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Multiple pterygium syndrome, Escobar variant

Hamamy syndrome

orphanaesthesia

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

SUPPLEMENT NR. 9 | 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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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

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Anaesthesia recommendations for

Multiple pterygium syndrome, Escobar variant

Disease name: Multiple pterygium syndrome, Escobar variant

ICD 10: Q97.8

Synonyms: Escobar syndrome; pterygium syndrome; multiple pterygium syndrome, non-lethal type; familial pterygium syndrome; pterygium colli syndrome; pterygium universale

Disease summary: Multiple pterygium syndrome, Escobar variant (MPSEV) is a rare congenital condition, which is inherited with an autosomal recessive pattern. It has an unknown incidence but is more common among children from consanguineous relationships. It is caused by a mutation in the CHRNG gene on chromosome 2q. This gene encodes the gamma subunit of the acetylcholine receptor (AChR), which is found in the foetus until around 33 weeks of gestation, when it is replaced by another subunit to form the adult AChR protein. The severity of the CHRNG gene mutation influences the severity of the condition and the complete absence of the gamma subunit will result in the lethal multiple pterygium syndrome.

The clinical features of MPSEV are variable, but the condition is characterised by pterygia (excessive webbing) typically affecting the neck, axilla, digits (syndactyly), antecubital fossa, popliteal and intercrural areas. Akinesia, which may be identified before birth, also frequently results in arthrogryposis (congenital contractures), causing a crouched stance, and muscle weakness. Other typical findings include growth retardation, ankyloglossia (adhesions between the tongue and the palate), syngnathia (congenital bands of tissue between the maxilla and the mandible), cleft palate, lumbar lordosis and scoliosis.

Typical facial features seen in patients with MPSEV are ptosis, down slanting palpebral fissures, epicanthal folds, micrognathia, long philtrum and low-set ears.

Other orthopaedic manifestations or associations that have been reported include cervical spine fusion, rib fusion, hip dislocation, foot deformities, camptodactyly, absent patellae, and pectus excavatum. There are case reports describing abnormalities of the ear bones and conductive hearing loss, and two case reports describe patients with MPSEV who had cardiac defects (atrial septal defects). Males with this condition can have cryptorchidism and females can have missing or underdeveloped labia majora. People affected by MPSEV may also have respiratory distress at birth due to lung hypoplasia.

Unlike other abnormalities of the AChR, MPSEV does not lead to myasthenic symptoms in later life as the gamma subunit is only expressed during foetal life. However, progressive webbing and scoliosis commonly cause significant reduction in lung capacity and an airway that is increasingly difficult to manage.

▶ **Citation:** Brooke J: Multiple pterygium syndrome, Escobar variant. Anästh Intensivmed 2021;62:S183–S190. DOI: 10.19224/ai2021.S183

Even though myasthenic features and abnormal muscle histopathology is not expected in CHRNG mutations, however, congenital diaphragmatic muscle weakness, diffuse myopathy, and myasthenic-like features have been frequently reported in CHRNG mutation patients which could be due to the role of γ-subunit AChR in muscle organogenesis.

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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Typiscal surgery

- Orthopaedic surgery - scoliosis correction, tendon transfers, joint surgeries, contracture releases,
- Plastic surgery - cleft palate repair, removal/reduction of pterygia, syndactyly release,
- Ophthalmic surgery - surgery to improve ptosis,
- Urological surgery – orchidopexy.

Type of anaesthesia

The type of anaesthesia will depend on the severity of the symptoms and the surgical procedure. General, regional and local anaesthetic techniques are safe to use.

A case report does describe a case complicated by malignant hyperthermia but several other case reports have described the uneventful use of volatile anaesthetics. Kachko et al. presented a case using epidural anaesthesia and stated that the risk of malignant hyperthermia in MPSEV is low.

There is little research on the function of the subunits of the adult AChR in MPSEV patients and some authors have avoided neuromuscular blocking agents due to concerns about their duration of action. However, case reports have described the uneventful use of both vecuronium and atracurium.

Short-acting agents, such as remifentanil, propofol and desflurane may be preferred in these patients as residual anaesthetic effects may impact post-operative upper airway control and respiratory function.

Where possible, regional or local anaesthesia should be used as an adjunct to general anaesthesia to reduce the use of drugs causing respiratory depression. Anatomical features such as kyphoscoliosis, lumbar lordosis and contractures may make regional anaesthesia and local anaesthetic blocks technically challenging, and so the use of ultrasound should be considered to aid placement.

Necessary additional pre-operative testing (beside standard care)

Prior to anaesthesia, patients with MPSEV should have a thorough pre-operative assessment with particular attention paid to assessing the airway and the respiratory, musculoskeletal and cardiovascular systems.

Additional pre-operative investigations will be dependent on the severity of the underlying disease and the surgical procedure. Specific investigations to be considered include:

- Nasendoscopy to evaluate airway anatomy
- Arterial blood gases and lung function tests to assess the degree of pulmonary involvement
- Chest X-ray to help assess for cardiorespiratory disease and assess the extent of scoliosis
- Neck X-ray due to the risk of cervical spine stiffness and fusion
- ECG and echocardiogram to assess for underlying cardiac defects and disease.

