_Disease_Search_diseaseGroup=PhelanMcDermidsyndrome&Disease_Disease_Search_diseaseType=Pat&Disease(s)/group%20of%20diseases=Monosomy22q133&title=Monosomy%2022q13.3&search=Disease_Search_Simple
- https://rarediseases.org/rare-diseases/phelan-mcdermid-syndrome
- Phelan-McDermid Syndrome Foundation (PMSF). www.pmsf.org
- Asociación Española Phelan-McDermid, www.22q13.org.es

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Date last modified: **April 2022**

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

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Editorial review 2022

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

Please note that this recommendation has not been reviewed by an anaesthesiologist and a disease expert but by two anaesthesiologists instead.

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DGAI
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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
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Tel.: 09522 943570 | Fax: 09522 943577
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Verlagsrepräsentanz
Jürgen Distler
Neuwieder Straße 9 | 90411 Nürnberg
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Titelbild
Dipl.-Designerin Monique Minde, Nürnberg

Erscheinungsweise 2023
Der 64. Jahrgang erscheint jeweils zum Monatsanfang, Heft 7/8 als Doppelausgabe.

Bezugspreise (inkl. Versandkosten):

- **Einzelhefte** 30,- €
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  Europa (ohne Schweiz) (inkl. 7 % MwSt.) 258,- €
  Schweiz 266,- €
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  Mitarbeiter aus Pflege, Labor, Studenten und Auszubildende (bei Vorlage eines entsprechenden Nachweises)
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