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The Hemodynamic Effects of Pancuronium and d-Tubocurarine in Anesthetized Patients

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Intravenous administration of d-tubocurarine (dTC) during general anesthesia may be followed by hypotension. Pancuronium bromide (Pavulon), a new nondepolarizing neuromuscular blocker, is reported to be free of this undesirable side-effect. This study compares the hemodynamic effects of dTC and pancuronium administered to the same patients during operation with halothane–nitrous oxide–oxygen anesthesia and controlled ventilation.

METHODS

Ten patients without cardiovascular disease, undergoing elective operations, were studied. All were premedicated with morphine (8–15 mg) and scopolamine (0.4 mg) 90 minutes before operation. Anesthesia was induced with methohexital (Brevital), 80–120 mg, followed by succinylcholine to facilitate tracheal intubation. Anesthesia was maintained with 0.5 to 1.0 per cent halothane and 60 per cent nitrous oxide in oxygen. Ventilation was controlled with a volume ventilator. Catheters were placed percutaneously in a radial or ulnar artery and external or internal jugular vein and connected to appropriate transducers.

After at least an hour of anesthesia, 0.08 mg/kg pancuronium (five patients) or 0.4 mg/kg dTC (five patients) was rapidly injected intravenously. Mean arterial pressure (MAP), mean central venous pressure (CVP) and elec-

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trocardiogram (ECG) were recorded continuously for 3 minutes before and 10 minutes after administration of the neuromuscular blocker. Cardiac output (CO) was measured by the dye-dilution method with indocyanine green dye and a Beckman cardio-densitometer immediately before and 3 and 10 minutes after administration of neuromuscular blocker. Stroke volume (SV = CO/HR) and systemic resistance (SVR = MAP – CVP/CO) were calculated. At least 180 minutes after the first injection, the other drug under study was administered, and all measurements were repeated at similar anesthetic concentrations and ventilation.

Four patients undergoing elective operations of shorter duration received only pancuronium. Measurements were made as described above.

RESULTS

Hemodynamic changes after pancuronium and dTC are summarized in figure 1. Pancuronium (5.2 ± 0.4 mg) significantly increased heart rate (HR), MAP, and CO (P < 0.01), while SV and SVR were not significantly changed. Administration of dTC (26 ± 3.3 mg) to the same patients resulted in a small increase in HR (P < 0.05), decreased MAP (P < 0.01), decreased CO (P < 0.01) at 10 minutes, and decreased SVR (P < 0.01) at 3 minutes. CVP decreased 1.2 to 2.8 torr following pancuronium and dTC. Differences between pancuronium and dTC control values for each measurement were not significant.
Fig. 1. Changes (average ±SEM) produced by 0.08 mg/kg pancuronium (n = 10) and 0.4 mg/kg dTC (n = 10) administered at zero time. HR, heart rate; MAP, mean arterial pressure; CO, cardiac output; SV, stroke volume; SVR, systemic vascular resistance; CVP, central venous pressure.

Changes after pancuronium or dTC were not affected by the sequence of drug administration.

Control values and hemodynamic changes in four additional patients receiving only pancuronium were similar to those described in figure 1. Two of these patients developed premature ventricular contractions concomitant with the increased HR and blood pressure following pancuronium. Arterial blood gases and serum potassium values were normal at this time. The arrhythmias persisted for at least 10 minutes before disappearing spontaneously.

DISCUSSION

During halothane-nitrous oxide-oxygen anesthesia and controlled ventilation all patients developed hypotension following dTC, while the same patients had increased MAP after administration of pancuronium. Since pancuronium is reported to be five times more potent than dTC, the doses used (0.08 mg/kg pancuronium and 0.4 mg/kg dTC) were comparable. Loh administered 0.12 mg/kg pancuronium during nitrous oxide-phenoperidine-oxygen anesthesia and found a significantly increased MAP 5 minutes after injection of the drug. In a comparable group of patients, 0.6 mg/kg dTC reduced MAP within 5 minutes, after which blood pressure returned towards control. Kelman and Kennedy found significantly elevated HR, blood pressure, and CO and unchanged total peripheral resistance after 0.07 mg/kg pancuronium. Other investigators found no significant change in blood pressure following pancuronium. The fact that
Pancuronium is devoid of histamine-releasing activity and does not produce significant ganglionic blockade probably explains the lack of hypotensive action.\(^6\)

Heart rate had increased an average of 10 beats/min one minute after administration of pancuronium and remained elevated throughout the 10-minute observation period. McIntyre and Cain\(^7\) reported a 7.9 beat/min increase with pancuronium. In our study the increased CO after administration of pancuronium was the result of the elevated HR. The increased HR and subsequently elevated MAP and CO may result from a specific cardiac vagolytic action\(^8\) of pancuronium.

