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Recurrence of Neuromuscular Blockade after Reversal of Vecuronium in a Patient Receiving Polymyxin/Amikacin Sternal Irrigation

MARK A. KRONENFELD, M.D.,* STEPHEN J. THOMAS, M.D.,† AND HERMAN TURNDORF, M.D.‡

Antibiotics such as neomycin, streptomycin, and polymyxin enhance the neuromuscular blocking properties of muscle relaxants.[1] We describe a case of recurrence of a vecuronium neuromuscular block attributable to a sternal irrigation consisting of polymyxin and amikacin in lactated Ringer's solution.

REPORT OF A CASE

Twenty-one days following aortic valve replacement and coronary bypass, a 72-yr-old, 75-kg man was scheduled for sternal debridement. His medications were iv cefoxitin one g four times a day and diazepam 5 mg by mouth at bedtime. Physical examination revealed a fairly vigorous man with a heart rate of 75 beats/min and an arterial blood pressure of 130/80 mmHg. His preoperative electrocardiogram showed nonspecific ST-T wave changes. Laboratory data included: hemoglobin 10 g/l, hematocrit 34%, serum sodium 135 mEq/l, serum potassium 3.9 mEq/l, serum chloride 109 mEq/l, blood bicarbonate 30 mEq/l.

The patient was NPO for approximately 10 h prior to arrival in the operating room, without iv fluid administration. Sixty minutes prior to surgery he was premedicated with morphine sulfate 4 mg im and hydroxyzine 25 mg im. Intraoperative monitoring included a modified V_5 ECG, blood pressure cuff, right radial arterial line, and a left ulnar peripheral nerve stimulator. An esophageal stethoscope and temperature probe were inserted after induction of anesthesia. Anesthesia was induced with fentanyl 3 μg/kg, thiamylal 3 mg/kg, and vecuronium 0.08 mg/kg iv. No further muscle relaxant was given. After intubation of the trachea, the response to tetanic and train-of-four (TOF) stimulation was totally suppressed. Anesthesia was maintained with 60% N_2O and approximately 1.5% enflurane. Near completion of the case the surgeons inserted a superior mediastinal catheter for sternal irrigation and a larger inferior mediastinal chest tube for drainage. The irrigation fluid consisted of 1 million units of polymyxin and one g of amikacin in 1 l of lactated Ringer's solution.

At the end of the procedure, prior to reversal of vecuronium, ulnar nerve stimulation demonstrated fade to tetanic stimuli at 50 Hz and loss of third and fourth responses to TOF. Approximately 1 h after induction and about 2 min prior to beginning sternal irrigation, neostigmine 0.05 mg/kg and glycopyrrolate 0.01 mg/kg were given iv. Within 5 min of reversal the patient was breathing spontaneously at 15 breaths/min with a tidal volume, measured with in-line spirometry, of 400–500 ml. There was a sustained response to tetanic stimulation, the TOF was fully recovered, and the patient was able to maintain a sustained head lift for 5 s. Despite these findings, his trachea was not extubated because of our concern over the possible effects of the antibiotic irrigation. During the next 5 min respiratory rate and tidal volume decreased until he required controlled ventilation. At this time the 1-l irrigation bag containing the antibiotics was noted to be three-fourths empty. Although the inferiorly placed mediastinal tube was placed to suction, less than 100 ml of the 750 ml infused was suctioned into the reservoir. There was no response to either tetanic or TOF stimulation. Edrophonium 1 mg/kg and atropine 0.02 mg/kg were given iv with no clinical change and no response to TOF. The trachea was left intubated, and he was mechanically ventilated. For sedation the patient received 4 mg of morphine sulfate iv in the recovery room. On arrival in the recovery room rectal temperature was 36.5° C, pH_a was 7.39, Pa_{O_2} 125 mmHg, Pa_{CO_2} 42 mmHg with an FI_{O_2} of 0.4, and serum potassium of 3.9 mEq/l. No other reversal drugs were given. His trachea was extubated 4 h later. At that time his inspiratory force was −35 cm H_2O, vital capacity 12 ml/kg, and head lift was sustained for 5 s. The patient did well with no untoward sequelae.

