orphanaesthesia

Anaesthesia recommendations for patients suffering from

Recessive myotonia congenita (Becker's disease)

Disease name: Recessive myotonia congenita

ICD 10: G71.1

Synonyms: Becker's disease

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 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 hyper-excitability of the muscle fibre membrane leading to bursts of aberrant action potentials.

Medicine in progress

Perhaps new knowledge

Every patient is unique

Perhaps the diagnostic is wrong

Find more information on the disease, its centres of reference and patient organisations on Orphanet: www.orpha.net

Disease summary

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, which is connected to specific types of mutations [5].

More than 150 different mutations have been reported in the CLCN1 gene, some of them associated to Becker's disease (recessive form, more severe) and other to Thomsen's disease (dominant form, milder). Laboratory diagnostic 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 share 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).

Facing surgery in patients with myotonia congenita or any other of myopathy, in addition to look for a diagnostic through NGS sequencing, some of the genes related to malignant hyperthermia (mainly RYR1 and CACNA1S genes) should be analysed.

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 therefore, tendencies to administer only malignant hyperthermia non-triggering anaesthetic agents for general anaesthesia. However, latest research shows that myotonic patients with malignant hyperthermia crisis can have mutations at two distinct genetic loci, one for myotonia and one for malignant hyperthermia susceptibility [5,7]. With respect to this knowledge, in case of necessity of general anaesthesia, we recommend using non-triggering anaesthetics, although the association with malignant hyperthermia is regarded as highly unlikely according to a recent review [8].

There is only one published only one case reporting use of midazolam for sedation of the rMC patient with no signs of adverse effect [6]. However, there is no evidence for safe administration of benzodiazepines for sedation. Therefore we recommend use of Target Controlled Infusions (TCI) of propofol or short acting opioids for sedation.

Necessary additional diagnostic procedures (preoperative)

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 of depth of neuromuscular blockade is strongly recommended for induction to 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].

Particular preparation for transfusion or administration of blood products

None.

Particular preparation for anticoagulation

None.

Particular precautions for positioning, transport or mobilisation

There is no specific approach for positioning, transport or mobilisation postoperatively in rMC patients. Early postoperative mobilisation is with benefit for rMC patients. Physiotherapeutists should also take into account the so-called “warm-up” phenomenon, which is typical for rMC patients.

Probable interaction between anaesthetic agents and patient’s long-term medication

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 neuromuscular blockade than expected. Benzodiazepines may increase **phenytoin** serum levels. **Quinine** enhances the neuromuscular effects of

suxamethonium. Administration of **dantrolene** may potentiate vecuronium-induced neuromuscular block.

Anaesthesiologic procedure

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

Neuroaxial techniques need no specific approach to rMC patient.

Particular or additional monitoring

Standard monitoring of vital signs should be performed in all types of anaesthesia including sedation. Monitoring of depth of 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 level of depth of neuromuscular blockade induced by rocuronium is measured at the end of surgery, sugammadex should be administered in appropriate dosage. For longer procedures, there is a need of proper temperature measurement and maintenance of normothermia since cold 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 neuromuscular blockade with active reversal using sugammadex is preferable.

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

Postoperative care

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

Information about emergency-like situations / Differential diagnostics

Total Body Rigidity

Triggers: succinylcholine

Prevention: avoidance of administration of succinylcholine

Total Body Rigidity is characterised by generalized skeletal muscle contraction. Spontaneous and controlled ventilation can be compromised. Treatment is administration of neuromuscular blockade and ensuring the airways by orotracheal intubation and proceeding of mechanical ventilation [21].

Situations that should be considered for differential diagnosis:

Malignant hyperthermia may be characterized by a dangerous, sudden hyperthermia, stiffness of skeletal muscles, hypotension, arrhythmias, and/or other complications, requiring immediate emergency intervention. There should be standardised protocol for appearance of malignant hypertermia in every hospital administering anaesthesia to the patient. Basic treatment involve administering of dantrolen IV and symptomatic therapy. It is described in detail in Supplement Nr. 10 - 2015 - Malignant hyperthermia.

Opioid-induced muscle rigidity is characterized by increased muscle tone progressing sometimes to severe stiffness. Rigidity can decrease pulmonary compliance and functional 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 neuromuscular blockade and ensuring the airways by orotracheal intubation and proceeding of mechanical ventilation [22].

If you need to provide neuromuscular blockade in short time after active reversal of neuromuscular blockade with sugammadex, you can use benzylisochinoline muscle relaxants (atracurium, cis-atracurium, mivacurium) or if Rapid Sequence Induction is needed you can use rocuronium again. But in that case is even more important to prove appropriate level of neuromuscular blockade with the objective monitoring of depth of neuromuscular blockade.

Ambulatory anaesthesia

We can't recommend ambulatory anaesthesia. Due to a risk of myotonic crisis, there is a need of postoperative monitoring of vital signs, appropriate analgesia and normothermia. 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, there is possible general anaesthesia regarding the above mentioned

pathophysiology of rMC. According to recent literature and available drugs, optional is use of combination of TCI propofol, rocuronium and sugammadex in appropriate dosages [23,24].

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

Literature and internet links

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Please note that this guideline has not been reviewed by two anaesthesiologists but by two disease experts instead.