

Anaesthetic management of a patient with myasthenia gravis for abdominal surgery using sugammadex

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Abstract

We report a case of a patient with tumor of the caecum with coexistent myasthenia gravis (a form according to Osserman II A), requiring general anesthesia for abdominal surgery. To reverse the neuromuscular block induced by vecuronium was used sugammadex.

Key words: sugammadex, myasthenia gravis, neuromuscular monitoring, vecuronium.

Introduction

Myasthenia gravis (MG) is a chronic autoimmune neuromuscular disease manifesting with weakness and fatigue of skeletal muscles after physical exercise, with a tendency to subside after periods of rest and typically after taking anticholinesterase medication. Myasthenia gravis is characterized by autoantibody attack of acetylcholine receptors at the motor end plate of striated muscles, which results in variable muscle weakness made worse by exercise [1]. Myasthenia gravis occurs in about 3-7 people per 100,000 – usually only sporadically.

The pathomechanism of the disease is associated with the formation of autoimmune complexes in acetylcholine receptors on the postsynaptic membrane of the neuromuscular junction. There is a close relationship between immune processes accompanying myasthenia gravis and the thymus, which has been found to contain production sites of B-cells synthesizing anti-receptor antibodies [2].

Of major clinical importance is the classification of myasthenia gravis developed by Osserman [3]. In 1958, Osserman proposed placing patients with myasthenia gravis in five groups: I – localized (ocular), II – generalized (mild or moderate), III – acute fulminating, IV – late severe, and V – muscle atrophy. Later, Osserman divided group II into the subclassification: A (mild) and B (moderate). Various modified criteria have been suggested over the years. This classification allows one to grade the disease and assess the perioperative risk and possible complications.

Myasthenic crisis may be defined as respiratory failure or delayed postoperative extubation for more than 24 h resulting from myasthenic weakness. Myasthenic crisis results from weakness of upper airway muscles leading to obstruction and aspiration, weakness of respiratory muscles leading to reduced tidal volumes, or from weakness of both muscle groups.

Over the last four decades, the prognosis for myasthenic crisis has dramatically improved from a mortality rate of 75% to the current rate of less than 5%. Common precipitating factors for myasthenic crisis include respiratory infections, aspiration, sepsis, surgical procedures, rapid tapering of immune modulation, beginning treatment with corticosteroids, exposure to drugs that may increase myasthenic weakness, and pregnancy [4].

Surgery and anaesthesia in myasthenic gravis patients are associated with an increased risk of death and severe complications. The risk is mainly related to a markedly higher sensitivity to muscle relaxants observed in this group of patients, even in periods of complete remission [5]. Myasthenia patients often require prolonged ventilation in the ICU setting [3, 6, 7]. A significant, though less common, perioperative risk in myasthenic patients is cholinergic crisis.

The most proper approach during anaesthesia in patients with myasthenia gravis is to apply deep inhalational anaesthesia without muscle relaxing agents. However, in abdominal and colorectal surgery sometimes it is necessary to use muscle relaxants in order to improve operating conditions – to have better access to the operational field.

The safety of using muscle relaxing agents in patients with myasthenia gravis undergoing major surgical procedures has so far been assessed as insufficient. Consequently, many anaesthesiologists routinely decided against using muscle relaxants in such clinical cases. The situation may change with sugammadex, a novel agent recently introduced into clinical practice. Sugammadex (ORG 25969) is a modified γ -cyclodextrin [8-11] (su refers to sugar and gammadex refers to the structural molecule γ -cyclodextrin). Unterbuchner *et al.* report the successful use of the modified cyclodextrin sugammadex in a myasthenic patient to reverse a vecuronium-induced deep level of neuromuscular block [12].

Case report

An 85-year-old white male patient was scheduled for right-sided hemicolectomy due to

caecal tumour. At the time of admission to the Department of General and Colorectal Surgery, the patient had no complaints.

The patient had been treated for myasthenia gravis (Osserman stage IIa) since 2004. He had a number of operations previously: appendectomy (1940), left inguinal hernioplasty (1995), right inguinal hernioplasty (2003) (reoperation in 2005 due to wound dehiscence). He received the following medications: Mestinon (Pyridostigmini bromidum) (3 × 1 tabl), Metazydyna (Trimetazidini dihydrochloridum), Vicebrol (Vinpocetinum), Zoxon (Doxazosini mesilas), Penestan (Finasteridum). The patient was in the optimum condition for surgery, with no absolute neurological contraindications to the operation and no abnormalities identified in laboratory tests.

The patient was scheduled for surgery under general endotracheal anaesthesia (ASA class III). The patient received no premedication due to existing contraindications to benzodiazepines. Induction of general anaesthesia was obtained with propofol at 2 mg/kg. The patient was intubated with spontaneous respiration. Intubation was uncomplicated. Immediately after the intubation, remifentanyl was given in a continuous intravenous infusion of 50-150 μ g/h. General inhalation endotracheal anaesthesia was performed according to procedures in place, using sevoflurane in an air/oxygen mixture with low gas flow. During anaesthesia, the patient's mechanical ventilation parameters were adjusted on the basis of standard anaesthesiological evaluation. Doses of anaesthetic agents were modified according to the clinical assessment of the depth of anaesthesia. Neuromuscular transmission was blocked with vecuronium administered at fractional doses of 1 mg until the required degree of relaxation (with nerve stimulation monitoring performed by the Datex-Ohmeda, mode TOF). Maintenance doses of 1 mg (0.015 mg/kg body weight) were administered every 50 min. Overall, 5 mg of vecuronium was administered during the 3-hour surgery. The management described above resulted in excellent circulatory stabilization (Table I).

