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Prolongation of a Pancuronium-induced Neuromuscular Blockade by Polymyxin B

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Several antibiotics prolong the neuromuscular blockades induced by nondepolarizing neuromuscular blockers.¹ We report an instance of pancuronium-induced neuromuscular blockade which was apparently prolonged as a result of intraoperative wound irrigation with Polymyxin B and, possibly, bacitracin. Pyridostigmine, neostigmine, edrophonium, and calcium chloride were either ineffective or incomplete antagonists of this blockade.

REPORT OF A CASE

A 76-year-old man was admitted in Nov. 1972 for open reduction and internal fixation of a right femoral neck fracture. His most recent operation had been a resection of a thoracic aortic aneurysm in 1968 under general anesthesia without known problems. No medication was taken prior to hospitalization. In the hospital, before operation, he received thiamine, multivitamins, stool softeners, codeine, and chloral hydrate. With the exception of congenital ocular palsies and the hip fracture,

physical examination disclosed no abnormality. Serum sodium, potassium, chloride, and bicarbonate were 135, 3.5, 97, and 27 mEq/l, respectively. Preoperative blood urea nitrogen and glucose levels were 18 and 105 mg/100 ml, respectively. Urine, chest and skull roentgenograms, and EKG were normal.

No preanesthetic medication was given. Anesthesia was induced and maintained with nitrous oxide, 60 per cent in oxygen, and an end-tidal halothane concentration of 0.75 per cent, the latter determined by gas chromatography. The trachea was intubated without the use of any other drug. Neuromuscular function was evaluated by supramaximal stimulation of the ulnar nerve at the wrist, measuring force of adduction of the thumb with a Grass FT-10 force-displacement transducer; results were recorded on a polygraph. A Grass S-44 stimulator delivered the stimuli at 0.3 pulses/sec with a 0.1 msec duration. Ventilation was controlled. Thirty-five minutes after induction of anesthesia, pancuronium bromide, 2.4 mg/m² (4.8 mg), was administered iv, resulting in 100 per cent depression of twitch height (fig. 1). Approximately 50 minutes later, arterial P_{O_2} , P_{CO_2} , and pH were 123 torr, 28 torr, and 7.55, respectively, with a base excess of +4. Esophageal temperature was 36.2 C. At this time the surgical wound was irrigated with 1 liter of 0.9 per cent sodium chloride containing Polymyxin B, 250,000 units, and bacitracin, 50,000 units.

Because 100 per cent depression of twitch height still existed 103 minutes after administration of pancuronium, and the end of the surgical procedure was anticipated, antagonism of the neuromuscular blockade was attempted by a bolus intravenous injection of pyridostigmine, 14.5 mg, and atropine, 0.6 mg (fig. 1). Because the twitch had returned to only 10 per cent of the con-

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TABLE 1. Summary of Neuromuscular Function, Medications, and Miscellaneous Variables during Attempted Antagonism of Pancuronium-induced Neuromuscular Blockade in the Presence of Polymyxin B and Bacitracin

Time after Pancuronium Injection*	Neuromuscular Function		Medications Given at Time Stated (iv)	Miscellaneous
	Per Cent of Control Twitch Height	Response to Tetanus 50 Hz		
50 min	0	↓	§	Wound irrigation†
103 min	0	↓	Pyridostigmine, 14.5 mg	Temperature 36.2 C
129 min	10	Unsustained	Pyridostigmine, 5.0 mg	
142 min	20	Unsustained	Pyridostigmine, 5.0 mg	
152 min	25	Unsustained	Tensilon, 10 mg	
157 min	30	Unsustained	Neostigmine, 1.0 mg	
175 min	45	Unsustained	Calcium, 100 mg	Operation completed
182 min	60	Unsustained	Calcium to 300 mg total	Spontaneous V _T 0.15 l
192 min	62	Unsustained	Calcium to 500 mg total	Spontaneous V _T 0.20 l
209 min	80	Unsustained	Calcium to 800 mg total	
215 min	80	Unsustained	Calcium to 1,000 mg total	
225 min	80	Unsustained	Calcium to 1,200 mg total	Spontaneous V _T 0.35 l; anesthesia discontinued. To recovery room
272 min	80	Unsustained	§	Assisted ventilation
292 min	80	Unsustained	Calcium to 1,300 mg total	No grip, no head hold
5 hr	80	Unsustained	Calcium to 1,400 mg total	Vital capacity 0.4 l
6 hr	80	Unsustained	§	
13 hr	↓	↓	§	Vital capacity 0.6 l Maximum inspiratory force <20 cm H ₂ O
21 hr	↓	Sustained (30 Hz)	§	Head lift >20 seconds Strong bilateral grip Vital capacity 1.0 l Maximum inspiratory force >40 cm H ₂ O Extubation of the trachea
23 hr	↓	↓	§	Discharged to ward

