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Case Report

Use of Sugammadex in Myasthenia Gravis and Becker Muscular Dystrophy: Four Cases

Yasemin Burcu ÜSTÜN, Binnur SARIHASAN, İsmail Serhat KOCAMANOĞLU, Seda YEĞIN, Hatice AZAR

Ondokuz Mayıs Üniversitesi Tıp Fakültesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, Samsun, Türkiye

Summary

Myasthenia gravis is an antibody-mediated autoimmune disease targeting nicotinic acid acetylcholine receptors in neuromuscular junctions. In myasthenia gravis, the number of nicotinic acid acetylcholine receptors is significantly reduced. This condition leads to muscular weakness and deserves special attention in terms of respiratory muscles. Becker muscular dystrophy is an X-linked recessive inherited disorder characterized by slowly progressive muscle weakness of the legs and pelvis. Sugammadex is a hydrophilic cyclodextrin molecule that has a lipophilic nucleus. It is an innovative molecule which terminates the effects of steroidal neuromuscular blocking agents via encapsulation. This is a report of the use of sugammadex in patients with MG and Becker muscular dystrophy. Three patients with myasthenia gravis; 55, 45 and 2.5 year-old; were enrolled the surgery under general anesthesia for the disc hernia repair, abdominal hysterectomy, and correcting of cataract, respectively. Additionally, a five-year-old patient with Becker muscular dystrophy was scheduled for circumcision and orchiopexy under general anesthesia. In all patients, rocuronium as a muscle relaxant and sugammadex for the reverse of rocuronium were administered. Tracheal extubation was achieved in all patients at the end of operations without complications. The use of a combination of rocuronium-sugammadex seems safe in muscle diseases without the development of any possible complications.

Key words: Anesthesia, Myasthenia gravis, Becker Musculer Dystrophy, Sugammadex

Myasteni Gravis ve Becker Muskuler Distrofisinde Sugamadeks Kullanimi: Dört Olgu

Özet

Myastenya gravis (MG), sinir kas kavşağında nikotinik asetil kolin reseptörlerini (nAKR) hedefleyen antikor aracılı bir otoimmün hastalıktır. MG'de, nAKR sayısı anlamlı olarak azalmıştır. Bu durum müsküler güçsüzlüğe yol açar ve respiratuvar kaslar açısından özel dikkat gerektirir. Becker müsküler distrofisi, bacak ve pelvis yavaş ilerleyici kas güçsüzlüğü ile karakterize X'e bağlı resesif geçişli bir hastalıktır. Sugamadeks, lipofilik çekirdeğe sahip hidrofilik bir siklodekstrin molekülüdür, steroid yapılı nöromuskuler bloker ajanların etkilerini enkapsülasyon yoluyla sonlandıran yeni bir moleküldür. Bu yazıda rokuronyum kullanılmış 3 myastenik ve 1 Becker muskuler distrofili hastada sugammadeks uygulama deneyimimizi sunduk. Myastenia gravisi olan 55, 45 ve 2.5 yaşındaki üç hasta sırasıyla; disk hernisi, abdominal histerektomi ve katarakt operasyonu için genel anestezi altında cerrahiye alındı. Ayrıca, Becker müsküler distrofi ile beş yaşındaki hastaya genel anestezi altında sünnet ve orşiopeksi planlandı. Tüm hastalarda, kas gevşetici olarak rokuronyum kullanıldı ve rokuronyumun etkisini geri döndürmek için sugamadeks uygulandı. Tüm hastalar, işlem sonunda komplikasyon olmadan ekstübe edildi. Kas hastalıklarda herhangi bir komplikasyon olmadan rokuronyum- sugamadeks kombinasyonunun kullanılması güvenli görünmektedir.