Peak hypotension occurred 3 minutes after administration of dTC. At this time CO was unchanged from the preinjection value, and pulse rate had increased only 4 beats/min. SVR was greatly decreased and probably was responsible for the reduction in MAP. A peripheral dilating action as the mechanism for dTC hypotension was suggested by the report of Longnecker et al.\(^9\) Ganglionic blockade or histamine release, or both, has been proposed as the cause of hypotension after dTC, and would be expected to act primarily on the peripheral vessels.

Preservatives in commercial dTC preparations reduce the contractile force of in-citro heart preparations,\(^10\)\(^11\) but have not been shown to be responsible for dTC-associated hypotension during anesthesia in man.\(^12\) Preservatives used for pancuronium differ from dTC preservatives, but have not been reported to have cardiovascular effects.

Anesthetic depth, surgical stimulation and blood volume may alter hemodynamic responses to neuromuscular blockers. Although end-tidal halothane concentrations were not measured in this study, the gas flows during injections of the two drugs were similar. All measurements were obtained during operation, but no observations were made during sudden changes in surgical stimulation. Measured blood losses were replaced with whole blood, and maintenance fluids were 3–5 ml Ringer's lactate solution/kg/hr. Microhematocrits were 40±2.3 per cent at the first injection and 37.5±1.5 per cent at the second injection. Nasopharyngeal temperatures during the two injections were similar (35–36.5 C).

Premature ventricular contractions occurred in two of four patients receiving only pancuronium. Although no patient receiving both pancuronium and dTC developed a similar arrhythmia, we feel that the two groups were comparable and that increased ventricular irritability in those receiving only pancuronium should not be implied. Dobkin et al.\(^13\) also found transient ventricular arrhythmias in five patients receiving pancuronium. A change in the ratio of parasympathetic to sympathetic tone secondary to pancuronium's cardiac vagolytic action may result in increased sympathetic activity and subsequent ventricular irritability.\(^14\) We have seen a similar response after administration of gallamine.

**Summary**

Hemodynamic responses after administration of pancuronium (0.08 mg/kg) and dTC (0.4 mg/kg) were evaluated in ten patients during operation with halothane-nitrous oxide-oxygen anesthesia and controlled ventilation. Pancuronium significantly increased HR, MAP, and CO, while SV and SVR were unchanged. In the same ten patients dTC resulted in a slight increase in HR, decreased MAP, decreased CO at 10 minutes, and decreased SVR at 3 minutes. Two patients developed premature ventricular contractions after administration of pancuronium.

Pancuronium bromide (Pavulon) was provided through the courtesy of Harry Strade, M.D., Organon Inc., 375 Mount Pleasant Avenue, West Orange, New Jersey 07052.

**References**

Transient Global Amnesia Following Spinal Anesthesia

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Transient global amnesia—a syndrome characterized by the occurrence of an isolated episode of transient amnesia in an otherwise healthy patient—was first described by Fisher and Adams in 1958.2 The number of additional cases reported since that time has been substantial,6-7 but in no instance does the syndrome appear to have been observed during the immediate postoperative period. As we have recently observed such an episode, initially misdiagnosed as an acute toxic psychosis, we believe it is important to bring the existence of this rare syndrome to the attention of anesthetists.

REPORT OF A CASE

A previously healthy 69-year-old woman was admitted with a history of two days of painless gross hematuria. Prior to admission an intravenous pyelogram had revealed a large filling defect in the left side of the urinary bladder, and a sessile bladder tumor had been observed at cystoscopy. Past medical history revealed only that she had undergone a partial hysterectomy under spinal anesthesia 23 years prior to admission, and had had iron-deficiency anemia for the past three years. No cause for the latter condition had been found, and it had responded well to iron therapy without recurrence. She admitted to no current symptomatology apart from the hematuria.

On physical examination, the arterial pressure was 140/60 mm Hg and the pulse rate 72 beats/min. The patient was oriented and in no acute distress, and without significant physical findings. The hemocrit was 40 per cent; fasting blood sugar, urea nitrogen, creatinine, and serum electrolytes were all within normal limits. Radiologic examination of the thorax revealed a normal heart and no acute pulmonary infiltrates, and an electrocardiograph was interpreted as being within normal limits. Premedication consisted of atropine sulfate, 0.5 mg IM, at 6:15 AM, and a spinal anesthetic (to which the patient had consented the previous evening) was administered uneventfully at 7:36 AM. Tetracaine, 8 mg, with 10 per cent dextrose, 0.8 ml, resulted in analgesia (no response to pin-prick) to the sixth thoracic dermatome. Cystoscopy and transurethral resection of a carcinoma of the bladder were performed without complication, arterial blood pressure and pulse rate remaining stable throughout. The patient entered the recovery room apparently in satisfactory condition at 8:50 AM and was given mannitol, 12.5 gm IV, at 8:51 AM, and trimethobenzamide hydrochloride (Tigan),

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