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Particular preparation for airway management

A difficult airway should be anticipated in all cases of MPSEV and a comprehensive plan for a difficult airway should therefore be in place prior to induction of anaesthesia. The airway should be assessed thoroughly pre-operatively including assessing mouth opening, micrognathia, ankyloglossia, neck webbing and neck movement.

The characteristics of MPSEV may make a standard facemask fit poorly and a 2-person technique may be required. The ability to accomplish adequate bag-valve-mask ventilation should be demonstrated prior to giving neuromuscular blocking agents.

Appropriate equipment for dealing with the difficult airway must be readily available and it may be necessary to have an ENT surgeon on standby to perform a tracheostomy as a last resort.

Unlike other congenital syndromes where management of the airway becomes easier, in MPSEV intubation becomes more difficult due to an increased deformity of the airway by the pterygia. An airway that has previously been easy to manage can become increasingly difficult with time. Detailed documentation of previous approaches to the airway is essential as these patients often present for multiple surgeries during their lifetime. Education about their airway should be provided to the patient and family in case they have to receive care at an outside or unfamiliar hospital.

Particular preparation for transfusion or administration of blood products

There is no definite recommendation for transfusion. Administration of blood products will depend on the type of surgery, the patient symptoms and advice from haematology clinicians.

Particular preparation for anticoagulation

There is no evidence to support the need for particular anticoagulation. Severe contractures may cause impaired mobility in patients and may suggest a higher risk of post-operative thrombosis.

Particular precautions for positioning, transportation and mobilisation

Caution must be taken while positioning the patient due to multiple contractures and possible scoliosis. Positioning should ideally be guided by the awake and cooperative patient.

Interactions of chronic disease and anaesthesia medications

None reported.

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Anaesthetic procedure

The anaesthesia of patients with MPSEV should be managed by an experienced anaesthetic team, familiar with the management of difficult airways. A comprehensive airway plan should be made and appropriate equipment and personnel available in case of difficulty.

Both inhalational and intravenous induction have been used successfully. When inhalational induction is used, intravenous access should be established prior to induction. Intravenous access may be difficult due to anatomical abnormalities and intraosseous access or central venous access may be required.

Extubation should be done in an awake patient wherever possible.

Particular or additional monitoring

Routine monitoring is needed in all MPSEV patients. Flexion contractures may make it difficult to obtain intravenous access and non-invasive blood pressures and this may mean the use of invasive monitoring and central venous access is necessary. Monitoring of neuromuscular blockade is recommended in all patients in whom neuromuscular blocking drugs are used.

Possible complications

Patients with multiple pterygium syndrome are at increased risk of failed or difficult intubation and ventilation may be difficult due to restrictive lung disease.

These patients may be sensitive to opiates and have a high risk of post-operative respiratory complications.

Post-operative care

Post-operative care will depend on the surgery performed and the severity of the clinical manifestations of the disease. Post-operative admission to an intensive care or high dependency care unit may be required for monitoring or ventilatory support, given the risk of post-operative respiratory failure. Mobilisation can prove difficult due to contractures and post-operative opiates should be used with caution.

Disease-related acute problems and effect on anaesthesia and recovery

All anaesthetists anaesthetising patients with Escobar should be familiar with difficult and failed intubation protocols.

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Ambulatory anaesthesia

The suitability of ambulatory anaesthesia will be guided by the severity of disease, the surgical procedure and the local guidelines. It is unlikely to be appropriate in any but the mildly affected.

Obstetrical anaesthesia

Pregnant women with MPSEV should have obstetric and anaesthetic care and multi-disciplinary team involvement led by an experienced consultant.

In the only case report of the obstetric anaesthetic management of a woman with MPSEV, the patient underwent an elective Caesarean section under general anaesthesia. Neuraxial anaesthesia was not possible due to extensive lumbosacral surgery with placement of hardware. Due to a potentially difficult airway, an awake fibre-optic intubation was performed and the anaesthetic was otherwise uneventful.

There are no case reports on labouring women with MPSEV, but the likely problem of a difficult airway suggests that the early implementation of epidural anaesthesia would be beneficial. However, spinal abnormalities may make this technically very challenging or impossible.

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This recommendation was prepared by:

Author

Jenny Brooke, Paediatric anaesthesiologist, Great Ormond Street Hospital London, UK
jbrooke82@googlemail.com

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This recommendation was reviewed by:

Reviewers

William D Stoll, Anaesthesiologist, Medical University of South Carolina, Charleston, SC, USA
stollwil@musc.edu

Ariana Kariminejad, Chief Genetic Counselor, Kariminejad-Najmabadi Pathology & Genetics Center, Tehran, Iran
arianakariminejad@yahoo.com

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

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E-Mail: info@aktiv-druck.de

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

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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
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E-Mail: mazyblue@klaus-steigner.de
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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