

Case Report

Potential of Neuromuscular Blockade Effect of Rocuronium for 4 Hours Due to Perioperative Gentamicin, Clindamycin and Magnesium Sulfate

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An 83 year old female was presented to the operating room for laparoscopic transverse loop colostomy for Ogilvie's syndrome. The laboratory work up was significant with magnesium level of 1.7 mg/dl. The patient received 100mg of lidocaine, 140mg of propofol and 40mg of rocuronium during intubation. Subsequently, patient had received clindamycin 600 mg and gentamicin 80 mg and 4 grams of magnesium by infusion over a period of 30 minutes. During surgery, the patient did not receive any additional dose of rocuronium. At the end of the procedure, which lasted about 3 hours, peripheral nerve stimulation showed no twitches. Patient stayed intubated and transported to post anesthesia care unit. Serum level of magnesium was checked and it was 3.2 mg/dl. After an hour (total of 4 hrs. from the time the patient received rocuronium), the patient had 4/4 twitches with negative fade and was extubated. It has been reported in articles that magnesium could cause potentiation of neuromuscular blockade effect of rocuronium ranging from 45 to 55 minutes. It is believed that this article could be the first published case report where supplemental magnesium given in the perioperative period, with concomitant use of amino glycoside antibiotics has led to prolongation of neuromuscular blockade for 4 hours.

Keywords: Prolongation of Neuromuscular blockade; Magnesium; Clindamycin; Gentamicin**Introduction**

Neuromuscular blocking agents (NMBA) are extensively used in the practice of anesthesia. They provide adequate intubating conditions and considered necessary for certain surgical procedures, where paralysis is required. Rocuronium, one of the commonly used neuromuscular blocking agents, is well known for its interaction with prolongation of neuromuscular blocking effect by magnesium [1-3] as well as antibiotics like amino glycosides [4]. Magnesium besides being commonly used in obstetrics is also used to treat patients with arrhythmias, electrolyte abnormalities and hypertension caused by pheochromocytoma [2,5]. The mechanism by which magnesium prolongs the effect of neuromuscular blocking agents is by preventing the release of acetylcholine at the neuromuscular junction [6]. Several clinical studies and some case reports have shown that the effect of non-depolarizing neuromuscular blocking agents including cisatracurium, vecuronium and rocuronium was prolonged after magnesium infusion [7-12]. However, patients in those studies and case reports had normal magnesium levels prior to infusion. Here, we present a case of an elderly patient, who had prolongation of neuromuscular blocking effect of rocuronium for four hours following single intubating dose; due to concomitant use of perioperative aminoglycoside antibiotics and a dose of magnesium to correct hypomagnesaemia. It is believed that this could be the first published case where supplemental magnesium could cause prolongation of neuromuscular blockade for 4 hours even in the face of hypomagnesaemia.

Case Presentation

An 83 year old female with a history of sigmoid volvulus status post sigmoid colectomy, was diagnosed with Ogilvie's syndrome. After failing conservative management, she was scheduled for laparoscopic transverse loop colostomy. She had multiple comorbidities including hypertension, diabetes mellitus, coronary artery disease, hyperlipidemia, cerebrovascular accident, peripheral vascular disease, hypothyroidism and dementia. Surgical history included right femoral to popliteal bypass and sigmoid colectomy without any anesthetic complications. The patient was on multiple medications including bisacodyl, colace, sub cutaneous heparin, hydrochlorothiazide, levothyroxine, lisinopril, nexium, zocor, and valproic acid. Patient was 63 inches tall and weighed 65.3 kilograms with normal vital signs. The laboratory work up on the day of surgery was significant with magnesium level of 1.7 mg/dL and the rest of the biochemistry and hematology values were within normal limits. The patient had low potassium on admission but was aggressively corrected before the surgery. The chest x-ray showed cardiomegaly and atelectasis; electrocardiogram showed sinus bradycardia with a rate of 56 and left bundle branch block. A resting transthoracic echocardiogram showed normal LV function 65-70% with mild pulmonary hypertension and mild tricuspid regurgitation with normal left ventricular size, wall motion, as well as normal valves. Airway examination did not show any abnormalities.

Patient received a 20 gauge intra venous access with lactated ringer as maintenance fluid and 0.5 mg of midazolam in pre-operative

holding area. In the operating room, standard monitors were used. Patient was pre oxygenated and received another dose of 0.5 mg midazolam. Anesthesia was induced with 100mg of lidocaine, 140mg of propofol and 40mg of rocuronium. The trachea was uneventfully intubated with a 7.0 mm single lumen end tracheal tube. The patient was ventilated with 50% oxygen and sevoflurane, maintaining an end tidal concentration between 1.5-2.5%. The patient received clindamycin 600mg and gentamicin 80mg prior to incision and a total of 250 mcg of Fentanyl administered in divided doses. Approximately 25 minutes after the intubation, 4 grams of magnesium was infused over 30 minutes. During the procedure, patient did not receive any additional dose of rocuronium, because peripheral nerve stimulation showed a train-of-four (TOF) of zero twitches at 2Hz.

At the end of the procedure, which lasted approximately 3 hours, peripheral nerve stimulation still showed no twitches. So, she was kept intubated and transported to post anesthesia care Unit (PACU) with mechanical ventilation and 75 mcg per kg per minute of propofol for sedation. On arrival to PACU, she had an arterial blood pressure of 137/74, heart rate of 93, and respiratory rate of 14 and temperature of 96.7°F with oxygen saturation of 100%. A blood sample for magnesium level was sent to the lab and the result showed that the magnesium level was 3.2 mg/dL. One hour after arrival to PACU, the patient had four out of four twitches with negative fade and negative post tetanic facilitation at 100 and was extubated when she met the extubation criteria. Patient was followed up for 24 hrs with no further complication.