Anahtar Kelimeler: Anestezi, Myasteni Gravis, Becker Muskuler Distrofi, Sugamadeks

INTRODUCTION

Myasthenia gravis (MG) is an antibody-mediated autoimmune disease targeting nicotinic acid acetylcholine receptors (nACR) in neuromuscular junctions. In MG, the number of nACR is significantly reduced. This condition leads to muscular weakness and deserves special attention in terms of respiratory muscles.[5] According to Osserman and Genkins classification the patients are divided into four groups, based on their clinical presentations.[12] Preoperative evaluation of patients with MG should include optimization of medical management, discussion of the potential impact of this treatment modality on neuromuscular blockers, preparation for the possible requirement for postoperative respiratory support, and detailed information for the patient.[2] Patients with MG show abnormal responses to muscle relaxants. They are resistant to succinylcholine, but extremely responsive to non-depolarizing neuromuscular blockers. In addition, anticholinesterases used in treating the disease can modify responses to muscle relaxants, decrease sensitivity to non-depolarizing drugs, prolong reaction time to succinylcholine and mivacurium secondary the inhibition of plasma cholinesterases. The effect of adjunctive use of anticholinesterase drugs at the end of the operation can be limited on residual block because of chronic cholinesterase inhibition.[10] Caution must be exerted when administering general anesthesia in muscular dystrophies (MDs) secondary to a mutation in the dystrophy gene, which progress with gradually increasing loss of muscular tissue and strength. Extubation is not always possible in patients who have diminished forced vital capacity and are not able to cough efficiently.[3]

Sugammadex is a hydrophilic cyclodextrin molecule that has a lipophilic nucleus. It is an innovative molecule which terminates the effects of steroidal neuromuscular blocking agents via encapsulation.[9,14] Only a limited number of reports related to sugammadex used in patients with neuromuscular disease are available, and there are only one report[6] on its use for patients with Becker muscular dystrophy (BMD). We have presented our experience with sugammadex usage in patients with MG and BMD.

CASE PRESENTATION

Case 1

A 55-year-old woman with a BMI of 37 kg m^{-2} presented for anesthesia before being operated on for discal hernia repair. She had been diagnosed with MG 27 years ago. The patient, who had no history of any operations, was in OGC Class-IIa. During preoperative evaluation, hypertension was found, and on ECG, AV block and T negativity at V3-V6 were detected. Her neurological examination revealed bilateral m. orbicularis oculi weakness, and the muscular strength of her affected proximal extremity was rated as 4/5. The patient was using losartan potassium + hydrochlorothiazide and pridostigmine.

Standard monitoring procedures were performed, including ECG recordings, noninvasive blood pressure measurements, and application of pulse oxymeter, capnography, and nasopharyngeal, and cutaneous thermal probes. Neuromuscular function was monitored by stimulation of the ulnar nerve using train-of-four (TOF-Watch SX Organon) tests. After preoxygenation, remifentanil 0.1-0.3 µg kg^{-1} min^{-1} (Ultiva, Glaxo Smith Kline, UK) was initiated. Following induction of anesthesia with propofol 2.5 mg kg^{-1} (Lipuro 1% B. Braun Melsungen AG, Germany), rocuronium 0.2 mg kg^{-1} (Esmeron N.V. Organon, Oss, Netherlands) was administered for muscular relaxation. When the TOF ratio was 0, at 60 seconds, the trachea was intubated. In addition to remifentanil,

sevoflurane 1-2% in an oxygen/air mixture was initiated. The first and second responses to ulnar nerve stimulation were obtained at 75 and 90 minutes into the operation, respectively. Then, rocuronium at 1/8 of its induction dose was re-administered. The TOF ratio became 0 again. The operation lasted 135 minutes, and at the end of the operation, or 45 minutes after the last dose of rocuronium, the TOF ratio was 15%. Twenty-five seconds and two minutes after a dose of 2 mg/kg sugammadex (Bridion Organon Oss, Holland), the TOF ratios were 75% and 100%, respectively. The trachea was extubated and the patient was transferred to the PACU without complication.

