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Coffin-Siris syndrom

Distal arthrogryposis type 3

orphanaesthesia

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

SUPPLEMENT NR. 13 | 2019

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.

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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 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.

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

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Disease background

First described by Gordon (1969) [1], distal arthrogryposis type 3 (DA3; MIM 114300) is a congenital non-progressive myopathy and includes contractures of the hands and ankle-foot complex, cleft palate, blepharoptosis, and abnormal spinal curvatures [2]. DA3 lacks these specific craniofacial findings seen in Freeman-Burian [3–4] or Sheldon-Hall syndromes (FBS or SHS) [5], but includes findings not present in distal arthrogryposis type 1, which generally manifested only distal extremity contractures. Limb malformations common to FBS, SHS, and DA3 include two or more of the following: talipes equinovarus, metatarsus varus, vertical talus, talipes equinovalgus, calcaneovalgus, camptodactyly, ulnar deviation of wrists and fingers, overlapping fingers or toes, and hypoplastic or absent interphalangeal creases. Major differential diagnoses include Distal arthrogryposis types 1A, 1B, 2B, 7, and 8; Marden-Walker syndrome; Schwartz-Jampel syndrome; and non-syndromic distal contractures. DA3 is distinguished from other conditions with apparent distal extremity contractures by presence of cleft palate, blepharoptosis, and abnormal spinal curvatures, and absence of additional features, especially ocular pathology and mental retardation [2]. DA3 is associated with allelic variation on the piezo-type mechanosensitive ion channel component 2 (PIEZO2; MIM 613629) gene, at 18p11.22–p11.21 [6]. DA3 is considered to belong to the group of phenotypically similar entities termed distal arthrogryposes [7–8]. Arthrogryposis multiplex congenita is a distinct entity from the distal arthrogryposes [2].

Most instances of DA3 are sporadic, but autosomal dominant inheritance has been established [2]. There is no apparent gender, ethnic, or geographical preference, and environmental and parental factors are not implicated in pathogenesis [2].

Although the literature on DA3 is negligible [9–10], general principles relevant to care of patients with DA3 arises from the better documented experience with FBS and DA1. This recommendation, developed through literature review and clinical experience, aimed to address the deficiency in available clinical guidance by providing essential outcomes-directed advice for evaluation and management of anaesthetic care for patients with DA3. The protocol for and results of the systematic review and meta-analysis underpinning this recommendation were described elsewhere [9–10]. AGREE II and GRADE Guidelines [11–12] were followed in the recommendation development process.

Typical surgery

Though not as severe as FBS or SHS, patients with DA3 frequently undergo many orthopaedic surgeries, primarily because attempts at operative deformity correction have suboptimal results and require subsequent revision. Several craniofacial manifestations of the syndrome also typically require operative treatment. Due to the wide variability of DA3 presentation and the lack of significant research, there is a great diversity of operative approaches employed for the following reasons: ankle-foot complex contracture correction, spinal curvature correction, hand contracture correction, cleft palate and blepharoptosis repair, and possibly additional craniofacial reconstruction. Less frequently, involvement of more proximal joints (e.g., recurrent dislocation or dysplasia of shoulders and hips, contracture of elbows, or patellar instability) or spine (rod insertion and vertebral fusion for abnormal curvatures) are the focus of operative interventions.

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Type of anaesthesia

Most case reports describe safely performed general anaesthesia techniques in these patients. In this case, anaesthesia is performed using volatile anaesthetics, propofol, opioids, ketamine and nitrous oxide. Beside this, general anaesthesia is not necessary in all cases. Because of some anatomical risks of difficult airway it may be desirable to avoid pre-medication, sedation, and general anaesthesia for appropriately selected patients with DA3 [13]. Though mild spinal deformities may be seen in DA3, this typically does not preclude epidural or spinal anaesthesia, which may have far fewer the syndromic-associated challenges and complications and a more favourable safety profile over sedation and general anaesthesia. Proper psychological preparation for patients undergoing surgery exclusively under local or regional anaesthesia does not differ substantively from any other pre-operative consent and preparation process [13].

Necessary additional pre-operative testing (beside standard care)

Anaesthetic care for patients with DA3 often presents a challenge and requires considerable pre-operative planning. Patients should be evaluated well in advance of proposed procedures, if possible. The anaesthesiologist performing the evaluation should also be the anaesthesiologist assigned for the procedure. A thorough and complete history should include questions about: current medications and allergies, reactive airways disease, gastro-oesophageal reflux disease (GERD), previous acute and chronic respiratory problems, prior anaesthesia and surgeries, seizures, and any symptoms of possible central nervous system dysfunction, especially increased intracranial pressure [14]. Examination includes: vital signs, developmental status, airway, spinal, neurological, and cardiopulmonary assessments [14]. It is important to explain to the patient and family possible risks and ensure questions are answered and concerns fully addressed [13–14]. Findings, concerns, and management plans must be discussed with participating surgeons [14].

