

Duchenne Muscular Dystrophy and Sugammadex

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Abstract

Cholinesterase inhibitors have been used to reverse neuromuscular blockade, but the complete spontaneous recovery of neuromuscular blockade in patients with Duchenne Muscular Dystrophy remains unclear. A 6-year-old boy was admitted to our clinic for adenoidectomy. Anesthesia was induced and maintained with an IV infusion of propofol and remifentanyl. Endotracheal intubation was performed after rocuronium. The duration of anesthesia was 35 min. At the end of the procedure, sugammadex was administered with IV. The recovery time was 160 s.

We have demonstrated that reversal of rocuronium-induced NMB by sugammadex in this Duchenne Muscular Dystrophy patient provides recovery without side effects.

Keywords: Muscular dystrophy; Duchenne; Sugammadex

Introduction

Duchenne Muscular Dystrophy (DMD) is the most common and severe type of muscular dystrophy, with an incidence of 1 per 3,500 live male births [1]. DMD is an X-linked recessive disease. The defect is located on the X chromosome at the Xp21 region, which contains the gene for dystrophin. Dystrophin, along with dystrophin-associated glycoproteins (DAGs), is involved in sarcolemmal stability. Lack or dysfunction of dystrophin leads to cellular and membrane instability, with progressive leakage of intracellular components and elevation of creatine phosphokinase (CPK) levels. Clinical pseudo hypertrophy of the muscle occurs when the dead muscle cells are replaced by fibro fatty infiltrates. Loss of muscle units accounts for the weakness and contracture [2].

Patients with DMD may require special care during anesthesia, and neuromuscular blockage (NMB) is of great concern in DMD patients. Depolarizing neuromuscular blocking drugs (NMBDs) are contraindicated because of risk of hyperkalemia, rhabdomyolysis or cardiac arrest [3-5]. Administration of non-depolarizing NMBDs is accompanied with a prolonged onset time and recovery after a single dose. However, in nearly all cases, reversal agents have been used, but the complete spontaneous recovery of neuromuscular blockade in patients remains unclear [6].

Sugammadex, a selective relaxant-binding agent, rapidly and completely reverses the effects of rocuronium and vecuronium. Administration of sugammadex results in rapid removal of free rocuronium molecules from plasma in rocuronium-induced NMB. Sugammadex does not affect acetyl cholinesterase, thus eliminating the need for anticholinergic drugs and their undesirable side effects (cardiovascular, pulmonary and gastrointestinal). The combination of rocuronium and sugammadex can completely eliminate residual paralysis. In a review of the current literature of sugammadex usage in pediatric patients with DMD, a small number of cases was found [6, 7]. In our case report, we discuss the results of dosing a patient with

DMD with sugammadex to reverse a rocuronium-induced profound neuromuscular blockage.

Case Presentation

A 6-year-old boy, weighing 20 kg, was admitted to our clinic for an adenoidectomy operation. The diagnosis of DMD was made when he was 3 years old. Physical examination showed normal development, but there was proximal muscle weakness. He was evaluated as mild DMD. Baseline creatine kinase (CK) levels were 9782 mg/dl (normally <190 mg/dl), and LDH was 804 U/L (normal range 240-480 U/L) as abnormal values in laboratory evaluation. The patient was consulted by pediatric cardiologist and was found that only minimal patent foramen ovale (PFO, 1-2 mm) in echocardiographic assessment with normal cardiac capacity.

The patient received 0.5 mg midazolam intravenously (IV) in the preoperative holding area before arrival into the operating room. Neuromuscular function, brain activity and temperature were monitored in addition to standard intraoperative monitoring (ECG, NIBP and pulse oximetry). Neuromuscular function was monitored using train-of-four (TOF) stimulation of the ulnar nerve (TOF module of Datex-Ohmeda S/5 compact anesthesia monitor, GE Healthcare, Finland). The brain was monitored using the bispectral index (BIS, BIS module of Datex-Ohmeda S/5 compact anesthesia monitor, GE Healthcare, Finland). After pre-oxygenation, anesthesia was induced and maintained with an IV infusion of propofol (10-4 mg.kg.h⁻¹, total amount of propofol was 68 mg) and remifentanyl (0.05 mcg.kg.min⁻¹, total amount of remifentanyl was 32 mcg). The infusion of propofol was started by doses of 10 mg.kg.h⁻¹. The infusion rate was decreased to 4 mg.kg.h⁻¹ each 10 unit reduction in the value of BIS. In the maintained period, propofol infusion was adjusted depending on BIS value of 40-60. The patient received an IV bolus injection of 8 mg rocuronium (doses of 0.4 mg.kg⁻¹) after the calibration and stabilization of neuromuscular monitoring was performed. This was followed by endotracheal intubation and mechanical ventilation with 50% oxygen and 50% air. Temperature was maintained at 35.8 - 36.4°C. End-tidal CO₂ was maintained at 28-36 mmHg. Propofol