* Dose of pancuronium was 2.4 mg/m² (4.8 mg).

† Hip wound irrigation with 1,000 ml sodium chloride, 0.9 per cent, containing Polymyxin B, 250,000 units, and bacitracin, 50,000 units, prior to initial pyridostigmine dose.

‡ Not monitored.

§ No medication given.

trol height 26 minutes later, additional antagonists were given over the next three hours, as summarized in table 1 (fig. 1). Although the surgical procedure was completed 150 minutes after administration of pancuronium, anesthesia was continued to allow frequent application of tetanic stimuli which would be painful if administered to a conscious patient.

Approximately four hours after pancuronium administration (and two hours after initial pyridostigmine administration), twitch had returned to only 80 per cent of the control height, and the response to a tetanic stimulus of 50 Hz for 5 seconds was unsustained. Anesthesia was discontinued at this time, with a spontaneous tidal volume of 0.35 l. The patient was transferred to the recovery room. Total doses of medications given in the operating room to antagonize the block were

pyridostigmine, 24.5 mg, neostigmine, 1.0 mg, edrophonium, 10 mg, and calcium chloride, 1,200 mg (table 1).

Neuromuscular function was monitored continuously in the recovery room for the next two hours, during which time an additional 200 mg of calcium chloride was administered without benefit. The patient responded to vocal commands with a slight nod of the head but was unable to lift his head off the bed or grip a pencil. Because spontaneous tidal volume was only 0.20 l, ventilation was controlled. Six hours after pancuronium administration, monitoring of neuromuscular block with the force-displacement transducer was discontinued with tetanus still unsustained. Thirteen hours after pancuronium, vital capacity had increased to 0.60 l but the maximum inspiratory force was less than 20 cm H₂O. Controlled ventilation was continued.

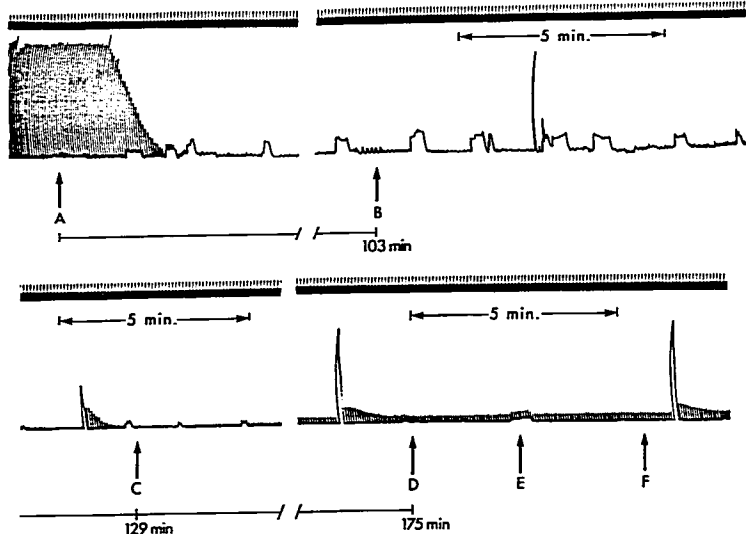


FIG. 1. 100 per cent depression of twitch height in response to administration of pancuronium bromide, 2.4 mg/m² (4.8 mg) (arrow A). Administration of pyridostigmine, 14.5 mg, and atropine, 0.6 mg, 103 min after pancuronium administration (arrow B). Because of an unsustained tetanus and the presence of posttetanic facilitation, additional pyridostigmine, 5 mg, was administered (arrow C). Calcium chloride, 100 mg each time, was administered at arrows D, E, and F. Irrigation of the surgical wound with Polymyxin B and bacitracin occurred between arrows A and B approximately an hour after pancuronium administration. Periodic baseline alterations are secondary to inflation of a blood pressure cuff on the monitored arm.

