

PARENTERAL NEOMYCIN AND MUSCLE RELAXANTS

TWO CASE REPORTS OF INTEREST

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The following 2 case reports lend weight to the suspicion that difficulty with reversal of curarization, and subsequent recurarization, may occur after parenteral administration of neomycin.

Case 1

A 57-year-old woman, weighing 51 kg., presented at St. Thomas' Hospital, London, for hemicolectomy for carcinoma of the colon. General and systemic examination revealed a thin but otherwise healthy woman. She had had 2 G of oral neomycin daily for 3 days, and another 1 G by mouth on the morning of the operation. Electrolytes were normal on the day of operation.

Anaesthesia. The premedication consisted of 50 mg. of pethidine and 25 mg. of phenergan. Anaesthesia was induced with 150 mg. of thiopentone and 30 mg. of curare, and maintenance anaesthesia consisted of N₂O and O₂ and 0.5% halothane. IPPR was provided by a Barnet ventilator, and a further 20 mg. of curare was given (total dose 50 mg.).

The operation and the anaesthesia were completely uneventful. Blood loss assessed at 1 pint was replaced, and 1 litre dextrose/saline and 500 ml. 5% dextrose/water were given during the course of the 2½-hour operation.

At the end of the operation 0.6 mg. of atropine and 1.25 mg. of neostigmine were given in repeated doses until a total of 5 mg. of neostigmine had been given. Response had been very sluggish but the patient recovered consciousness and was apparently ventilating well. In view of the difficulty in reversing the curare after 2½ hours on the operating table, it was decided to keep the patient under observation in the recovery room. Twenty-five minutes later it was reported that the patient was having difficulty with respiration. Obvious signs of curarization were evident—the patient had tracheal tug, intercostal paralysis, was extremely restless, unconscious and cyanosed; pulse 70/min., bounding; blood pressure 135/80 mm.Hg.

The patient was reintubated without any difficulty and put back onto a ventilator. A Medelec nerve stimulator revealed a neuromuscular block of the non-depolarizing type. Blood was immediately taken and sent to the laboratory for pH and electrolyte analysis. The further progress of the patient was monitored with the nerve stimulator.

Fifty mEq. of Na(HCO₃)₂ were given empirically with no improvement. Ten ml. of calcium gluconate were then administered in an effort to antagonize the suspected neomycin block. Slight improvement was noted. A further 10 ml. of calcium gluconate were given 20 minutes later and ventilation was continued. The patient only recovered consciousness 3 hours after the relapse. Six hours after operation full muscular strength returned and the patient made an uneventful recovery. The blood taken revealed only a mild respiratory acidosis. Electrolytes were normal.

Case 2

A healthy, well-built man, weighing 80 kg., was admitted to Karl Bremer Hospital with signs suggestive of chronic intestinal obstruction thought to be due to adhesions following a bowel resection and postoperative radiotherapy 1 year previously. Pre-operative examination revealed no abnormalities. There was no dehydration, the electrolytes and haematocrit were within normal limits.

Anaesthesia. Premedication consisted of 75 mg. of pethidine and 50 mg. of phenergan. Anaesthesia was induced with 300 mg. of thiopentone and 45 mg. of curare, and maintenance anaesthesia consisted of N₂O and O₂, with intermittent pethidine to a total of 50 mg., and a further 15 mg. of curare (total 60 mg.).

The operation and anaesthesia were once again uneventful, blood loss assessed at 1 pint was replaced, and 1 litre of 5% dextrose/water and 1 litre of Ringer's lactate were infused during the course of the 2½-hour operation.

Resection of an adherent loop of bowel was performed. Just before closure of the peritoneum, 1 G of neomycin was injected into the lumen of the bowel in the region of the anastomosis. The surgeon's attention was drawn to the possible dangers of this manoeuvre but he replied that he considered absorption of a significant amount unlikely. However, 10 ml. of calcium gluconate was injected prophylactically.

Reversal of the curare was, as in the first case, difficult and protracted—the response being very sluggish indeed. A total of 6.25 mg. of neostigmine was necessary. The patient was sent to the recovery room, recovered consciousness and spoke to the anaesthetist, who allowed the patient to be returned to the ward. There was some portage delay and the patient's progress back to the ward was (fortunately!) somewhat prolonged. Outside the lift on the theatre floor the nurse noticed that the patient was experiencing difficulty with respiration. She reported this fact to the anaesthetist who rushed to the scene and found the patient deeply cyanosed and *in extremis*. The pulse was impalpable, the heart beat inaudible and the pupils widely dilated, i.e. cardiac arrest had occurred.

External massage, positive-pressure ventilation and injection of intracardiac adrenalin proved immediately successful. The patient was taken back to theatre, blood was taken for analysis, and 50 mEq. of Na(HCO₃)₂ and 100 G of mannitol were administered empirically to combat metabolic acidosis and cerebral oedema, respectively.

The patient, although making spontaneous respiratory movements, was not ventilating adequately, a curarized pattern still prevailing. A further dose of 1.25 mg. of neostigmine and 10 ml. of 10% calcium gluconate produced no response. The patient was ventilated via the endotracheal tube with a Bird respirator and 6 hours later was able to ventilate adequately on his own. Consciousness had returned 2 hours after arrest. Subsequent recovery was uneventful and the patient was discharged without any recollection of this un-

pleasant episode and with no detectable residual impairment of cerebral function.

DISCUSSION

These 2 cases would certainly appear to incriminate neomycin. The points in favour of this would seem to correspond to a well-documented pattern, namely:

1. Difficulty in reversing curarization, i.e. neostigmine resistance.
2. Loss of consciousness despite adequate ventilation.
3. Reversal with passage of time.
4. Improvement with calcium gluconate in the first place would lend weight to this argument, although, in the second place it afforded no protection and gave no response.

Metabolic acidosis is of course held to be the cause of many of these cases of resistant curarization and recurarization. There does not seem to be any reason to suspect its presence in either of these cases, and indeed administration of sodium bicarbonate did not afford any improvement.

Electrolyte imbalance is considered an unlikely cause as both haematocrit and electrolyte figures were within normal limits.

It is claimed that neomycin is minimally absorbed, if at all, after parenteral administration. While cases of this sort are well documented following intraperitoneal instillation, one may be lulled into a false sense of security when the parenteral route is used. In the first case the bowel was apparently normal so absorption was not anticipated. In the second case the bowel was inflamed as a result of the radiotherapy and the injection was made in the region of raw anastomosis. It would appear that although good results have been reported following the use of calcium gluconate the most certain method is to allow 'time to heal' while ensuring adequate ventilation by artificial means.

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