infusion was stopped 5 min before the end of surgery. Remifentanyl infusion was stopped at the end of surgery. The duration of surgery was 15 min. Neuromuscular monitoring showed first twitch reaction in the post-tetanic count (PTC 1), and reversal NMB was then performed by administration of 80 mg sugammadex (4 mg.kg⁻¹). The recovery time to reach a TOF ratio of 90% was 160 s. The patient was extubated after 2 min. The duration of anesthesia was 35 min. The perioperative clinical features of the case are presented in Table 1. The patient's recovery from anesthesia was uneventful, and he was discharged to the postoperative recovery ward. He was observed for 2 h in the recovery room. Residual block or vital sign abnormalities were not observed. The patient was discharged to the ward and went home the next day.

Discussion

We observed full reversal of neuromuscular blockage without side effects that sugammadex was used for rocuronium induced neuromuscular blockage in this DMD patient.

One of the major problems in the anesthetic management of patients with DMD is neuromuscular blockage. The administration of standard doses of non-depolarizing NMBDs in DMD patients leads to a prolonged onset time and a prolonged recovery [8-10]. The reasons for these extended times are unclear, although possible changes in the pharmacokinetics and, depending on the underlying disease, changes in neuromuscular junctions are evident [9].

Another problem of anesthetic management of DMD patients is reversal of neuromuscular block. Despite the prolonged duration of non-depolarizing NMBDs does not change effect time of anticholinesterases. There is a risk of possible recurarization in this situation [8]. Besides cholinesterase inhibitors has undesirable side effects (bradycardia, hypotension, bronchoconstriction, and emesis). These side effects may cause more problems in DMD patients compared to normal patients. Sugammadex was approved in the European Union in 2008 for the reversal of moderate (reappearance of the second twitch of the train-of-four [TOF] response [T₂]; sugammadex 2.0 mg.kg⁻¹) and deep (1-2 post-tetanic counts; sugammadex 4.0 mg.kg⁻¹) NMB induced by rocuronium or vecuronium [11]. Sugammadex does not interfere with acetyl choline receptors or anticholinesterase. Therefore it does not cause cardiovascular fluctuation and pulmonary side effects.

There are a small number of case reports on the usage of sugammadex in DMD patients [6,7]. In presented case from De Boer, the patient received 1.0 mg.kg⁻¹ rocuronium and 4.0 mg.kg⁻¹ sugammadex, and the recovery time was found 70 sec [6]. They administered a high dose of rocuronium for rapid intubation to protect the airway. Induction dose of rocuronium in DMD patients is controversial. A reduction to a standart dosage of NMBD is recommended because of increased sensitivity [8]. We chose to use rocuronium 0.4 mg.kg⁻¹ for this reason. However, we recorded a recovery time of 160 sec, despite our use of 0.4 mg.kg⁻¹ rocuronium (less rocuronium but a longer recovery time). In Yabuzaki's report, they received rocuronium 0.6 mg.kg⁻¹ and sugammadex 4 mg.kg⁻¹ to two patients (one of them mild, other severe DMD [7]). They found that a recovery time 156 sec in mild and 423 sec in severe DMD patient. There may be degradation of muscle fibers and replacement by fatty and fibrous tissue with the progression of the disorder in DMD patients. These changes could be accompanied by decreased neuromuscular junctions and receptors. The stage of the disease may

influence the effective doses of NMBDs and the reversal agent [8]. This may be the reason for the dose-response differences between previous cases and our case, and the effective doses of sugammadex may differ in these patients.

When inhalational agents or succinylcholine are used in DMD patients, there are increased risks of rhabdomyolizis, hyperkalemic cardiac arrest or perioperative metabolic reactions (malignant hyperthermia- like syndrome) [12]. We selected the propofol-TIVA technique with BIS monitoring in order to decrease these risks. In addition to neuromuscular monitoring is necessary to have the anesthetic management of these patients. We preferred to use of TOF acceleromyelography after loss of consciousness before neuromuscular block because of disturbing effect of TOF stimulator.

Conclusion

We know that neuromuscular blockage is a serious problem in DMD patients. Succinylcholine should not be used in these patients also non depolarizing NMBD have got prolonged effect time. When anticholinesterases used for reversal agent there is a risk of postoperative residual curarization in DMD. We administered sugammadex for reversal of rocuronium-induced NMB. In this DMD patient resulted in full recovery without side effects. We believe that there is a correlation between severity of disease and recovery time of neuromuscular blockage. Additional studies are required to determine the effective sugammadex dose in DMD patients.

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