Some suggest that malignant hyperthermia (MH) does not have an association [15–16] with most myopathies in which anaesthetically related hypermetabolic states resembling MH have been reported. Unless there is specific concern, an anaesthetic technique considered MH-safe is not required for patients with DA3.

An expanded metabolic panel and 12-lead electrocardiogram are appropriately included in pre-operative screening for many patients who carry a potentially higher risk for anaesthesia or sedation and prevent misinterpretation of the pre-existing status as being associated with intra-operative changes. As arterial puncture for blood gases may be infeasible, point-of-care capillary blood testing can be helpful for baseline and subsequent assessment when available. Alternatively, pulse oximetry on room air is a valuable non-invasive modality for assessing pulmonary gas exchange, and venous serum bicarbonate is reflective of the state of carbon dioxide exchange.

Notably, DA3 is not associated with any cardiac muscle pathology.

Particular preparation for airway management

In patients with DA3, cleft palate, some degree of micrognathia, class II malocclusion, dental crowding, highly arched hard palate, and limited cervical spine flexibility may make endotracheal intubation and use of airway adjuncts difficult. While some providers may elect to attempt use of a Laryngeal Mask Airway (LMA) to avoid a difficult intubation, successful

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introduction and seating of an LMA may be difficult or infeasible in DA3 patients. A smaller LMA device than typically used for the patient's age may be necessary.

Other techniques of oral or nasal intubation include: indirect video intubation (GlideScope, C-Mac, etc.) or a flexible fibre-optic bronchoscope guided technique. In institutions with limited facilities, blind nasal intubation may be attempted but risks airway trauma. These patients are most safely cared for in hospitals with the full range of airway equipment that may be needed. Patients can spontaneously ventilate with positive airway pressure support delivered through a soft nasopharyngeal airway in one nare, while fibre-optically guided intubation is performed through the other nare or the mouth. Care must be taken to avoid the palatal cleft. Similarly, prior operative repair of a cleft palate may have resulted in unknown nasal narrowing or obstruction, making a nasal intubation difficult or impossible. Mask ventilation may be possible as well, but patients must be evaluated for adequate sealing pre-operatively, given the anatomical challenges involved. If an LMA can be introduced, fibre-optic intubation can be performed through the LMA. Tracheotomy may be needed but is technically challenging in emergent or unusually challenging intubations. Surgical backup should be arranged for the most difficult airways. There are multiple anaesthetic techniques available for airway management, including spontaneous breathing of inhalational agents or intravenous infusion of propofol, dexmedetomidine, or both.

Particular preparation for transfusion or administration of blood products

No reports in the literature or known clinical experience indicate any unusual problems or needed precaution for patients with DA3 needing transfusion or administration of any blood components.

Particular preparation for anticoagulation

While many patients have reduced pre-operative mobility and, therefore, are at a somewhat higher pre-operative thrombogenic risk, no reports in the literature or known clinical experience indicate any disorder of coagulation associated with DA3.

Particular precautions for positioning, transportation and mobilisation

Carefully evaluate patients pre-operatively to assess the extent of contractures. Any range of motion limitations found should be discussed with surgeons to plan the best positioning for the patient during surgery. If possible, positioning before induction of anaesthesia is recommended but may not be feasible. Patients should always be placed in a position of respiratory comfort, with avoidance of unnatural mobilisation under anaesthesia, kept warm, and provided with generous padding to avoid pressure points. Use of padded dressings is recommended for areas at risk for pressure injury (sacrum if supine; breasts and iliac crests if prone). Thin patients and those with extended inpatient confinement are at higher risk for loss of skin integrity. Patients with skin complications should be seen by a plastic surgeon. Active forced air heating systems should be used to maintain patient normothermia during anaesthesia and surgery, as many of these patients may have reduced adipose tissue and be at increased risk of hypothermia.

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Interactions of chronic disease and anaesthesia medications

There are no syndrome-specific chronic medications for patients with DA3, and there is no syndrome-specific treatment. Therapeutic interventions focus on improving functional outcomes. There is no cure, although DA3 is believed to be non-progressive.

Anaesthetic procedure

The evidence does not support an association between MH and DA3 [15–16]. Nonetheless, in some clinical situations hyperpyrexia was described, but a recommendation to avoid MH-triggering agents cannot be given.

