Effectiveness of sugammadex in reversing prolonged neuromuscular block in a patient with acquired immune deficiency syndrome (AIDS) taking streptomycin—A case report—

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The duration of the effect of muscle relaxants is extended in patients with acquired immunodeficiency syndrome (AIDS); however, a specific mechanism for this effect has not yet been discovered. In addition, streptomycin is known to prolong the action of muscle relaxants by blocking activity at neuromuscular junctions. Here, we report the case of a patient with AIDS taking streptomycin for pulmonary tuberculosis for which sugammadex was effective in reversing prolonged paralysis induced by rocuronium and vecuronium for video-assisted thoracoscopic surgery (VATS) lung wedge resection. (Anesth Pain Med 2015; 10: 124-127)

Key Words: AIDS, Aminoglycoside, Rocuronium, Sugammadex, Vecuronium.

Different clinical situations can enhance the effect of muscle relaxants. Notably, the action of muscle relaxants is significantly prolonged in patients with acquired immunodeficiency syndrome (AIDS) caused by human immunodeficiency virus (HIV) infection, although a specific mechanism for this effect has not yet been determined [1]. Conventional acetylcholinesterase inhibitors used to reverse the effects of muscle relaxants are greatly limited due to their mechanism of action [2]. On the other hand, sugammadex is highly selective for rocuronium and vecuronium (aminosteroidal agents) and reverses the action of muscle relaxants through an antagonistic effect [3-8]. Here, we report a case in which sugammadex was effective in reversing prolonged paralysis caused by rocuronium and vecuronium in a patient with AIDS taking streptomycin for pulmonary tuberculosis.

CASE REPORT

The patient in this case report was a 45-year-old, 170 cm-tall male patient weighing 60 kg. The patient was classified as American Society of Anesthesiologists physical status 2. The patient’s hepatic aspartate amino transferase level was 60 IU/L, alanin aminotransferase was 21 IU/L, total bilirubin was 1.0 mg/dl, blood urea nitrogen was 11.0 mg/dl, and creatinine was 0.7 mg/dl. We decided to employ VATS for a wedge resection of the lung after suspecting miliary tuberculosis, tuberculous lymphadenitis in the mediastinal and right supraclavicular lymph nodes, and pneumocystis carinii pneumonia following the diagnosis of HIV. The patient took antiviral agents and was administered 1 g of streptomycin and steroidal agents one day before the surgery and again on the day of the surgery.

Upon arrival in the operating room, the patient’s noninvasive blood pressure, continuous electrocardiography (lead II), end-tidal CO₂ pressure, pulse oximetry, and body temperature were monitored. The patient’s level of consciousness was continuously monitored with a bispectral index (BIS) monitor (Model A 2000, Aspect Medical System, Natick, MA, USA). Induction was performed by intravenous infusion with an effect-site target concentration of 5 μg/ml propofol and 5 ng/ml remifentanil. Supramaximal current was measured with a TOF-Watch SX® (Merck Sharp & Dohme Corp., Glostrup, Denmark) and the
state of muscle relaxation was continuously monitored starting with the loss of consciousness until the end of anesthesia. The \(T_4/T_1\) ratio after loss of consciousness was 100\%, after which the dose of rocuronium was increased in 0.1 mg/kg increments according to TOF. A total of 36 mg (0.6 mg/kg) of rocuronium was used for intubation with a left-sided double lumen bronchial tube (Broncho-Cath\(^\circ\), Mallinckrodt Medical Ltd., Athlone, Ireland). After intubating with the left-sided double lumen bronchial tube, the exact location was confirmed using a fiber optic bronchoscope. An arterial catheter was placed in the right radial artery (in the lateral recumbent dependent portion), and another catheter was placed in the external jugular vein (in the independent portion). The tidal volume was set to 7 ml/kg; the positive end expiratory pressure was set to 5 cmH\(_2\)O, and the respiratory rate was regulated at 35–40 mmHg as measured with a capnograph. The patient was placed in a lateral recumbent position for surgery, and the placement of the double lumen bronchial tube was reconfirmed with the fiber optic bronchoscope. After intubation, the effect-site target concentrations of propofol and remifentanil were maintained at 3 \(\mu\)g/ml and 3 ng/ml, respectively. Every time \(T_1\) or \(T_2\) appeared in the course of the neuromuscular monitoring, 0.01–0.02 mg/kg of vecuronium was added for the surgery and mechanical ventilation. The total amount of vecuronium used during surgery was 2 mg, and the operation lasted 90 minutes. The surgery was completed 135 minutes after induction. Prior to the end of surgery, manual ventilation was performed with 20 cmH\(_2\)O for 10 seconds, 30 cmH\(_2\)O for 15 seconds, and 40 cmH\(_2\)O for 15 seconds consecutively. Prior to the end of the surgery the surgeon blocked the intercostal nerves with bupivacaine. Next, after the end of the surgery, 25 mg of pethidine was administered twice for pain control, with more administered as needed.

