orphanaesthesia

Anaesthesia recommendations for

Myasthenia gravis

Disease name: Myasthenia gravis (MG)

ICD 10: G70.0

Synonyms: Myasthenia gravis (juvenile and adult form) autoimmune (receptor-binding antibodies)
Additional forms of myasthenia:
- Isolated ocular myasthenia (autoimmune)
- Congenital Myasthenia (presynaptic, postsynaptic)
- Neonatal Myasthenia (maternal antibodies in newborns)

Disease summary: Myasthenia gravis (MG) is an autoimmune disorder with increasing frequency and recognition and is present in the pediatric and adult population. The juvenile form of MG is the most common and is similar to the adult form. It is caused by antibodies against the acetylcholine receptor at the postsynaptic neuromuscular junction. 75% of this cases occur after the age of ten [1]. The clinical expression differentiates between the ocular and the generalized form. The first clinical signs are painless weakness followed by ptosis and diplopia. Ptosis and diplopia images as the only clinical presentation occurs in the isolated ocular form of myasthenia gravis. If muscular weakness progresses within the next year a generalized form is present with the potential for respiratory muscle involvement. The first line of treatment are oral cholinesterase inhibitors, such as pyridostigmine. However, high doses could induce cholinergic crises. Thymectomy mainly as an endoscopic procedure is currently done in young onset acetylcholine-receptor antibody positive patients with generalized myasthenia [2, 3]. Due to the immunological origin of the disorder, immunesuppressant substances could be helpful. Mainly steroids are used, but also azathioprine, ciclosporin, methotrexate and cyclophosphamide could be used in poor-responders or as steroid-sparing agents for chronic use.

Congential myasthenic syndromes are genetically, mainly recessive, transmitted disorders. This group is clinically very heterogeneous, children present shortly after birth with a feeding problem and muscular hypotonia. As a severe symptom is respiratory insufficiency is well described and children often need artificial ventilation. A few children respond to therapy with acetycholinesterase-blockers. The defect could be located presynaptic (eg. Cholinacetyl-Transferase Defect CHAT), synaptic (eg. mutations in the gene encoding for Collagen Q COLQ) and postsynaptic (eg. disturbances in fast or slow channels in acetylcolinrezeptors or mutations in the gene encoding for the Rapsyn gene). A special feature in CHAT defects are recurrent apnea in children suffering from simple infectious diseases. These children require fast intubation and artificial ventilation.

Transient Neonatal Myasthenia gravis occurs in approximately 12% of the newborns of mothers with MG and improves within the first weeks of life as the antibody concentration decreases. The first signs are often muscular hypotonia, feeding problems and respiratory

distress. The characteristic presentation of MG is fatigability of voluntary muscles – depending on the extent of the disease – which typically worsen with continued daily activity.

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

Typical surgery

- Thymectomy
- General surgery
- Obstetrics and gynaecology
- Tracheostomy

Type of anaesthesia

Loco-regional anaesthesia is possible, depending on surgery. There is no evidence regarding the role of local anaesthetics but theoretically ester local anaesthetics might lead to problems in patients with MG and an anticholinesterase medication due to inhibition of metabolism. [4] High blood levels of any of the local anaesthetics can cause muscular weakness.

Epidural techniques with bupivacaine in patients with MG and trans-sternal thymectomy had been reported uneventful. Spinal anaesthesia is possible. [5]

Analgo-sedation should be performed very carefully as any sedative or muscle relaxing medication can cause respiratory depression (Table 1).

General anaesthesia is possible and necessary.

Induction with propofol, barbiturates, etomidate or ketamine are described as uneventful in patients with MG [6, 7]. Opioids analgesics do not depress neuromuscular transmission and remifentanil`s short elimination half-time makes it more titratable in myasthenic patients [8].

Benzodiazepines should be avoided due to increase of myasthenic symptoms.

Volatile anaesthetics can be used but may cause muscle relaxation and show reduced train of four (TOF) responses in MG patients like in all other patients. There is no difference in the use of sevoflurane or isoflurane.[12, 13]

The myasthenic patient is very sensitive to any neuromuscular blockade. The use of small doses for priming or defasciculation is not appropriate as the use of long acting muscle relaxants like pancuronium. In myasthenic patients the ED95 of vecuronium has an individual variability and varies between 5% to 90% of the normal dose, the same applies to atracurium and cisatracurium.

There is an increased sensitivity to any non-depolarizing muscle relaxants. Dose has to be reduced by 2 to 8 times. The TOF-ratio before the administration of the muscle relaxant can give an adequate information of the needed dose, but still the duration of the neuromuscular block can be prolonged.

Succinylcholine as a depolarizing muscle relaxing agent can be used, but be aware that patients with MG have a reduced response and need higher doses of succinylcholine 1.5 to 2.0 mg/kg.

The metabolism of mivacurium and succinylcholine can be affected by the preoperative use of pyridostigmine and therefore the duration of the neuromuscular blockade can be prolonged. [9, 10][11].

A good alternative might be the intubation with propofol and remifentanil.