Oral midazolam is routinely used for pre-medication, and intravenous midazolam is often used for mild procedural sedation. Nitrous oxide was used for induction and maintenance of anaesthesia. If maintenance of spontaneous respiration is essential, nitrous oxide is used in conjunction with ketamine to achieve and maintain surgical anaesthesia. If vascular access is established before induction, propofol is frequently used for induction and maintenance of surgical anaesthesia. Intravenous infusion of either propofol or dexmedetomidine or both can be used to establish moderate sedation, with preservation of spontaneous ventilation for airway management and surgical anaesthesia. Spontaneous ventilation also can be maintained with nitrous oxide, ketamine, propofol, dexmedetomidine, or low-dose infusion of short-acting opioids, such as remifentanil.

Lidocaine with or without epinephrine for local anaesthesia, bupivacaine or ropivacaine for local anaesthesia, spinal, or epidural anaesthesia may be used. If performing spinal or epidural anaesthesia, a paediatric size needle and catheter is used, even for adults, as most patients with DA3 are small. When using lidocaine or bupivacaine for anaesthesia without adjuvants, no special precautions are required, except for precautions related to the actual operative intervention itself. Peripheral nerve blocks, either single bolus injection or with catheter placement, may be used for extremity surgery and continued post-operatively for analgesia.

Distal extremity contractures and the consequent poor quality of veins may make establishing peripheral intravenous access challenging in many patients with DA3, and if present, limited cervical mobility complicates neck vein access. Use of a small gauge catheter, 22 or less, is generally required. Need for the use of a small-gauge vascular catheter may impair transfusion, intravenous hydration, medication administration, and blood draw efforts. With increased use of ultrasound-assisted peripheral vein cannulation, central line placement has a diminished role in providing vascular access for these patients, but still may be necessary in a greater frequency than in the general population.

Particular or additional monitoring

While standard modern anaesthesia monitoring modalities (e.g., heart rate, oxygen saturation, blood pressure, end tidal carbon dioxide ($ETCO_2$), respiratory rate and depth, and temperature) are sufficient, vigilance is needed for monitoring in patients with DA3. Muscle rigidity or relaxation is not a reliable indicator of anaesthesia depth or neuromuscular blockade effectiveness, as syndromically affected muscles, especially those exhibiting overt contracture, are unaffected by anaesthesia and muscle relaxants. Oxygen saturation and $ETCO_2$ must be closely observed, especially if obstructive sleep apnoea or intercostal muscle pathology causing restrictive pulmonary disease is suspected. As clip sensors may

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not fit well, flexible adhesive oxygen saturation sensors are preferred and readily available in all institutions. They are applied circumferentially and fit any digit in the largest or smallest of patients. If a urinary catheter is used for monitoring, during a long surgery, or when epidural anaesthesia-analgesia is used, a paediatric size is typically chosen, even for adults, as most patients with DA3 are small. If present, the character of dysphasia caused by orofacial anatomical abnormalities and muscle contractures should be documented before administration of any medication is noted to reduce potential mischaracterisation of dysphasia during pre-medication, sedation, or monitored anaesthesia when spoken-to patient responses are required.

Possible complications

Possible complications of general anaesthesia or sedation in patients with DA3 include hyperpyrexia and hypermetabolic syndrome. Other complications that are more likely to present include rhabdomyolysis without hyperpyrexia, challenging peripheral vascular access, impaired operative access due to ineffectiveness of neuromuscular blockade, and orotracheal intubation difficulty due to anatomic abnormalities. Airway abnormalities leading to difficult intubation includes: small mouth, cervical spine immobility, and stiffness of the orofacial musculature. While primarily reported in FBS, post-operative or post-sedation pneumonia may be caused by hypoventilation (atelectasis). Meticulous anaesthetic care usually prevents aspiration, but opioid effects should be monitored closely to prevent respiratory depression and post-operative airway complications, especially in patients with unrepaired cleft palate. If present, spinal deformities may complicate epidural and spinal anaesthesia, but rarely preclude it.

Post-operative care

Because of the high potential for postoperative complications (apnoea, over-sedation, hypoventilation and respiratory distress) most patients are observed in the intensive or intermediate care unit for at least some time, especially after major surgery.

Disease-related acute problems and effect on anaesthesia and recovery

These patients require meticulous respiratory therapy in the post-operative period, which may include incentive spirometry, chest physiotherapy, with or without the use of a cough assist machine, and implementation of bilevel positive airway pressure, if airway obstruction or hypoventilation occur. If a culture is required, such as in empiric treatment failure, consider if bronchoscopy is necessary to obtain a clean specimen, such as patients with poor tussive ability. If general anaesthesia with intubation is necessary, the anaesthesiologist should use recruitment manoeuvres and endotracheal suctioning prior to extubation to maximise lung volume and reduce the risk of atelectasis.

Special settings or types of anaesthesia

The general principles for the anaesthetic care of patients with DA3 previously described apply, with proper balancing of risks and benefits, to all types and settings of anaesthesia, including obstetric, ambulatory, or emergent.

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