Discussion

Anesthesiologists are facing with the challenges of evaluating and managing elderly patients who typically suffer from multiple co-morbidities. This patient population is at risk of poly pharmacy and drug interactions, which do not exclude medications commonly used to provide anesthesia. In addition, elderly population is at risk of electrolyte disturbances and need for intravenous replacement. Magnesium replacement is of most importance in the surgical population due to its effects on cardiovascular, endocrine, neurological systems and electrolyte homeostasis [5,13]. Furthermore, there is evidence that hypomagnesaemia could be seen in patients after surgery irrespective of prior magnesium levels [14].

In general, the patients who are diagnosed with Ogilvie's syndrome usually have electrolyte disturbances, which include hypokalemia and hypomagnesaemia. It is known that treatment of hypokalemia is ineffective without concomitant correction of hypomagnesaemia [15]. Therefore, those electrolyte abnormalities need to be corrected aggressively prior to surgery.

Studies have shown that prolongation of neuromuscular blockade caused by magnesium ranged from 45 to 55 minutes [7,8,10-12]. However, the timing of the magnesium dose and duration of infusion also influences the duration of blockade. Fuchs showed that if magnesium was given to patients receiving vecuronium at recovery from block to a train of four ratio of 0.7 or 1 hour after recovery to a train of four ratio of 0.7, there was significant prolongation of neuromuscular block in the latter. In our patient, prolongation of the neuromuscular block lasted for 4 hours, evidenced by no return of twitch with TOF.

Magnesium's prolongation of neuromuscular blockade was thought to be caused by the prevention of the presynaptic release of acetylcholine [1,3,5,6]. Recent study showed that magnesium produces a concentration dependent inhibition of the adult muscle type acetylcholine receptors acting as a noncompetitive inhibitor [15]. The study was done with vecuronium and as expected, it showed enhanced neuromuscular blockade with magnesium. Interestingly, the study also showed that in the range of therapeutic concentration of magnesium could not attain a significant neuromuscular inhibition. The patient's magnesium level prior to correction was 1.7 mg/dL, which was low based on the laboratory values. After replacement of magnesium, it was probably slightly over corrected, resulting in a magnesium level of 3.2 mg/dL. However, there remains a question that if magnesium was corrected to a normal level, still significant prolongation effect of neuromuscular blockade could be observed.

In regards to amino glycoside antibiotics, they cause acetylcholine receptor channel block at the end plate in decreasing acetylcholine release at the motor nerve terminal and enhancing the effects of non-depolarizing agents [16]. The use of clindamycin and gentamicin which have been involved in affecting neuromuscular blocking agents could have most likely caused the prolongation by decreasing acetylcholine release at the motor nerve terminal or a clinical synergistic effect of paralysis in this patient. We believe that the dramatic prolongation of the NMBD effect in this case was caused by the concomitant use of amino glycoside antibiotics [4] in addition to magnesium infusion.

The patient's multiple comorbidities and the use of different medications could have also influenced the recovery from neuromuscular blocking drugs; but the most likely cause of this prolonged effect of rocuronium was magnesium and the perioperative amino glycoside antibiotics. It is important to point out that one year prior to this event; the patient was given the same paralytic agent without any prolongation of paralysis. Furthermore, during the rest of the procedure, the patient did not receive other medications with known effect on neuromuscular blockade. The patient was taking valproic acid as part of her home medications, which is an antiepileptic, could have caused resistance to non-depolarizing neuromuscular blocking agents. Interestingly enough, Kim [17] showed in a randomized double blind controlled trial that the effects of valproic acid on neuromuscular blocking effects were attenuated by the use of magnesium. However, patients in that study still showed some degree of prolongation of neuromuscular blockade after the use of magnesium. Fawcett [18] presented a case of recurarization caused by magnesium given for atrial fibrillation after the patient had recovered from neuromuscular blockade. This effect was recently confirmed by Hans [9] in a randomized control trial, that magnesium could re-establish neuromuscular blockade after spontaneous recovery from intubating dose of rocuronium. This patient received 4 grams of magnesium to correct hypomagnesaemia approximately 30 minutes after the dose of rocuronium. When considering the patient weight of 63 kg (the dose of 64 mg/kg), the dosage given to this patient which was consistent with doses used in previous clinical trials [8,10,11].

Conclusion

In summary, elderly patients are increasingly seen in the operating room for surgical management. Due to the physiologic changes in addition to co-morbidities place them at higher risk for intra and

post-operative complications. Use of magnesium continues to be a common practice in patients with electrolyte disturbances, who are presenting for emergency surgery. Our understanding of magnesium's neuromuscular effects and interaction with neuromuscular blocking agents has improved. The use of pre-operative antibiotics is a gold standard to prevent post-operative infections. In addition, due to allergic reaction to penicillin, amino glycosides and clindamycin are common agents used in the operating room. We suggest that during perioperative replacement of magnesium, close vigilance and attention is required to the infusion speed and avoidance of concomitant medications with similar effects on neuromuscular blocking agents. Routine use of neuromuscular monitoring is mandatory in all patients who receive any type of neuromuscular blocking agent. Furthermore, NMBA prolongation should be suspected when TOF does not return to the expected period of time and if so, adequate ventilator support is necessary.

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