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Case Report Open Access

Rocuronium and Sugammadex in a Myasthenic Patient Undergoing Laparoscopic Cholecystectomy

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Background

MG is a chronic autoimmune disease that targets the neuromuscular junction, leading to a decreased number of cholinergic receptors available for interaction with AcetylCholine (ACh). Clinically the condition is characterized by asymmetric and fluctuating weakness of the skeletal muscles that worsens upon exertion and that may determine sudden respiratory and oropharyngeal failure (myasthenic crisis) that can occur in the perioperative period. The therapeutic options are [1,2]:

- AcetylCholinEsterase Inhibitors (AChEI) e.g. pyridostigmine and neostigmine, to enhance the probability of ACh interaction with its receptors by prolonging the biological half-life of the neurotransmitter
- Immunosuppressive drugs
- Plasmapheresis
- Thymectomy

Responsiveness of MG patients to muscle relaxant drugs is unpredictable. Suxamethonium chloride (succinylcholine) can be used for rapid sequence induction and intubation (RSI) but higher than normal doses are required (1.5-2 mg/Kg). Because of their interaction with anticholinergic drugs succinylcholine and mivacurium often cause prolonged skeletal muscle relaxation. Caution is advisable in using non-depolarizing muscle relaxant drugs (NDMRs) because of the unpredictability of the effects and irregularities of the resulting hyposthenia. This in turn may cause muscular function monitoring through peripheral neurostimulation to be unreliable and NDMRs have to be administered in small successive doses until the desired effect is achieved. The interactions of NDMRs with anticholinergic drugs taken by the patient and the inhibitors of the anesthesiological muscular blockade may lead to a prolonged skeletal muscle relaxation therefore the patient has to be made aware of the possible necessity of post-operative mechanical breathing aiding [3]. It appears therefore clear that the anesthesiological management of myasthenic patients remains a challenge.

Case Report

A male patient (41 yo, h172 cm, w82 Kg) was elected for a Laparoscopic Cholecystectomy procedure (LC), following diagnosis of lithiasic cholecystitis. The patient's clinical history reported an Endoscopic Retrograde CholangioPancreatography (ERCP) executed to remove a calculus from the biliary tract. From the anamnesis emerged that the patient was affected by MG, diagnosed 2 years before with exquisitely ocular symptoms (diplopia, presently absent) and that after chronic cortisonic treatment (suspended) the patient was being treated with pyridostigmine (60 mg every 4 h per os, without night administration), the last dose administered on the day prior the operation. Pre-operative anesthesiological treatment was omitted.

Neurological counsel framed the absence of symptoms and thymoma and ensured the effectiveness of the pharmacological treatment and the routine pre-operative exams evidenced no notable data, except for the expected cholestasis signs. Combination antibiotic therapy with piperacillin/tazobactam [4] was established. The anesthesiological examination reported an ASA (American Society of Anaesthesiologists) risk score of 2, relative to a generalized mild to moderate pathological condition.

After pre-oxygenation and administration of sufentanil (15 μg) and 1.25 mg of droperidol (antiemetic) [3] narcosis was induced through Propofol (200 mg) and, prior verification of the possibility to ventilate the patient with a face mask, 20mg of rocuronuim (corresponding to the ED95, dose responsiveness of 95%) were infused. Oro-tracheal intubation was rapidly carried out with no events, after 90 seconds. Narcosis was then maintained with sevoflurane (1.5% Inspired Concentration, FI) and remifentanil (0.5 μg/Kg/min).

A nasogastric feeding tube (NGT) allowed emptying of the stomach while protection of the gastric mucosa was assured by treatment with omeprazole. The LC proved difficult to perform but the operation was carried out in about two hours. At the end of the procedure 300 mg of sugammadex were administered (just above 4 mg/kg) and the patient was awaken from anesthesia, extubated and, after the tongue depressor test [3], led to the post anesthesia care unit (PACU) where the vital parameters were kept under constant monitoring. Post operative pain therapy contemplated the use of tramadol, metoclopramide and anti-inflammatory drugs. After a few hours under observation the patient was transferred to the Surgery Department where discharge was programmed for the second post-operative day.