Case 2

A 45-year-old woman with a BMI of 27 kg m^{-2} was scheduled for abdominal hysterectomy because of myoma uteri. The patient, who had been diagnosed with MG 15 years ago, had undergone uncomplicated myomectomy and thymectomy operations 20 and 15 years ago, respectively. Pridostigmine, prednisolone, and azathioprine were being used. Her neurologic evaluation revealed bilateral weakness of m. orbicularis oculi, and a slight decrease in bilateral pharyngeal reflexes. The muscular strength of her affected proximal extremity was rated as 4/5, or OGC class II-b.

After standard montorization anesthetic induction was achieved using propofol 2 mg kg^{-1}, remifentanil 0.1-0.5 µg kg^{-1} min^{-1} and rocuronium 0.25 mg kg^{-1}. Twenty seconds later, the TOF ratio was 0, and the trachea was intubated. For the maintenance of anesthesia, sevofluorane 1-2%, and remifentanil 0.1-0.3 µg kg^{-1} min^{-1} in an oxygen-air mixture was infused. At the end of the operation (96 minutes), after obtaining a second response to TOF stimulation, sugammadex 2 mg kg^{-1} was administered. After achieving TOF ratios of 62% and 72.2%, at 60 and 90 seconds respectively, the trachea was extubated. Her TOF ratio was 100% at five minutes.

Case 3

A 2.5-year–old infant, weighing 13.5 kg, was scheduled for an operation, with a diagnosis of cataract. He had experienced ptosis of the left, and then the right, eyelid when he was 22 months old. He had been diagnosed with MG 8 month ago. His history revealed an inguinal hernia repair when he was four months old, with no subsequent complication. He was using pridostigmine. Bilateral ptosis was detected, OGC Class-I. After standard monitorization, anesthetic induction was performed using propofol 2.5 mg kg^{-1}, fentanil 1 µg kg^{-1} and rocuronium 0.15 mg kg^{-1}. When the TOF ratio was 0, after 30 seconds, the trachea was intubated. Anesthesia was maintained with 1-2% sevoflurane in an oxygen-air mixture. At the end of the operation (35 minutes), two responses were elicited to the TOF stimulation, and then sugammadex 2 mg kg^{-1} was administered. Forty-five seconds later, the TOF ratio was 100% and the trachea was extubated.

Case 4

A five-year-old male patient, weighing 20 kg, was scheduled for circumcision and orchiopexy, with the diagnoses of phimosis and undescended testis. One year before this, he had complained of difficulty in walking and climbing steps, and a diagnosis of BMD had been established. His preoperative laboratory values were within normal limits.

After standard monitorization, propofol 2.5 mg kg^{-1} was administered and anesthesia was maintained with propofol 8-12 mg kg^{-1} h^{-1} and remifentanil 0.1-0.2 µg kg^{-1} min^{-1}. Then, rocuronium 0.5 mg kg^{-1} was injected incrementally according to the value of the TOF ratio. After ratio 0 was achieved, the trachea was intubated and the lung was ventilated with 2:3 oxygen/air mixture. At 25 minutes into the operation, the TOF ratio was recorded as 23% and rocuronium 0.15 mg kg^{-1} was administered. The operation was terminated 15 minutes after the last dose of rocuronium. At the end of

the surgery, a TOF ratio of 18% was recorded and sugammadex 2 mg kg^{-1} was administered. Seventy seconds later, the TOF ratio reached to 80%, and at the end of second minutes TOF ratio was 100% and the patient was extubated.

Informed written consents from all patients, or their parents, were obtained. In all patients, the TOF ratios were 100% after administration of propofol. No postoperative respiratory complication was observed in any of the patients during two hours at the PACU.

