A Possible Hazard of Prolonged Neuromuscular Blockade by Amikacin

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Prolonged neuromuscular blockade is a well-known adverse effect that follows administration of antibiotics. The aminoglycoside group of antibiotics producing neuromuscular blockade in man includes bekamycin, dibekacin, dihydrostreptomycin, kanamycin, neomycin, ribostamycin, spectomycin, and tobramycin. Amikacin sulfate is structurally related to the aminoglycoside group of antibiotics. The neuromuscular blocking properties of amikacin sulfate in man have not been previously reported. Therefore, this study was undertaken to determine the neuromuscular blocking properties of amikacin sulfate in anesthetized patients.

Methods

Thirteen adult patients, ASA class I–II, of both sexes, without known neuromuscular disease, were studied after informed consent was obtained. All were premedicated with meperidine, 50–70 mg, and atropine, 0.5 mg, given im approximately an hour before induction of anesthesia. After peridural anesthesia was attained, anesthesia was induced with thiaylal, 5 mg/kg. Succinylcholine, 1 mg/kg, was given iv and endotracheal intubation performed. Each patient then received nitrous oxide and oxygen (5:1:1 mixture) via a semiclosed circle absorber system. Supplemental pentazocine, 30–60 mg, was given iv to maintain a stable level of light anesthesia. Some patients were also given pancuronium. Ventilation was assisted or controlled manually to maintain end-tidal PCO₂ in the range of 35–45 torr.

The median nerve was stimulated at the elbow and wrist through subcutaneous needle electrodes using a Nihon Kohden SEN-1101 stimulator and a stimulus isolation unit with supramaximal square waves of 0.2-msec duration. The electrical stimuli were applied continuously with either 0.2 Hz or 2 Hz for 2–15 seconds. The resultant force of adduction of the middle finger was measured with a force-displacement transducer (Shinkoh U-gage) and recorded on a Nihon Kohden polygraph.

After a control period of at least 15 minutes, amikacin sulfate, 100 or 200 mg, was administered iv as a single rapid bolus to seven patients. Six other patients were given amikacin sulfate, 100 mg iv, when twitch tension after pancuronium administration had recovered to 50 per cent of the control level. The antagonizing effects of edrophonium and calcium chloride on combined amikacin–pancuronium-induced neuromuscular blockade were also studied.

Results

Amikacin sulfate alone did not depress twitch tensions and train-of-four ratios in six of seven patients. In one patient, iv administration of amikacin sulfate, 100 mg, caused decreases in twitch tension and train-of-four ratio. Train-of-four ratios before and after administration of amikacin sulfate were 75 and 69 per cent, respectively. Calcium chloride antagonized this blockade. This patient, a 55-year-old woman, weighing 58.5 kg, was scheduled for vaginal hysterectomy. She had no clinical symptoms of muscular weakness.

When twitch tension after pancuronium had recovered to 50 per cent of the control level, iv injection of amikacin sulfate, 100 mg, slightly augmented pancuronium blockade. The combined amikacin–pancuronium-induced blockade was antagonized by edrophonium, 10 mg, and by calcium chloride, 400 mg.

Discussion

Amikacin sulfate is a semisynthetic, water-soluble antibiotic produced by an acyl substitution of an amino group of kanamycin. It is markedly active against strains of gentamicin-resistant Pseudomonas aeruginosa and Proteus species. Amikacin sulfate is not bound to plasma proteins and is eliminated by the kidney almost exclusively.

The main pharmacologic mechanism of neuromuscular blocking action by the aminoglycoside group of antibiotics is inhibition of the release of acetylcholine from nerve endings, an effect similar to that of low calcium or high magnesium concentration. The neuromuscular blockade of this group of compounds is reversible with calcium and with neostigmine when the blockade is incomplete. Our results suggest that the characteristics of neuromuscular blocking properties of amikacin sulfate are similar to those of other members of the aminoglycoside group.
In our present study we observed one patient who had decreases in twitch tension and train-of-four ratio after amikacin sulfate, 100 mg, alone. Train-of-four ratio in a control period in this patient was 75 per cent, while those of the other 12 patients in this study were approximately 100 per cent. Słomiński et al. recorded twitch responses with trains of 2-Hz stimuli for 90 seconds in 30 normal subjects and 23 patients with myasthenia gravis. They found that while the force of twitch gradually increased (positive staircase) in normal subjects, twitch tension decreased by 20–40 per cent, most markedly after 10 seconds, in patients with myasthenia gravis. We previously reported that the mean values for train-of-four ratios with 2-Hz stimuli in 15 normal patients and eight patients with myasthenia gravis during nitrous oxide-oxygen and halothane anesthesia were 100.3 and 77.9 per cent, respectively. Thus, it is probable that this patient has "mild myasthenic state" or myasthenia gravis.

In conclusion, the present study suggests that amikacin sulfate would produce undesirable prolonged neuromuscular blockade in circumstances of overdosage or excessive absorption in myasthenic patients.

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Carden-tube Insertion

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Microlaryngoscopy for investigation of the larynx has created a challenge to find an effective method for airway management of the anesthetized patients. The Carden tube was developed to facilitate microlaryngoscopy.

Along with others, we have encountered some difficulties with insertion of the Carden tube. Cooke et al. reported a relatively easy method for inserting this tube. We have found the following modification of their technique for the placement of the Carden tube to be simple and effective.

A standard endotracheal tube stylet is lubricated and a 25-cm piece of ⅛ inch ID plastic suction tubing is slipped over the stylet with the distal end of the stylet

Fig. 1. Carden tube, suction tubing and stylet in place for endotracheal intubation.

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