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Recessive myotonia congenita (Becker's disease)

Wolf-Hirschhorn syndrome

orphanaesthesia

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

SUPPLEMENT NR. 14 | 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.

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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.

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Anaesthesia recommendations for

Recessive myotonia congenita

(Becker's disease)

Disease name: Recessive myotonia congenita

ICD 10: G71.1

Synonyms: Becker's disease

Disease summary: Becker's disease is an autosomal recessive type of myotonia congenita, non-dystrophic myotonia, first described in the 1970s by Peter Emil Becker [1]. The worldwide prevalence of myotonia congenita is about 1:100,000 while in some countries (e.g. Norway) the incidence may be 10 times higher [2,3]. It is linked to mutations in CLCN1 (the same as the autosomal dominant in Thomsen's disease), the gene encoding the skeletal muscle chloride channel. The mutation in Becker's disease leads to a reduced flow of chloride ions during repolarisation leading to sustained muscle contraction [4]. The reduced chloride conductance of the mutated chloride channels in Becker's myotonia causes hyperexcitability of the muscle fibre membrane leading to bursts of aberrant action potentials.

The clinical picture is characterised by slowed relaxation following forceful voluntary contractions (myotonic stiffness). Myotonia tends to improve with exercise, the so-called 'warm-up' phenomenon. It usually presents during the first or second decade of life with slow progression in later decades.
Symptoms are more severe than in Thomsen's disease and usually involve the lower limbs first. Muscle hypertrophy is a common symptom. Sometimes it is accompanied by gradually progressive weakness and by peculiar transient episodes of proximal weakness, involving the hands and arm muscles in particular, and is connected to specific types of mutations [5].

More than 150 different mutations of the CLCN1 gene have been reported, some of them are associated with Becker's disease (recessive form, more severe) and others to Thomsen's disease (dominant form, milder). Laboratory diagnostics of myotonia congenita is based on sequencing the CLCN1 gene. Identification of mutations in the CLCN1 gene in the patient and parents differentiate between the two clinical forms of the disease. Since the disease shares symptoms with paramyotonia congenita and other diseases with myotonia, the pool of genes involved in the differential diagnosis is large enough to sequence all of them at the same time, currently by the new techniques of sequencing (NGS).

In addition to searching for a diagnosis based on NGS sequencing, some of the genes related to malignant hyperthermia (mainly RYR1 and CACNA1S genes) should be analysed if patients with myotonia congenita or any other of myopathy who are facing surgery.

Medicine is in progress

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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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Typical surgery

There is no typical surgery, unlike in patients suffering from other neuromuscular disorders like myotonic dystrophy. Possible complications of recessive myotonia congenita (rMC) are joint problems and frequent falls with injury which both can result in orthopaedic/traumatic surgery.

Type of anaesthesia

There is no definite recommendation for either general or regional anaesthesia.

If the procedure enables using neuroaxial anaesthesia (spinal/epidural/combined spinal-epidural) or peripheral nerve blockade, it should be considered as first choice of anaesthesia in indicated cases considering the pathophysiology of myotonia congenita and possible malignant hyperthermia (MH) susceptibility [6].

There are some concerns about the risk of malignant hyperthermia in patients with myotonia congenita and thus tendencies to administer only malignant hyperthermia non-triggering anaesthetic agents for general anaesthesia. However, latest research shows that myotonic patients with a malignant hyperthermia crisis can have mutations at two distinct genetic loci, one for myotonia and one for malignant hyperthermia susceptibility [5,7]. Based on this knowledge, we recommend using non-triggering anaesthetics if general anaesthesia is necessary, although the association with malignant hyperthermia is regarded as highly unlikely according to a recent review [8].

There is only one published case report advocating the use of midazolam for the sedation of a rMC patient without signs of an adverse effect [6]. However, there is no evidence that an administration of benzodiazepines to produce sedation is safe. Therefore, we recommend the use of target-controlled infusions (TCI) of propofol or short-acting opioids for sedation.

Necessary additional pre-operative testing (beside standard care)

Because individuals with myotonia congenita Becker may be at increased risk for adverse anaesthesia-related events, testing of at-risk individuals during childhood to clarify their genetic status is appropriate [9]. Every patient with rMC should have neurological examination before anaesthesia, especially before neuroaxial techniques of peripheral nerve blocks.

Particular preparation for airway management

Monitoring the depth of the neuromuscular blockade is strongly recommended when inducting general anaesthesia. Avoidance of succinylcholine is essential to avoid all possible complications including muscle rigidity and subsequent “can't-intubate-can't-ventilate” scenarios [10,11].

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Particular preparation for transfusion or administration of blood products

None.

Particular preparation for anticoagulation

None.

Particular precautions for positioning, transportation and mobilisation

There are no specific precautions necessary for the post-operative positioning, transport or mobilisation of rMC patients. Early post-operative mobilisation benefits rMC patients. Physiotherapists should also take into account the so-called “warm-up” phenomenon typical for rMC patients.