DISCUSSION

Certain antibiotics have neuromuscular blocking properties that become clinically significant when given to patients receiving muscle relaxants.[1–3] This case describes an interaction involving the antibiotics polymyxin and amikacin.

Prolongation of other nondepolarizing neuromuscular blockers by polymyxin and amikacin have been reported.[4–9] Polymyxin enhances the blockades produced by *d*-tubocurarine, pancuronium, and succinylcholine.[8,10] One report describes the potentiation of pancuronium by polymyxin to have lasted 21 h, or about five times longer than what we observed with vecuronium.[9]

The neuromuscular blocking action of polymyxin is both prejunctional and postjunctional. In the frog, polymyxin decreases the quantal release of acetylcholine, as well as causes a postjunctional receptor blockade of acetylcholine-activated channels.[7] Additionally, the bacteriocidal action of polymyxin results from its interaction with cell membrane phosphatidylethanolamine, causing an irreversible alteration in membrane permeability.[11] This action on nervous tissue or muscle changes transmembrane potentials and may also contribute to a neuromuscular block.

Due to the complicated nature of the polymyxin block, most attempts at reversal with calcium and or anticholinesterases have met with little success.[5] Because reversal of an antibiotic neuromuscular blockade of this nature is

* Instructor of Anesthesiology.
† Associate Professor of Anesthesiology.
‡ Professor and Chairman.

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Address reprint requests to Dr. Kronenfeld.

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unreliable, ventilation should be controlled until the block dissipates spontaneously and standard criteria for extubation of the trachea are met.

Amikacin sulfate, the other antibiotic in our patient's sternal irrigation, is structurally related to the aminoglycoside group of antibiotics. The aminoglycosides decrease sensitivity to acetylcholine.§ Hashimoto *et al.*, however, reported that an amikacin block could be effectively reversed with calcium chloride, which augments presynaptic quantal release of acetylcholine. This would implicate a presynaptic site of action for amikacin sulfate.[4,7]

The reparalysis seen during sternal irrigation containing one million units of polymyxin and one g of amikacin was quite dramatic. The failure of our trial at reversal was not unexpected, but had been unreported with this combination of antibiotics and vecuronium. Calcium was not used to effect reversal because it is an unpredictable antagonist and, when successful, the reversal is unlikely to be sustained.

It is unknown why the prolonged paralysis seen in our patient lasted only 4 h compared with 21 h reported with pancuronium. At first one is tempted to attribute this to the shorter duration of vecuronium compared with pancuronium. However, a recent case report described a prolonged neuromuscular block with vecuronium and gentamicin to have lasted 49 h.[12]

In conclusion, this is the report of a patient whose neuromuscular blockade reappeared and was prolonged after apparent reversal of a vecuronium neuromuscular block. This occurred during sternal irrigation with polymyxin and amikacin in lactated Ringer's solution. The neuromuscular block in our patient lasted approximately 4 h. Based on this case, the possibility of unsuccessful reversal of the combination of vecuronium and these antibiotics should be considered. If this occurs, the patient should be ventilated until the block dissipates and standard tracheal extubation requirements are met. With our use of this regimen, our patient did well with no untoward sequelae.

§ Viby-Mogensen J: Interaction of other drugs with muscle relaxants. Sem Anesthesiol 4:52–64, 1985.

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Erratum

In the article "Postoperative Hepatic Dysfunction after Halothane or Enflurane Anesthesia in Patients with Hyperthyroidism" by H. Seino, S. Dohi, Y. Aiyoshi, T. Mizutani, K. Nakamura, and H. Naito (ANESTHESIOLOGY 64:122–125), under Materials and Methods, fifth line in the third paragraph, the correct dose of diazepam is 10 mg, not 100 mg.