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Discussion

Following is described what appears to be one of the few cases of a myasthenic patient treated with sugammadex to antagonize a rocuronium-induced neuromuscular blockade. Traditional antagonists act by inhibiting Acetylcholin Esterase (AChE) activity, enormously increasing the quantity of ACh available for interaction with the cholinergic receptors in the neuromuscular junction. This in turn leads to competitive inhibition by ACh of the NDMRs used to maintain the neuromuscular paralysis. This mode of action enhances cholinergic transmission, including that of the sympathetic nervous system, requiring administration of an anticholinergic drug, e.g. atropine, to contrast the effects of such stimulation (bradycardia, sialorrhea, etc.).

The novel mode of action of sugammadex allows sequestering of steroidal NDMRs within its lipophilic core without altering the cholinergic transmission or risking a cholinergic crisis. Adverse effects don't appear to be more severe that those recorded with neostigmine and placebo [5]. Sugammadex is a non-AChE inhibitor of steroidal NDMRs, with a high affinity for rocuronium. Structurally it is a novel modified γ-cyclodextrin, which binds the curare to form an extremely stable complex excreted with urine [6]. Decurarization takes place rapidly and allows the use of rocuronium in RSI as an alternative to succinylcholine [3,7]. It is reasonable to think at rocuronium and sugammadex for the anaesthesia of a myasthenic patient: at least three cases are reported in scientific literature [8-10].

Initially acceleromyography was chosen to monitor the degree of curarization [11] but, despite sudden unavailability of the appropriate instruments, the cholelithiasis developing in cholecystitis required removal of the gall bladder, resorting to clinical monitoring for the assessment of the degree of paralysis. Propofol (200 mg) and rocuronium (20 mg) administered at the induction of narcosis readily allowed intubation, but after approximately 20 minutes the patient fighting the ventilator prompts administration of a further 50 mg of Propofol and 20 mg of rocuronium to obtain adequate operational conditions.

No further administration of curare was needed during the length of the procedure, the initial muscle relaxation proving satisfactory. Two hours later, lacking reliable data on the intensity of the neuromuscular blockade, administration of a reversing drug is decided, choosing the specific antagonist of rocuronium, sugammadex. This allowed avoiding the use of neostigmine that, even though not often, may induce in MG patients cholinergic crises that are hardly differentiable from the myasthenic ones [1,2] and that would complicate the clinical management of the patient [6].

LC represents the gold standard for cholecystitis treatment [4]. The chance of a rapid worsening of the myasthenic patient's conditions, especially in the perioperative period [1], and the required induced pneumoperitoneum, that impedes normal breathing, provided the *rationale* for the recourse to a general anesthesia with skeletal muscle relaxation and mechanical ventilation [12], so much so because the surgical procedure was expected to be difficult.

Recent research reports alternative techniques of spinal anesthesia being available [13,14] for LC, but the peculiar physiopathology of MG compels to extreme caution in considering such procedures.

In MG, whereas not possible to employ locoregional anesthesia, the myorelaxant action of halogenated anesthetics should be considered as it may reduce the necessity of using curares [3]. Anesthesia was therefore maintained with sevoflurane and remifentanil, an ultra-short-acting opioid with rapid metabolism and rapid reduction of blood concentration after cessation of infusion [3], both suspended at the end of the surgical procedure to minimize the risk of pharmacologically-induced post-operative respiratory failure. In PACU strict monitoring of the vital parameters was continued together with surveillance of the state of consciousness and the effectiveness of the pain therapy.

Restoration of pyridostigmine treatment was achieved through the NGT, expecting re-establishment of its action in about 30-60 minutes [1]. Its uptake and effects were monitored during several hours following the procedure. The best post-operative course prediction reference is the patient's condition prior to the operation and in this case it was optimal. Moreover it is uncommon for the neuromuscular functions of a myasthenic patient managed with adequate perioperative procedures to spontaneously worsen during the post-operative period. In such a case it would be needed to assess and correct the reversible metabolic cause, infective or pharmacological, responsible for the worsening [2]. After thorough assessment of the patient's conditions, five hours after leaving the operation theater the patient was transferred to the Surgery Department where he was discharged after a few days.

Conclusion

Considering the outcome of the operation and the reported cases in scientific literature, the use of rocuronium and sugammadex in patients affected by MG appears to be effective and safe. Further investigations are probably needed to effectively circumscribe its application in the concerned pathology.

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