Case Report

Use of rocuronium and sugammadex under neuromuscular transmission monitoring in a patient with multiple sclerosis

ABSTRACT

Multiple sclerosis (MS) is a potentially disabling disease characterized by demyelinating lesions in the central nervous system. One of the anesthetic challenges encountered in surgical patients with MS is the management of neuromuscular blockade (NMB) and its reversal. We report a case of a 31-year-old female patient suffering from MS, who underwent gynecological surgery under general anesthesia with sevoflurane, fentanyl, and rocuronium which was successfully reversed with sugammadex. Neuromuscular transmission (NMT) monitoring was used to guide the intraoperative doses of rocuronium and also the reversal of NMB by the use of sugammadex to ensure a safe tracheal extubation. In addition, delivered volatile was titrated according to anesthetic depth monitoring (Bispectral Index) while esophageal temperature was also monitored for the maintenance of normothermia. Postoperatively, a multimodal analgesic scheme offered a high-quality analgesia and sleep, minimization of anxiety, and increased patient satisfaction. At 1-month follow-up, the patient's course was uncomplicated without any MS exacerbation. We consider that the use of rocuronium and sugammadex under NMT monitoring may represent a useful and safe choice in patients with MS.

Key words: Anesthesia; multiple sclerosis; neuromuscular transmission monitoring; rocuronium; sugammadex

Introduction

Multiple sclerosis (MS) is an immune-mediated, chronic, and potentially disabling disease characterized by demyelinating lesions in the central nervous system. Its course may be relapsing-remitting or progressive, and common symptoms include visual impairment, sensory and motor deficits, balance and genitosphincter disorders, fatigue, spasticity, and pain.[1] Depression or bipolar disorder may also accompany MS.[1]

Anesthesia for MS patients may be challenging, especially regarding the management of neuromuscular blockade (NMB), since early and complete recovery of muscle strength is particularly important for these patients. Literature on the safety and efficacy of rocuronium and sugammadex in patients with MS is limited.[2] After obtaining written consent, we report the case of a patient with MS who received general anesthesia with NMB induced by rocuronium and reversed with sugammadex under the guidance of neuromuscular transmission (NMT) monitoring.

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Case Report

A female patient (31 years, 62 kg, 164 cm) suffering from MS and bipolar disorder was scheduled for myomectomy under general anesthesia. Two years before, she had been diagnosed with MS, manifested as weakness and numbness of the upper and lower limbs. Symptoms had resolved after steroid

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treatment, and since then, she occasionally had abnormal sensations – numbness and tingling in her extremities. She received the immunomodulatory drug glatiramer acetate for the MS and lamotrigine as maintenance therapy for the bipolar disorder. The rest of her medical history and laboratory tests was unremarkable. Neurological clinical examination revealed hyperactive deep tendon reflexes of lower extremities without clonus and hypesthesia to light touch on the right side. She had never received general or neuraxial anesthesia.

Preoperatively, the patient was informed about surgery, anesthesia, perioperative risks, and plans of management. She continued her medications perioperatively and received additionally bromazepam 3 mg per os the evening before surgery and midazolam 2 mg intravenously (IV) in the operating room. Cefuroxime 1.5 g plus metronidazole 500 mg IV was given as antibiotic prophylaxis. The temperature in the operating theater was set at 22°C.

Apart from routine monitoring (electrocardiogram, blood pressure, pulse oximeter-S/5 Anesthesia Monitor, Datex-Ohmeda, Helsinki, Finland), NMT monitoring of the adductor pollicis muscle was also implemented through the respective NMT module of S/5 anesthesia monitor. The train-of-four (TOF) response (stimuli of 2 Hz, 0.2 ms, at 60 mA) was monitored throughout the procedure. In addition, anesthesia depth was assessed through Bispectral (BIS) Index Monitor (BIS A-2000; Aspect Medical Systems, Newton, MA, USA) and core temperature through an esophageal probe.