Table I. Data of cardiovascular parameters during anaesthesia

Parameters	Heart rate [beats/min]	Non-invasive blood pressure [mmHg]
Induction	96	136/80
Start of the operation	90	110/58
Every 15 min during 3 h of the operation	88; 86; 80; 75; 76; 78; 76; 72; 70; 70; 72	110/60; 112/59; 110/60; 100/58; 100/60; 100/60; 102/62; 100/62; 110/58; 112/62; 112/60
End of the operation	72	112/68
Extubation	72	120/80

The patient underwent right-sided hemicolectomy due to a caecal tumour with a diameter of approx. 8 mm infiltrating the mesentery.

Emergence from anaesthesia was initiated at the time of placement of the final skin suture. Sugammadex (Bridion) in a 3 mg/kg bolus was administered to reverse the neuromuscular block. Neuromuscular block reversal was monitored by the Datex-Ohmeda monitor simulation and clinical signs. Five min after Bridion administration, the patient regained efficient pulmonary respiration and full logical contact was re-established. The patient was extubated 6 min after Bridion administration.

Upon emergence from anaesthesia and extubation, the patient was transferred to the recovery room of the Anaesthesia and Intensive Care Department. Full verbal contact and recovery of consciousness with the patient was maintained at the time of transfer to the recovery room. The patient's respiratory function and circulatory status were uncompromised. Postoperative analgesia was provided with remifentanyl administered in a continuous infusion. The patient stayed in the recovery room of the Anaesthesia and Intensive Care Department for 20 h before being transferred to the Department of General and Colorectal Surgery. During 6 days postoperative stay in the Department of General and Colorectal Surgery, the patient received 100 mg of Ketoprofen intravenously three times per day. The patient was discharged on the 7th postoperative day.

Discussion

Myasthenia gravis patients, particularly those undergoing major surgery and/or suffering from concomitant disorders, require special individual management in preparation for surgery [5], appropriate selection and administration of anaesthesia, and close monitoring postoperatively [13]. This also applies to other groups of patients with nervous system disorders including myopathies and other muscular diseases [14, 15].

Sensitivity to non-depolarizing neuromuscular blocking drugs is known to vary greatly between myasthenic patients. Several studies using a cumulative technique have shown the ED₉₅ for vecuronium to range from 6 µg/kg to 44 µg/kg. Ocular myasthenic patients were less sensitive to vecuronium than generalized myasthenic patients. During general anaesthesia, neuromuscular monitoring is essential to avoid problems of prolonged neuromuscular block in myasthenic patients. Vecuronium is a muscle relaxing agent usually applied during the surgery in our hospital.

Epidural anaesthesia is less controllable in cases of intraoperative haemorrhage. Epidural anaesthesia causes sympathetic blockade with blood vessel

dilation and venous stasis; thus hypovolaemia as a result of a haemorrhage is more difficult to compensate than general endotracheal anaesthesia, especially in elderly patients.

The best way of preparing a patient for a surgical procedure is to recognize and understand both the underlying medical condition and coexisting diseases. Proper awareness of these makes it possible to arrange individual pre-, peri- and postoperative management. The procedure was followed in the case reported here. Each stage of perioperative care was thoroughly analysed and planned.

Currently used neuromuscular transmission blockers are considered safe, with the recovery of normal muscle function occurring after a period specific to each drug. Acetylcholinesterase inhibitors are used to accelerate the recovery of normal neuromuscular transmission following administration of non-depolarizing neuromuscular blockers. The time of administration of these agents is of major importance, since administered prematurely, they can paradoxically result in neuromuscular block reversal. As many as 60% of patients undergoing surgery under general anaesthesia are believed to be likely to experience problems with residual activity of skeletal muscle relaxants (PORC – postoperative residual curarization) [16-18]. The launch of sugammadex, an agent reversing neuromuscular block induced by steroid muscle relaxants, holds out hope to steadily reduce the incidence of PORC [19]. Unquestionable benefits of the drug include: rapid neuromuscular block reversal regardless of its depth [20-22], documented drug safety and tolerance [23-25], and – above all – an innovative mechanism of action [25]. All the beneficial qualities of sugammadex offer the possibility for using the drug in patients who are expected to have problems with proper ventilation and gas exchange.

In the case described here, sugammadex made it possible to perform a safe general anaesthesia procedure with skeletal muscle relaxants without prolonging mechanical ventilation. The medical literature contains isolated reports on the use of sugammadex (with success) in patients with myasthenia and other muscular dystrophies [12].

The authors of this report believe that sugammadex as an agent used for muscle relaxation in delivering anaesthesia to MG patients during abdominal surgery could one day be recognized as the gold standard. Sugammadex, used in combination with objective neuromuscular monitoring, can be applied to reverse vecuronium-induced neuromuscular blockade in patients with myasthenia gravis.

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