After the end of the surgery, the patient showed signs of spontaneous breathing within 5 minutes of \(T_2\) appearance. At this time, 2.5 mg of neostigmine and 0.4 mg of glycopyrrolate were injected for reversal of neuromuscular blockade. However, the patient’s spontaneous breathing reached a tidal volume of 400 ml after 30 minutes of manual assisted ventilation, after which the patients TOF ratio recovered from 60 to 80\%, although this was not considered a reliable measurement due to possible distortion as a result of the patient’s movement.

At this point, we proceeded with extubation upon determining that the neuromuscular relaxation was reversed, as the patient was able to open his eyes when called, nod to answer questions, and lift his head. However, within three minutes of the extubation the patient suffered from dyspnea and his oxygen saturation again fell to 93\%. We therefore applied manual assisted ventilation through an oxygen mask. As the patient complained of dyspnea up to 20 minutes after extubation and the oxygen saturation level during the spontaneous breathing had fallen to 93\%, we injected 1 mg/kg of propofol and performed an intubation with a laryngeal mask airway (LMA). The oxygen saturation level during the spontaneous breathing was maintained at 95\% even after LMA intubation, and the manual assisted ventilation was therefore continued. The BIS value was 95 one hour after extubation but only \(T_1\) and \(T_2\) appeared on the TOF, and the patient continued to complain of dyspnea. At that time, the patient’s visual analogue scale (VAS) pain score was between 4 and 5 of 10. Thus, the overall duration wherein only \(T_1\) and \(T_2\) were observed was approximately 100 minutes. We then injected 2 mg/kg of sugammadex for complete reversal of neuromuscular blockade. Dyspnea disappeared and the TOF reached 99\% thirty seconds after the injection of the sugammadex. Finally, the patient was moved to the intensive care unit, where no residual muscle relaxation was observed.

**DISCUSSION**

The action of neuromuscular relaxants is prolonged in most AIDS patients, although the reason for this effect is not well understood [1]. Furthermore, it is well known that the effects of neuromuscular relaxants in neuromuscular blockade are enhanced in patients taking streptomycin. Specifically, streptomycin acts as an antagonist of calcium to inhibit the secretion of acetylcholine in nerve terminals, thereby enhancing the effects of nondepolarizing muscle relaxants [9].

In a previous study, 5 patients with AIDS and 8 patients without infection were infused with 0.08 mg/kg of vecuronium during general anesthesia, and patients with AIDS showed a significantly prolonged duration of paralysis, on average 67 minutes, compared to that of the control group, which was 32 minutes. In that study, the duration of paralysis was defined as the time for 25% recovery of the \(T_1\) [1]. In our case, the duration with only \(T_1\) and \(T_2\) was about 100 minutes. Thus, we tentatively concluded that the extended duration of muscle relaxation due to delayed reversal of muscle relaxation was a result of both the underlying AIDS disease and a separate factor. In this case, we suspected that the other factor was the preoperative injection of streptomycin.

With respect to the effect of antibiotics on the delay of
reversal of muscle relaxation, a previous study was conducted with 70 patients receiving either a single, large preoperative dose of gentamicin, a moderate dose of gentamicin, or no gentamicin, which were associated with a mean time from cessation of vecuronium infusion to extubation of 34.7 minutes, 27.4 minutes, and 19.4 minutes, respectively [10]. In our case, the patient was administered 1 g of streptomycin one day before the surgery and on the day of the surgery, and the duration with only T1 and T2 was about 100 minutes. Importantly, these findings are consistent with our observation of delayed recovery from treatment with muscle relaxants as a result of streptomycin, and thus may explain the extended delay in recovery in AIDS patients treated streptomycin.