Anesthesia was induced with propofol 2.5 mg/kg and fentanyl 2 μg/kg IV and was maintained with sevoflurane in a N_2O/O_2 mixture ($FiO_2 = 0.45$) targeting to BIS values between 40 and 50. Fentanyl 200 μg was given at incremental doses for analgesia. Intraoperative BIS values fluctuated between 26 and 57, and sevoflurane inhaled concentration was adjusted accordingly from 0.9% to 1.4%. Rocuronium 1 mg/kg IV was given to facilitate tracheal intubation which was attempted after 2 min when the TOF response became 0. No further doses of rocuronium were required intraoperatively, but interestingly, posttetanic counts remained >1 at all times. At the end of surgery (65 min duration), the 3rd TOF response (T_3) reappeared, and sugammadex 2 mg/kg was administered. The T_4:T_1 ratio became 0.9 in 45s, and the patient's trachea was extubated.

Intraoperative esophageal temperature fluctuated between 35.7°C and 36.5°C. Paracetamol 1 g, parecoxib 40 mg, and morphine 1 mg/kg were administered IV for postoperative analgesia. In addition, a patient controlled analgesia IV pump was connected to deliver morphine (0.5 mg/h basal rate, 1 mg extra boluses, and 15 min lockout interval). Paracetamol 1 g × 3 g and parecoxib 40 mg × 2 mg daily were also prescribed. Postoperative pain, anxiety, sleep quality, and satisfaction were assessed by a 10-point numerical rating scale [Table 1]. Temperature was also recorded regularly. The patient remained normothermic, had an uncomplicated course, and was discharged home after 2 days. At 1-month follow-up, she was in very good condition without MS exacerbations.

Discussion

The main perioperative concern for MS patients is worsening of symptoms since surgical stress, anesthesia, anxiety, pain, and hyperthermia may precipitate attacks.[1]

Preoperative approach includes a thorough assessment of MS type/course, neurological deficits, and medical treatment which may interfere with anesthetic drug activity and hepatic metabolism.[1] The patient's clinical condition should be optimized while elective surgery should be postponed in case of symptom exacerbation. The patients should receive detailed information on treatment options, perioperative risks, and management plan. A tailored anesthesia should include a safe technique, carefully chosen drugs/adjuvants, dose titration to individual needs, and avoidance of hyperthermia.[1] In this regard, monitoring of anesthetic depth, NMB, and temperature may be useful.

There are no controlled trials comparing general versus regional anesthesia in patients with MS. Neuraxial techniques are preferred in obstetrics[1] while general anesthesia is commonly used in other cases. Since the demyelinated neural tissue is sensitive and susceptible to local anesthetic toxicity, epidural anesthesia may probably be preferred over spinal due to the lower drug concentrations that develop in the spinal cord. Among IV anesthetics, propofol,[2-5] thiopental,[6] and etomidate[7] have been safely used for anesthesia induction. Similarly, most volatiles, namely,

Table 1: Postoperative assessment of analgesia, anxiety, sleep quality, and satisfaction

Measurements	Postoperative					
	1 h	2 h	6 h	12 h	24 h	48 h
Pain at rest (0-10)	3	3	2	0	1	0
Pain during cough (0-10)	6	6	5	3	3	3
Cumulative morphine consumed (mg)	10	12	17	35	56	104
Anxiety/stress (0-10)	0	0	0	0	0	1
Sleep quality (0-10)	NA	NA	NA	NA	8	8
Satisfaction (0-10)	9	9	9	9	9	9

NRS: Numerical Rating Scale (0-10); NA: Not applicable

halothane,[4] isoflurane,[6] sevoflurane,[2,3,5,8] and desflurane[7] have been used uneventfully for the maintenance of anesthesia, with the latter two agents being associated with fast and smooth emergence.[7,8] Moreover, sevoflurane was administered for both anesthesia induction and maintenance in a patient with MS exacerbation.[9] Opioid analgesia with fentanyl[2-4,8] or remifentanil[3,5,7] has been used without complications, apart from chest wall rigidity - without further sequelae - observed in a spontaneously breathing patient receiving remifentanil infusion.[5] Since case reports represent the main source of information, there is no strong evidence regarding the optimal general anesthetic for patients with MS. Nevertheless, monitoring of anesthesia depth is undoubtedly useful for dose titration and avoidance of overdosing or intraoperative awareness.[9] In this regard, BIS could be a helpful tool in the anesthetic management of patients with MS.[3]

