

voir fittings or labels to which industrial gas producers must adhere. Such standards, combined with continuous monitoring of the oxygen concentration in the anesthetic circuit and in the central oxygen supply line, would contribute to the safety of oxygen administration.

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## Inability to Reverse Pancuronium Blockade in a Patient with Renal Failure and Hepatic Disease

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Gallamine is used with caution or not at all in the management of patients with renal failure, since renal excretion is the major pathway for its elimination.<sup>1</sup> In usual clinical doses, *d*-tubocurarine has not been associated with similar prolonged elimination, presumably because of hepatic mechanisms for its elimination. For similar reasons, the new nondepolarizing neuromuscular blocking agent, pancuronium bromide, has been suggested to be particularly appropriate for use in the anephric patient. This report describes prolonged muscular weakness following pancuronium in an anephric patient who, in addition, had hepatic dysfunction secondary to acute biliary obstruction.

## REPORT OF A CASE

A 45-year-old Negro woman who had renal failure and peptic ulcer disease was to undergo

drainage of a large pancreatic pseudocyst under general anesthesia. Three weeks earlier a rejected renal transplant had been removed, with fluroxene-nitrous oxide anesthesia. Liver function tests had been normal at that time. Muscle relaxation had been achieved with *d*-tubocurarine, 21 mg, which was easily reversed with neostigmine, 2.5 mg, 45 minutes after the *d*-tubocurarine had been given. In the postoperative period, the patient had had numerous episodes of hypotension which were promptly treated with the intravenous administration of fluids and albumin. Chronic hemodialysis was also re-established.

At the end of the first postoperative week, the patient developed an abdominal mass and became jaundiced. Liver enzyme values were slightly increased, and the diagnosis of pancreatic pseudocyst with acute biliary obstruction was made. Her medications included prednisolone, nystatin, folic acid, and Aquamephyton. Physical examination revealed that the patient was debilitated, lethargic, and cushingoid, with scleral icterus. The blood pressure was 75/50 mm Hg, heart rate 100/min, temperature 38.4 C (rectal), and central venous pressure 2 cm H<sub>2</sub>O. Weight was 60 kg. There was marked pitting pretibial edema. The chest was clear. Examination of her heart disclosed no abnormality except sinus tachycardia. A Scribner hemodialysis shunt was present in the left arm. A roentgenogram of the chest was clear and an electrocardiogram was normal. Abnormal laboratory values were: Na 134 mEq/l, K 2.9 mEq/l, Cl 86 mEq/l, total protein 5.6 g/100 ml, albumin 2.6 g/100 ml, bilirubin 8.9 mg/100 ml, BUN 79 mg/

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100 ml, creatinine, 10.5 mg/100 ml, Hct 33 per cent, SGOT 52 units/ml, LDH 412 units/ml.

The patient received no premedication prior to exploratory laparotomy. A rapid infusion of lactated Ringer's solution was begun and anesthesia was induced with sodium thiopental, 175 mg. Following succinylcholine, 100 mg, and endotracheal intubation, fluroxene, 4 per cent, with 50 per cent oxygen and nitrous oxide was administered. Arterial and central venous pressures, electrocardiogram, heart sounds, and ventilation were monitored continuously during operation. The blood pressure decreased from 70/50 to 50/40 mm Hg. The inflowing fluroxene concentration was reduced to 1 per cent, and blood pressure stabilized at 65/45 mm Hg for the remainder of the operation. The central venous pressure fluctuated between 5 and 7 cm H<sub>2</sub>O. Approximately 10 minutes after induction, after spontaneous respirations had returned, pancuronium bromide, 3 mg (0.05 mg/kg) was administered to produce relaxation for the operative procedure. Thereafter, ventilation was mechanically controlled. Arterial blood-gas values during this time were P<sub>o</sub>, 95 mm Hg, P<sub>co</sub>, 44 mm Hg, pH 7.40, and HCO<sub>3</sub> 26.3 mEq/l.

