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**Paraganglioma &
Pheochromocytoma
Pena-Shokeir syndrome**

orphan^anesthesia

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

SUPPLEMENT NR. 15 | 2017

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 OrphanAnesthesia 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
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OrphanAnesthesia –

**a common 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 recommendations 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.

**A survey of until now in A&I
published guidelines can be
found on:**

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orphan anesthesia

Anesthesia recommendations for patients suffering from **Pena-Shokeir syndrome**

Disease name: Pena-Shokeir syndrome

ICD 10: Q87.8

Synonyms: Pena-Shokeir syndrome, Type I (OMIM 208150). Fetal akinesia sequence. Arthrogryposis multiplex congenita with pulmonary hypoplasia.

Pena-Shokeir syndrome (PSS) (OMIM 208150) is a rare, early lethal disorder with an estimated incidence of 1:12,000 [1-3]. Approximately one hundred cases have been reported [3]. It was first identified by Pena and Shokeir in 1974 [1], although early descriptions resulted in the eponym, it has recently been suggested that Pena-Shokeir is not a specific unitary diagnosis or syndrome, but rather a description of a clinically and genetically heterogeneous phenotype from variable etiology, resulting from the reduction of movements in the uterus due to an intrinsic pathology regardless of the cause, and was subsequently included among the phenotypes associated with the fetal akinesia/hypokinesia deformation sequence (FADS) [4]. In some families it has been suggested a recessive autosomal inheritance, and identified homozygosity for a frameshift mutation in the RAPSN gene, and homozygous truncating mutation in the DOK7 gene [5]. In pathogenesis has also identified several infants with PSS, born of mothers with myasthenia gravis [6]; or associated with other autosomal dominant diseases [7].

Medicine in progress



Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

► **Citation:** Bakan M: Pena-Shokeir syndrome. Anästh Intensivmed 2017;58:S628-S634. DOI: 10.19224/ai2017.S628

Disease summary

Prenatal diagnosis of PSS is feasible as early as 14th week of gestation [8,9]. The abnormal neural development results in fetal akinesia/hypokinesia (decrease in fetal movements), with secondary arthrogryposis (contractures of the joints) and skeletal dysplasia. Prenatal ultrasonography may reveal polyhydramnios, short umbilical cord, and pulmonary hypoplasia. In addition to neurogenic arthrogryposis, PSS is characterized by intrauterine growth restriction, various cranio-facial anomalies (microcephaly, micrognathia, cleft-palate deformity, ocular hypertelorism, low-set and malformed ears, and a depressed nasal tip) camptodactyly, and pulmonary hypoplasia [3]. Skeletal deformities like scoliosis, kyphoscoliosis, pectus carinatum, congenital hip dislocation, rocker-bottom feet, and syndactyly may accompany. These manifestations vary in severity, but are usually severe. Pulmonary hypoplasia is obligatory in PSS and cannot be found in others subtypes of fetal akinesia such as the arthrogryposis multiplex congenital (AMC). Involvements of cardiovascular, genitourinary (cryptorchidism), endocrine, and gastrointestinal systems have been reported [3,10]. In most cases, intelligence was impaired.

Approximately 30% of affected infants are stillborn, otherwise in live births death generally occurs during neonatal period or soon thereafter due to developmental delay, and respiratory and neurological problems. The ultimate prognosis for children with PSS is mostly dependent on the severity of pulmonary hypoplasia.

Two variants of this syndrome have been described and are commonly referred to as PSS Type I and II. Pena-Shokeir syndrome Type II (cerebro-oculo-facio-skeletal syndrome) differentiated from PSS Type I by the presence of microcephaly, ocular findings (microphthalmia, blepharophimosis, and/or cataracts), and by the lack of pulmonary hypoplasia [2,11].

Differential diagnosis:

- Cerebro oculo facio skeletal syndrome 1; COFS1 (OMIM [214150](#)) COFS syndrome; Pena-Shokeir syndrome, Type II: is an autosomal recessive progressive neurodegenerative disorder characterized by microcephaly, congenital cataracts, severe mental retardation, facial dysmorphism, and arthrogryposis.
- Lethal congenital contracture syndrome; LCCS (OMIM [253310](#)), is the most severe, neonatally, lethal form of arthrogryposis.

Typical surgery

Patients with PSS may have to undergo many surgical interventions if they able to survive [12]. Tracheostomy [12, 13, 14] is frequently performed in infants with cranio-facial anomalies and/or pulmonary hypoplasia to achieve patency of the airway and for long-term mechanical ventilation. Vocal cordotomy [15], cleft palate repair [12,16], artrolysis [14], correction of other skeletal deformities may be performed.

Type of anaesthesia

There is no definite recommendation for either general or regional anaesthesia. General anaesthesia management for 7 cases was reported in the literature [12-16]. Difficult tracheal intubation [12,16,17], reactive airway [12,13], perioperative respiratory complications [12], and malignant hyperthermia [12,17] must be considered during anaesthesia management of PSS. Inhalational anaesthesia with sevoflurane was used in most cases. Total intravenous anaesthesia with propofol and remifentanil after sevoflurane induction was described in one case without any incident [16].