Interactions of chronic disease and anaesthesia medications

There are no interactions between anaesthetic agents administered for GA and mexiletine or acetazolamide. Carbamazepine may antagonise the effects of non-depolarising muscle relaxants (e.g. pancuronium). Their dosage should be raised and patients monitored closely for a more rapid recovery from a neuromuscular blockade than expected. Benzodiazepines may increase phenytoin serum levels. Quinine enhances the neuromuscular effects of suxamethonium. Administration of dantrolene may potentiate a vecuronium-induced neuromuscular block.

Anaesthetic procedure

General anaesthesia has to be performed as total intravenous anaesthesia. We recommend a target-controlled infusion for eligible drugs because of good control of the plasma/effective concentration. For a patient with chloride-channel myotonia, propofol appears to be the ideal anaesthetic agent, given its antimyotonic effect resulting from modulations of voltage-gated sodium channels within the sarcolemma membrane of the skeletal muscle. Propofol should be administered via the large forearm vein as this reduces the incidence of pain [8]. For neuromuscular blockade, rocuronium seems to be the ideal drug owing to the availability of the selectively relaxant-binding agent sugammadex at the end of surgery at any level of neuromuscular blockade [12,13,14].

Neuroaxial techniques need no specific approach to rMC patients.

Particular or additional monitoring

Standard monitoring of vital signs should be performed in all types of anaesthesia including sedation. Monitoring of the depth of the neuromuscular blockade is strongly recommended for induction to general anaesthesia, maintenance of anaesthesia and after the end of surgery to avoid residual neuromuscular blockade. If any depth level of a neuromuscular

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blockade induced by rocuronium is measured at the end of surgery, sugammadex should be administered in an appropriate dosage. For longer procedures, there is a need of proper temperature measurement and maintenance of normothermia since low temperature can worsen myotonia in rMC patients [9].

Possible complications

Anaesthesiologists should be aware of the risk of using suxamethonium in patients with chloride-channel myotonia in whom administration of suxamethonium can cause sustained total body rigidity and subsequent difficulty in airway management [10,11]. Patients with myotonic dystrophy also have myotonic response to neostigmine and increased sensitivity to non-depolarising neuromuscular blocking agents [15–20]. In such cases, rocuronium for a neuromuscular blockade with an active reversal by means of sugammadex is preferable.

In rare cases, injections of adrenaline or selective beta-adrenergic agonists in high doses may aggravate myotonia [9].

Post-operative care

The risk of reintubation because of muscle weakness or myotonic reaction can be obviated by using sugammadex and monitoring in the recovery room including monitoring of the depth of the residual neuromuscular blockade for at least 2 hours post-operatively. Normothermia should be maintained.

Disease-related acute problems and effect on anaesthesia and recovery

Total Body Rigidity

Triggers: succinylcholine

Prevention: avoidance of succinylcholine administration

Total Body Rigidity is characterised by generalised contraction of skeletal muscles. Spontaneous and controlled ventilation can be compromised. Treatment consists in the administration of the neuromuscular blockade and securing the airways by orotracheal intubation and continuation of mechanical ventilation [21].

Situations that should be considered for differential diagnosis:

Malignant hyperthermia may be characterised in terms of a dangerous, sudden hyperthermia, stiffness of skeletal muscles, hypotension, arrhythmias, and/or other complications, requiring immediate emergency intervention. There should be a standardised protocol for the appearance of malignant hypertermia in every hospital administering anaesthesia to the patient. Basic treatment involves the administration of dantrolen IV and symptomatic therapy. It is described in detail in European Malignant Hyperthermia Group guideline from the year 2010 [25].

Opioid-induced muscle rigidity is characterised by increased muscle tonus sometimes progressing to severe stiffness. Rigidity can decrease pulmonary compliance and functional

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residual capacity, may diminish or preclude adequate ventilation, and may cause hypercarbia, hypoxia, and an elevated ICP. Opioid-induced rigidity also increases pulmonary artery and central venous pressures and pulmonary vascular resistance. It has been demonstrated that vocal cord closure is primarily responsible for difficult ventilation with bag and mask that follows opioid administration. It can be also treated by administration of a neuromuscular blockade and ensuring the airways by orotracheal intubation and proceeding mechanical ventilation [22].

Ambulatory anaesthesia

We cannot recommend ambulatory anaesthesia. Due to the risk of a myotonic crisis, postoperative monitoring of vital signs, appropriate analgesia and normothermia is required. However, one-day surgery is acceptable in our opinion.

Obstetrical anaesthesia

The most common type of obstetrical procedure with the need of anaesthesia is caesarean section. First choice for most of obstetrical procedures should be any kind of neuroaxial anaesthesia: epidural/spinal/spinal-epidural. In case of contraindication for neuroaxial techniques, general anaesthesia is possible regarding the above mentioned pathophysiology of rMC. According to recent literature and available drugs, the use of a combination of TCI propofol, rocuronium and sugammadex in appropriate dosages is optional [23,24].

It is important to avoid excessive and prolonged pain perception during vaginal delivery. Therefore any kind of analgesia should be administered for delivery: neuroaxial (epidural) analgesia, remifentanil in PCA mode, nitrous oxide (Entonox®) and/or other systemic or established analgesic approach in every obstetrical ward.

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