DISCUSSION

Anesthesia management of the patient with neuromuscular disease is challenging and requires specific management; however, safe and successful outcomes are achievable. Patients with MG or muscular dystrophy can need respiratory support during the postoperative period.[15,17] Acetylcholinesterase inhibitors antagonize the block slowly, or inadequately, if administered when the block is relatively dense, when reversal of block is attempted soon after the administration of the neuromuscular blocker agent or in the presence of potent volatile anesthetics. In addition, acetylcholinesterase inhibitors stimulate the muscarinic receptors resulting in bradycardia, arrhythmias, increased secretions and contraction of smooth muscle. Some authors have suggested intubation and anesthesia without resorting to muscle relaxants, in order to avoid postoperative respiratory failure related to the usage of muscle relaxants and the other complications related to acetylcholinesterase inhibitors.[1] However, anesthesia without muscle relaxants might not always be suitable for some surgical procedures. With the use of sugammadex, we avoided the use of the classical antagonist neostigmine, which can cause a cholinergic crisis in a patient with myasthenia. Moreover, the use of sugammadex prevents the need for postoperative mechanical ventilation, often the consequence of using non-depolarizing neuromuscular blocking drugs.

Only a limited number of case reports about the use of sugammadex in MG are available. Following rocuronium, sugammadex had been administered to a 69-year-old myasthenic patient undergoing laparoscopic cholecystectomy, and a TOF ratio of 100%, at 30 seconds, was recorded.[11] The authors suggested that need for acetylcholine esterase inhibitor use would be eliminated through reversal of neuromuscular blockade due to rocuronium administration by routine sugammadex usage. Similarly, in our first case, 25 seconds after sugammadex, the TOF ratio increased to 75%.

In a myasthenic patient undergoing radical prostatectomy, rocuronium 0.25 mg kg^{-1} was used. At the end of the operation, two responses to TOF stimulation had been obtained and, 210 seconds after sugammadex administration, a TOF ratio of 100% had been recorded.[16] We also gave 2 mg kg^{-1} sugammadex in Case 2 and Case 3, following two responses to TOF stimulation. In Case 3, a faster response to sugammadex administration was obtained, in spite of shorter operative time. Despite similar responses to TOF stimulation obtained at the end of the operation, differences in the times to recovery of muscular strength could be due to the administration of different doses of rocuronium during induction of anesthesia (0.25 mg kg^{-1} versus 0.15 mg kg^{-1}). In addition, faster response to sugammadex in Case 3 might be related to the pediatric age of the patient who demonstrated only a mild form of eyelid ptosis.

The use of neuromuscular blocking drugs lead to prolonged spontaneous recovery even after a single dose of neuromuscular blocking drug.[7,8] However, the combination of rocuronium-sugammadex was used in a patient with Duchenne muscular dystrophy without postoperative respiratory complications. Boer and colleagues[4] injected 1 mg kg^{-1} iv

rocuronium into a nine-year-old child with humerus fracture and Duchenne muscular dystrophy. At the end of the operation (35 minutes), only a single twitch could be obtained as a PTC. However, 70 seconds after the administration of 4 mg kg^{-1} sugammadex, the TOF ratio was 90%, and they extubated the child three minutes later without any complication. The anesthetic considerations for the muscular dystrophies are similar in many respects.[13] This is the first reported case in the literature in which sugammadex was given in a patient with BMD. At the end of the operation on our patient who had BMD, the TOF stimulation yielded a TOF ratio of 18%, and two minutes after 2 mg kg^{-1} sugammadex the patient was extubated. Reversal of rocurunium-induced neuromuscular block by sugammadex in our four patient with MG and becker muscular dystrophy was rapid, efficient, and without signs of postoperative residual neuromuscular block.

As a result of our experiences with patients who have MG and BMD, we think that a rocuronium-sugammadex combination can be chose for the routine management of these patient after careful adjustment of appropriate and safe dosages, based on the severity of the disease.

Correspondence to:
Yasemin Burcu Üstün
E-mail: ysmbrcustun@gmail.com

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