There is one report of a parturient with PSS who had caesarean delivery under spinal anaesthesia [17]. Patients with PSS may have scoliosis, kyphoscoliosis that might be difficult to perform neuroaxial anaesthesia. Regional or local anaesthesia can be done.

For brief and less invasive procedures monitored care anaesthesia with spontaneous or assisted mask ventilation may be considered.

Necessary additional diagnostic procedures (preoperative)

Anaesthetic data regarding previous operations and intubations provide valuable information regarding intubation risks, which have to be anticipated. Special questions regarding recurrent aspirations, pneumonia and reflux is part of every anamnesis.

Particular preparation for airway management

It is important to assume that difficult airway management might be encountered. Micrognathia is frequent. Cleft palate deformity may complicate laryngoscopy. In anaesthesia management of 6 cases described in the literature, mask ventilation was described as without problem. Difficult intubation was described in two cases. Direct laryngoscopy revealed Cormack-Lehane grade II in other two.

For a safe airway management, it is essential to use a difficult airway algorithm and have a skilled theatre team. Airway devices (face mask, oral and nasal airways, laryngeal mask airway, endotracheal tube, etc.) in various sizes have to be prepared. If available, a smaller size fiberoptic bronchoscope will be precious. Urgent tracheostomy must be considered.

Particular preparation for transfusion or administration of blood products

Most surgical procedures performed in PSS are not related with excessive blood loss.

Particular preparation for anticoagulation

There is no evidence to support the need for anticoagulation.

Particular precautions for positioning, transport or mobilisation

Positioning patients for surgery may be difficult with the pre-existing contractures. Extra precautions have to be taken when positioning under anaesthesia.

Probable interaction between anaesthetic agents and patient's long term medication

No specific treatment is available for those affected by Pena-Shokeir syndrome. Patients may use anti-epileptic therapy.

Anaesthesiologic procedure

Sedative premedication should be administered cautiously for patients with respiratory insufficiency and airway difficulty. Respiratory depression after chloral hydrate administration was described [12]. Additional secretions might increase the risk of respiratory complications. The use of an antimuscarinic (atropine or glycopyrrolate) might be beneficial, especially in patients undergoing oropharyngeal surgery or requiring fiberoptic guided intubation. If sedation with ketamine is considered the antisialogouge action of antimuscarinics is well-appreciated.

Inhalational induction has to be used due to the poor venous quality and possible difficult airway management. Oral premedication with midazolam before inhalational induction may be appropriate. Although a 'cannot ventilate, cannot intubate' situation was not described before, it may be reasonable to prefer inhalational induction with sevoflurane and nitrous oxide to ensure mask ventilation for some clinicians. Sevoflurane use only for induction or throughout the whole procedure was described in most cases.

As a precaution, the use of succinylcholine can be renounced due to the risk of malignant hyperthermia. Intubation without a neuro-muscular blocker or low-dose rocuronium (0.2-0.3 mg/kg) can be considered. If sugammadex is available, clinicians feel free to use higher doses of rocuronium to ease laryngoscopy.

Pulmonary condition of the patient must be considered during mechanical ventilation. High frequency jet ventilation was described for endoscopic laser cordectomy of a patient [15].

Particular or additional monitoring

The type of monitoring should be chosen according to the type and extent of surgery. As a part of standard monitoring, the surveillance of temperature and end-tidal carbon dioxide are of particular importance, even in case of small interventions.

Possible complications

Multiple attempts for endotracheal intubation may cause airway injury and oedema. Perioperative respiratory complications and malignant hyperthermia must be considered during anaesthesia management of PSS.

Postoperative care

Degree of postoperative monitoring is depending on surgical procedure and preoperative condition of the patient. Although it is not mandatory, intensive care may be necessary.

Information about emergency-like situations / Differential diagnostics

caused by the illness to give a tool to distinguish between a side effect of the anaesthetic procedure and a manifestation of the diseases, e.g.:

Malignant hyperthermia was mentioned in the medical history of two patients with PSS, but the conditions and triggering agents were not well-documented [12,17]. A hyper-metabolic state which may be a stress response to anaesthesia and/or surgery, with an increase in body temperature and end-tidal CO₂, and consecutive acidosis, may confused with malignant hyperthermia [18]. To be cautious, PSS has to be recognised as a risk factor for malignant hyperthermia, especially if myopathy is suspected.

Ambulatory anaesthesia

There are no recommendations regarding an outpatient procedure in the case of PSS. Outpatient anaesthesia in paediatric patients with PSS should be an exception and only be carried out after having thoroughly weighed benefits and risks. A minimal intervention under sedation with non-triggering agents would be an example.

Obstetrical anaesthesia

Most descriptions of anaesthesia in the case of PSS refer to paediatric patients. Recently one parturient with PSS had caesarean delivery under spinal anaesthesia had been published. If a female patient with PSS will able to survive to be an adult, it will be a great possibility that she had undergone anaesthesia several times in her childhood and therefore her medical history can easily be taken. Though these patients had multiple co-morbidities, if regional anaesthesia is not contraindicated, they can receive labour epidural analgesia and regional anaesthesia for caesarean section deliveries. If there is skeletal deformities like scoliosis present, ultrasonography guided placement of regional technique (epidural or spinal) may be considered.

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