No additional pancuronium was necessary during the subsequent two hours of operation. Antibiotics were not administered. As the operation neared completion, atropine, 0.5 mg, followed by neostigmine, 2.5 mg, was given to reverse the neuromuscular blockade. Response to neostigmine was minimal. Spontaneous respirations returned, but with a tidal volume of only 100 ml at a rate of 40/min. When the inhalation agents were discontinued, the patient could open her eyes, the endotracheal tube was well tolerated, her grip was weak, and she could not raise her head. Positive-pressure ventilation was continued. Five hours after pancuronium administration, two 10-mg doses of edrophonium did not improve grip strength or head lift. Ten hours after pancuronium administration, the patient's status was essentially unchanged and hemodialysis was begun. Her temperature at this time was 37.4 C (rectal), and serum potassium was 2.9 mEq/l. After 30 minutes of hemodialysis the patient became agitated, began to swallow and chew on the bite block, and vigorously fought the ventilator. She could raise her head, and her grip strength was good. She had a tidal volume of 300 ml, vital capacity of 750 ml, and an inspiratory force of -25 cm H<sub>2</sub>O. Postdialysis serum potassium was 3.0 mEq/l. Arterial blood-gas analysis with the patient breathing 40 per cent oxygen showed P<sub>o</sub>, 89 mm Hg, P<sub>co</sub>, 38 mm Hg, pH 7.41, and HCO<sub>3</sub> 26 mEq/l. The trachea was extubated and the patient did well thereafter.

#### DISCUSSION

Recent reports<sup>2-4</sup> have shown that patients in renal failure receiving single doses of pancuronium in the clinical range of 0.04 to 0.10 mg/kg have not had unusually prolonged

neuromuscular blockade. Miller<sup>4</sup> reports that pancuronium-induced neuromuscular blockade lasts 20 to 40 minutes longer in patients with renal failure than in patients with normal renal function. Thus, the ten hours of neuromuscular blockade in our patient after a single dose of only 0.05 mg/kg pancuronium raises the question whether factors other than failure of renal excretion might have accounted for the persistent paralysis. These additional factors could include decreased biliary excretion or hepatic metabolism of pancuronium resulting from this patient's biliary obstruction, an increased sensitivity at the myoneural junction resulting from her renal disease, a malnourished and debilitated condition, or an increased sensitivity to pancuronium resulting from her low serum protein and potassium levels or from other unassessed electrolyte abnormalities.

The proportion of pancuronium excreted by kidney and liver in normal man is unknown.<sup>5</sup> There is evidence that the liver eliminates pancuronium not only by biliary excretion, as is the case with *d*-tubocurarine, but also by metabolism.<sup>5,6</sup> In our patient the biliary excretion pathway was blocked by the obstruction from the pancreatic pseudocyst. Hepatic metabolic function was also impaired, as evidenced by abnormal values for liver enzymes.

Renal failure may increase the sensitivity of the myoneural junction to muscle relaxants. In one patient with renal failure we observed satisfactory relaxation for both endotracheal intubation and subsequent operation after a 10-mg test dose of succinylcholine. Subsequent determination of plasma pseudocholinesterase revealed normal levels. The present patient did not have obviously abnormal sensitivity to succinylcholine, since she resumed breathing spontaneously within 10 minutes after receiving 100 mg of the drug. However, the apparent intensity of the block following 0.05 mg/kg pancuronium suggests that increased sensitivity to the drug may be a factor contributing to its prolonged duration of action.

This patient did have slightly low serum protein levels. However, Stovner, Theodorsen, and Bjelke<sup>7</sup> could not demonstrate a correlation between pancuronium requirement and

serum protein level. Although our patient was also hypokalemic, Miller, Stevens, and Way<sup>5</sup> could not demonstrate a significant correlation between serum potassium levels and time to 5 per cent recovery of control twitch height with 2.4 and 3.6 mg/m<sup>2</sup> pancuronium, and found only a slight negative correlation with 1.2 mg/m<sup>2</sup>. Nor was return of muscle strength following dialysis associated with an appreciable change in serum potassium concentration.

We were pleasantly surprised by the lessening of our patient's weakness after only 30 minutes of dialysis. The pancuronium ion has a molecular weight of 544 and thus qualifies as a "middle molecule" (MW 350-2,000) for dialysis purposes. Shreiner and Teehan<sup>8</sup> state that middle molecules permeate hemodialysis membranes poorly. In fact, gallamine, an even smaller molecule (MW 384), has required two episodes of dialysis over three days before all signs of residual neuromuscular blockade disappeared.<sup>1</sup> A more appealing, albeit undocumented explanation for this patient's rapid recovery with dialysis would be an improvement in electrolyte balance, perhaps for calcium or magnesium ions, rather than elimination of residual pancuronium.

In summary, we have described an anephric patient with a markedly prolonged neuromuscular blockade from pancuronium. Three weeks previously the patient had had no prolongation of neuromuscular blockade after administration of *d*-tubocurarine, 21 mg. In the interim, the patient developed a pancreatic pseudocyst, resulting in biliary

obstruction with evidence of hepatocellular dysfunction. Both pancuronium and *d*-tubocurarine have been used safely in anephric patients, and both have renal and hepatic pathways of elimination. Concomitant hepatic disease in the anephric patient may be a cause for prolonged neuromuscular blockade when these drugs are used even in moderate dosages for surgical relaxation.

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