Sugammadex has been shown to accelerate recovery time from treatment with muscle relaxants. Specifically, a study employing 118 patients without AIDS nor preoperative streptomyocin were randomly allocated to receive sugammadex 2 mg/kg or neostigmine 50 µg/kg with glycopyrrolate 10 µg/kg at the appearance of T2. In that study, the time to recovery of TOF ratio to 0.9 was 1.8 (range 1.6-2.0) minutes with a 14.8 (range 12.4-17.6) minute geometric mean [11]. In our case, the patient received 2.5 mg of neostigmine and 0.4 mg of glycopyrrolate at the appearance of T2. However, the time with only T1 and T2 lasted for about 100 minutes. Therefore, this strongly supports our conclusion that underlying disease of AIDS and preoperative injection of streptomycin delayed the duration of reversal of muscle relaxation. In addition, as the patient’s liver function and renal function were close to the normal range, the possibility that the muscle relaxant treatment was not eliminated from the body was considered very low.

Conventional acetylcholinesterase inhibitors used for the reversal of neuromuscular blockade can have several limitations due to their mechanism of action. Specifically, acetylcholinesterase inhibitors have a ceiling effect with respect to increasing the concentration of acetylcholine and recovering muscle strength, and are not effective in reversing deep muscle relaxation [2].

In our case, 2.5 mg of neostigmine and 0.4 mg of glycopyrrolate were administered for reversal of neuromuscular blockade after signs of spontaneous breathing appeared 5 minutes after the end of the surgery with appearance of T1 and T2 on TOF. However, the tidal volume of the spontaneous breathing only reached 400 ml after 30 minutes of manual assisted ventilation. At this time, TOF was recovered from 60 to 80%, but the TOF was considered unreliable due to the possibility that the patient’s movements distorted TOF measurements. Thus, extubation was performed based on clinical evidence, which consisted of the patient’s ability to nod in the affirmative to questions and being able to lift his head when asked, both of which indicated that reversal of the neuromuscular blockade was possible. However, the fact that only T1 and T2 were present in the TOF was taken to indicate that the clinical situation and neuromuscular monitoring results may not be coherent in patients with AIDS. Indeed, such discrepancies have already been reported in motor neuron diseases such as amyotrophic lateral sclerosis [3]. Moreover, AIDS patients display patterns of motor neuron diseases similar to amyotrophic lateral sclerosis, although the mechanism of this presentation has not been clearly identified [12].

Sugammadex forms a very stable host-guest complex with both rocuronium and vecuronium, allowing for a quick reversal of various types of muscle relaxation [4-8]. Thus, sugammadex constitutes a safe alternative for patients with myasthenia gravis, amyotrophic lateral sclerosis, and other neuromuscular diseases with various causes and mechanisms in clinical situation [3,7]. In this way, sugammadex is an effective tool to eliminate any postoperative residual muscle relaxation when patients’ respiratory functions are impaired after postoperative reversal of neuromuscular blockade.

Additional factors that prolong the reversal of neuromuscular blockade may be considered. In thoracoscopic surgery, it is generally critical to consider the arterial blood acid-base balance related to the body temperature and one-lung ventilation. In our case, no significant abnormalities were identified for body temperature and arterial blood tests performed from the induction stage until the end of surgery. Spontaneous hypoventilation due to decreased consciousness and residual atelectasis can be considered as causes of desaturation. In our case, the patient’s BIS value was 95. In addition, manual bagging was performed with 20 cmH2O for 10 seconds, 30 cmH2O for 15 seconds, and 40 cmH2O for 15 seconds consecutively in order to prevent residual atelectasis [13]. Thus, we were able to rule out the effect of hypoventilation and residual atelectasis. Further, because dyspnea and neuromuscular monitoring showed rapid improvement within 1 minute of administration of sugammadex, we determined that the probability of other factors reversing the neuromuscular blockade was relatively low.

The incidence of patients infected with HIV progressing to AIDS has decreased remarkably owing to the recent development of new treatment options. Previous studies have reported cases of delayed reversal of a neuromuscular blockade...
in patients with AIDS or those who were only administered aminoglycoside antibiotics. We believe, however, that patients with two or more factors that may prolong neuromuscular blockade, such as the one described in this report, are relatively rare. Indeed, this case study illustrates that conventional reversal strategies may present limitations in reversing prolonged paralysis caused by a combination of factors, although sugammadex remained effective in safely reversing the neuromuscular blockade.

In conclusion, when aminosteroidal muscle relaxants are used in cases of suspected prolonged neuromuscular blockade in patients with AIDS who are also being treated with streptomycin, sugammadex is the drug of choice.

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