Antagonisation of muscle relaxants with neostigmine or pyridostigmine may be difficult due to risk of cholinergic crisis and must be titrated carefully.

The use of rocuronium and reversal with sugammadex may be a good and safe alternative, but there a more data needed at the moment.

Necessary additional pre-operative testing (beside standard care)

Basic medication

- Anticholinesterase medication could be stopped, if this does not influence the respiratory situation. The need for muscle relaxants during the operation can be reduced
- Steroids: Should be given and covered preoperatively
- Immunsuppressants

Blood count and electrolytes

Lung function test should be done preoperatively (classification of MG [18]) and blood gas analysis. Chest X-Ray or CT-Scan before Thymectomy for detection of tracheal compression or deviated trachea.

Plasmapheresis could be useful in patients with autoimmune triggered MG (juvenile or adult form). This is typically performed prior to surgery in patients with unstable disease.

Premedication should be avoided in patients with severe reduced respiratory reserve, in cases with isolated ocular form of MG reduced doses of benzodiazepine are acceptable.

Particular preparation for airway management

No specific problems expected. Be aware of the possibility of postoperative need of mechanical ventilation or prolonged time of extubation.

Particular preparation for transfusion or administration of blood products

Not reported.

Particular preparation for anticoagulation

No special features.

Particular precautions for positioning, transportation and mobilisation

No special features.

Interactions of chronic disease and anaesthesia medications

No special features.

Anaesthetic procedure

If possible, regional techniques should be preferred. General anaesthesia as balanced or total intravenous anaesthesia can be used if reduced doses of muscle relaxants are used.

In case of thymectomy, epidural techniques for intra- and postoperative analgesia should be intended.

Particular or additional monitoring

Standard monitoring for normal operative procedure and extended monitoring according to the underlying operation.

Monitoring of the neuromuscular blockade is mandatory:

The preferred monitoring of neuromuscular transmission is electromyogram (EMG) and mechanomyogram (MMG) or calibrated acceleromyography (AMG) and train of four (TOF). TOF should be performed in the awake patient preoperatively and the ratio of T4/T1 (fade ratio) should be 1.0. In MG patients the ratio could be < 0.9 and shows a reduced need for depolarizing muscle relaxants. The use of calibrated AMG is recommended and the TOF ratio should reach preoperative values [15].

Possible complications

Prolonged neuromuscular block with respiratory insufficiency.

Post-operative care

Should be adapted to the underlying operations and comorbidity. The need for postoperative ventilation is dependent on the operation and the preoperative clinical extent of the MG. Possible criteria are a duration disease longer than 6 years, respiratory complications in the past medical history and a reduced vital capacity < 50% according to age.

Adequate postoperative pain control, pulmonary toilet and the avoidance of drugs that interfere with neuromuscular transmission (Table 1). Anticholinesterase medication has to be continued in the postoperative phase. The dose has to be titrated and the intravenous dose if needed has to be in an equivalent dosage.

Patients should stay in a post-anaesthesia care unit or an intensive care unit.

Lists, summarizing substances which are definitely deteriorating myasthenia gravis are available (table 1, www.dgn.org, www.myasthenia.org). Especially antibiotics, anticonvulsant drugs, beta-blocker and psychopharmacological medications are of special interest.

Disease-related acute problems and effect on anaesthesia and recovery

Patients may suffer cholinergic or myasthenic crises (both causing respiratory failure and muscle weakness), which may be difficult to differentiate. These can be triggered by infection or antibiotic therapy as well as by neuromuscular blocking agents or benzodiazepines.

Probatory administration of cholinesterase inhibitors can help to differentiate between both forms.

Ambulatory anaesthesia

Ambulatory anaesthesia is unsafe and should be avoided.

Obstetrical anaesthesia

Obstetrical anaesthesia can be performed as general as well as regional anaesthesia. Like in most neuromuscular disorders MG can deteriorate during pregnancy [16].

Maternal antibodies in MG can pass the placenta barrier and give the possibility for impaired newborns with muscular hypotonia or respiratory distress after birth.

Annex 1

Table 1. Drugs with possible influence on Myasthenia gravis

Class	Drugs
Analgesics	flupirtine, morphine
Antiarrhythmics	chinidine, ajmaline, procainamide, mexitile, ß-blocker (pindolol, propranolol, timolol topical)
Antibiotics	aminoglycosides, macrolide, ketolide, lincomycine, fluoroquinolone, sulfonamide, tetracycline
Antidepressants	amytryptiline, lithium
Anticonvulsants	benzodiazepine, carbamazepine, ethosuximide, gabapentin
Antimalarial Drugs	chinidine, chloroquine
Antirheumatic Drugs	d-penicillamine, chloroquine
Ca-channel Inhibitor	verapamil, nifedipine, diltiazem
Diuretics	loop-diuretics, acetazolamide
Local anesthetics	ester type
Magnesium	high dose therapy e.g. obstetrics
Psychopharmaceutical	chlorpromazine and other phenothiazines, benzodiazepine

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