The NMB agents are preferably omitted in selected patients and surgical procedures.[5,9] Maintenance of spontaneous breathing in a patient with MS through a laryngeal mask under sevoflurane anesthesia has been described.[5] On the other hand, an NM blocker is usually required to facilitate tracheal intubation in MS patients even though intubation without NMB has also been reported.[10] Succinylcholine,[11] atracurium,[4,6,12] vecuronium,[7,8] and rocuronium[2,3] have been used with various responses. Succinylcholine should better be avoided because it may induce hyperkalemia due to upregulation of skeletal acetylcholine receptors.[1,11] The same mechanism is also involved in a resistance to nondepolarizing neuromuscular (NM) blockers which may be seen in MS.[4,12] Brett *et al*. described a characteristic resistance to atracurium 0.4 mg/kg, manifested as an abnormally slow establishment of NMB not deep enough to facilitate tracheal intubation; two additional doses of atracurium (0.2 mg/kg each) were required to provide acceptable conditions.[12] On the contrary, muscle mass reduction and weakening - due to the disease *per se* or drugs used for spasticity (i.e., baclofen) - may predispose patients to an increased sensitivity to nondepolarizing NM blockers.[1,4]

There are limited data about the response of MS patients to rocuronium.[2,3] Two case reports do not describe if resistance or sensitivity to rocuronium was encountered, and no details are given about patients' TOF response (i.e., time to become zero) after small intubating doses (0.5 and 0.6 mg/kg, respectively).[2,3] In our patient, a resistance to rocuronium was manifested as a delay in the onset and maximum action of rocuronium, with a TOF = 0 being achieved 2 min after administration of a high intubating dose (1 mg/kg). In addition, at no time during surgery did the NMB become intense, with posttetanic counts remaining >1.

In any case, NMT monitoring is useful in assessing MS patients' response - resistance or sensitivity - and thus titrating NMB drug doses.[2,4,10] Furthermore, NMT monitoring is valuable in assessing muscle strength at recovery and confirms the absence of residual NMB which in MS patients may become catastrophic.[2,3] Although reversal of NMB in patients with MS is usually achieved with neostigmine,[4,6] spontaneous recovery with omission of reversal agents has also been reported.[3,7,12] It should be noted though that any degree of NMB - even intense blockade - induced by rocuronium or vecuronium can be reversed with an appropriate dose of the selective reversal agent sugammadex. This modified γ-cyclodextrin encapsulates the free molecules of rocuronium or vecuronium in the plasma, reduces their concentration in the NM junction, and reverses rapidly the NBM.[13] Sugammadex does not cross the intact blood–brain barrier, and central neural or peripheral muscular effects are not expected by its use. Theoretically, these unique properties render it advantageous over neostigmine, especially in patients with NM disorders. Nevertheless, published data on its clinical use, safety, and efficacy in MS patients are scarce.[2] Sinikoglu *et al*. gave sugammadex 2 mg/kg to a patient with MS who underwent repeated operations; each time, sugammadex was given at a stage of significant spontaneous recovery of NM junction, thus at T_4/T_1 ratios ≥0.5. A T_4/T_1 ratio of 1 was achieved in 85–140 s (mean time: 109.8 ± 21 s) while the time needed for T_4/T_1 to increase from 0.5 to 0.9, which is recommended for safe tracheal extubation, was 44 s.[2] In our patient, we administered sugammadex 2 mg/kg at a significantly deeper NMB thus when 3 TOF responses were recorded. The above dose is recommended for reversal of NMB with TOF ≥2.[13] Notably, T_4/T_1 became 0.9 in just 45 s, significantly faster than previously described[2] or expected according to drug characteristics (median time is around 2 min).[13] The observed resistance to NMB agent may have played a role.

Among other drugs, anxiolytics and antibiotics are required to reduce the impact of aggravating factors, such as emotional instability and infections.[3] Postoperatively, high-quality analgesia (i.e., a multimodal scheme) and sleep are extremely important. Body temperature should be monitored closely since even minor increases (i.e., by 0.5°C) may worsen neural conduction.[6] Body heating should be avoided (i.e., room temperature control, blankets, and fluids) while fever/infections should be treated promptly with antipyretics and antibiotics.[3,4]

In patients with MS, the use of rocuronium and sugammadex under NMT monitoring may represent a useful and safe

choice. In addition, anesthetic depth and body temperature monitoring are helpful in optimization of anesthesia and perioperative care in these patients.

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Conflicts of interest
There are no conflicts of interest.

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