Twenty-one hours after administration of pancuronium the patient was able to lift his head off the pillow for at least 20 seconds, and bilateral grip strength was equal to that of the observer. His maximum inspiratory force was greater than 40 cm H₂O. Vital capacity was 1.0 l and chest roentgenogram was normal. Sustained response to a tetanic stimulus of 30 Hz for 5 seconds from a Neurodyne was elicited. With spontaneous respiration and without an endotracheal tube, arterial P_{O₂}, P_{CO₂}, and pH were 122 torr, 41 torr, and 7.40, respectively, with oxygen administered at a flow rate of 5 l/min through a nasal cannula. The patient recovered without further complication.

DISCUSSION

In this patient, whose surgical wound was irrigated with polymyxin B and bacitracin, neuromuscular blockade by pancuronium was prolonged approximately 21 hours. The

block produced by succinylcholine has been reported to be prolonged by Polymyxin B and bacitracin.² In both patients prolongation must be ascribed to Polymyxin B, since bacitracin is probably devoid of neuromuscular blocking properties.¹ Neuromuscular blockade from Polymyxin-B alone has been reported in both medical and surgical patients not receiving anesthetic or other neuromuscular blocking drugs.¹ It also potentiates *d*-tubocurarine- and succinylcholine-induced blockades.¹ A Polymyxin B neuromuscular blockade is prolonged by neostigmine and not antagonized by calcium.³ We, too, had little success antagonizing this block with pyridostigmine, 24.5 mg, edrophonium, 10 mg, neostigmine, 1.0 mg, and calcium chloride 1,400 mg (fig.

1). In the absence of antibiotics, the effect of pancuronium, 2.4 mg/m², is readily antagonized by pyridostigmine, 14.5 mg. Possibly, administration of these acetylcholinesterase inhibitors actually prolonged the pancuronium-polymyxin B neuromuscular block. The prompt initial improvement after administration of calcium chloride (increase in the twitch height from 45 per cent to 80 per cent of control) suggests partial antagonism of this antibiotic-pancuronium neuromuscular blockade.

Since tetanus (50 Hz) normally is sustained approximately 2.5 hours after pancuronium,⁴ the prolonged block might have resulted from Polymyxin B alone. This seems likely, since urinary levels of Polymyxin B (excretion in urine is the major route of elimination) peak about 24 hours after an intramuscular injection.⁵

If administration of antibiotics to patients with nondepolarizing neuromuscular blockade is indicated, perhaps alternative antibiotics, such as the cephalosporins which are devoid of neuromuscular blocking properties⁴ and have both gram-positive and gram-

negative antibacterial activity, might be administered.

In summary, we have reported a prolonged block from pancuronium in the presence of Polymyxin B. Acetylcholinesterase inhibitors did not antagonize, and perhaps increased, that block. Calcium chloride partially antagonized the block.

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Improper Oxygenation during Bronchofiberscopy

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A flexible bronchofiberscope was introduced by Ikeda¹ in 1968. The instrument has been utilized during both general and topical anesthesia.^{2,3} The relative ease with which this flexible instrument may be inserted into the airway has led to increased use of bronchoscopy by less experienced personnel.⁴

Troubled by episodes of hypoxia during performance of bronchoscopy using topical anesthesia, Harken *et al.*⁵ advocated insufflating oxygen through the cuff hose of

an endotracheal tube in which a window had been cut into the cuff. The bronchofiberscope was then introduced down the central lumen of the endotracheal tube, which had been previously inserted under topical anesthesia following the method of Ikeda.¹

At our institution a nasopharyngeal airway, rather than an endotracheal tube as advocated by Wanner *et al.*,² is used to pass the bronchofiberscope.

The following case led us to look into a safe, reliable method for oxygen administration during bronchoscopy through a nasopharyngeal airway using local anesthesia.

REPORT OF A CASE

A 75-year-old man was scheduled for bronchoscopy because of persistent pneumonitis and atelectasis of the right lower lobe

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