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Cardiovascular Effects of Scopolamine during Morphine–Oxygen and Morphine–Nitrous Oxide–Oxygen Anesthesia in Man

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Incomplete amnesia and awareness sometimes complicate morphine (0.5–3.0 mg/kg) or morphine (0.5–1.0 mg/kg)–nitrous oxide anesthesia.[1] Scopolamine is often employed as a supplement during both of these techniques to prevent awareness. The cardiovascular effects of this drug during morphine anesthesia have not been investigated, however. In this study we measured the effects of intravenous administration of 0.5 mg scopolamine on cardiovascular dynamics during morphine–oxygen and morphine–nitrous oxide–oxygen anesthesia in 19 patients undergoing open-heart or major vascular operations.

METHODS

Informed written consent was obtained at the time of the pre-anesthetic visit. Operations included mitral- or aortic-valve replacement, coronary artery–vein bypass, or abdominal aortic replacement. No patient was receiving beta-adrenergic receptor-blocking drugs, but five were taking digitalis preparations. Premedication consisted of morphine (5–10 mg), pentobarbital (50–100 mg), and atropine (0.3–0.6 mg), intramuscularly, 90 minutes before the scheduled time of operation. Intravenous infusion was started and catheters were placed into the right atrium and aorta percutaneously. Computerized analysis of the central aortic pulse–pressure curve was used to calculate cardiac output, stroke volume, mean arterial blood pressure, and peripheral arterial resistance.[2]

Patients breathed 100 per cent oxygen or 50 per cent nitrous oxide in oxygen while morphine was administered intravenously at 5–10 mg/min until they became unresponsive. When the patient became unresponsive, pancuronium bromide, 0.5 mg/kg, was administered intravenously and the trachea intubated. Controlled ventilation was maintained with a volume-limited ventilator and Pa_{CO_2} kept between 30 and 35 torr. Additional increments of pancuronium bromide, 1–3 mg, were administered as needed. When additional anesthesia was needed, morphine was given intravenously in 10-mg increments. After each increment of morphine or pancuronium, a 30-minute period of equilibration elapsed before data were collected.

Data were obtained before the operation began after establishment of a steady state of anesthesia, and also during the operation. Periods chosen for data collection during the operation included those during which surgical stimulation was minimal. Recordings were made before and 5, 10,and 15 minutes after scopolamine, 0.5 mg, iv. Data were analyzed for significance using Student's t test for paired groupings.

Postoperatively, all patients were questioned with respect to awareness of the operative procedure.

RESULTS

Ten patients received an average of 0.7 mg/kg morphine plus 50 per cent nitrous oxide in oxygen; nine patients received 2.3 mg/kg morphine plus 100 per cent oxygen. The two groups had mean ages of 51 ± 7 and 53 ± 8 years, respectively. Changes in cardiovascular dynamics after scopolamine are given in tables 1 and 2. During morphine–nitrous oxide–oxygen anesthesia, scopolamine produced significant increases in heart rate, stroke volume, cardiac output, and mean arterial blood pressure, as well as reducing peripheral vascular resistance and central venous pressure. All changes were maximal 5 minutes after administration and somewhat less at 10 minutes. Cardiac output was still slightly elevated and peripheral vascular resistance decreased 15 minutes after scopolamine in these patients; however, all other variables had returned to normal.

Scopolamine produced transient (only at the 5-minute recording) increases in heart rate and decreases in stroke volume in patients anesthetized with morphine and oxygen, but did not significantly alter cardiac output, peripheral vascular resistance, or arterial or central venous blood pressure at any time.

No patient was aware of any aspect of the operation when questioned postoperatively.

DISCUSSION

In unanesthetized adult patients, scopolamine, 0.3–0.8 mg, iv, increases heart rate and cardiac output, increases or does not change stroke volume and arterial blood pressure, and decreases peripheral vascular resistance.[3–5]

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TABLE 1. Cardiovascular Effects of Scopolamine during Morphine–Nitrous Oxide–Oxygen Anesthesia (Mean ± SD)

	Control	Minutes after Scopolamine 5	10	15
Heart rate (beats/min)	78 ± 12	88† ± 13	86* ± 11	81 ± 13
Stroke volume (ml)	42 ± 13	50† ± 9	47* ± 10	43 ± 11
Cardiac output (l/min)	3.2 ± 1.6	4.4† ± 1.3	4.0* ± 1.2	3.5* ± 1.2
Peripheral vascular resistance (PRU)	272 ± 41	231† ± 29	243† ± 36	259* ± 24
Mean blood pressure (torr)	99 ± 11	107* ± 12	106* ± 11	103 ± 9
Central venous pressure (torr)	8 ± 2	6* ± 2	7* ± 1	7 ± 2

* $P < .05$, † $P < .025$, Student's t test for paired data, compared with control values.

TABLE 2. Cardiovascular Effects of Scopolamine during Morphine–Oxygen Anesthesia (Mean ± SD)

	Control	Minutes after Scopolamine 5	10	15
Heart rate (beats/min)	75 ± 13	84* ± 11	81 ± 13	77 ± 14
Stroke volume (ml)	48 ± 9	43* ± 8	44 ± 11	46 ± 11
Cardiac output (l/min)	3.6 ± 1.4	3.7 ± 1.6	3.7 ± 1.5	3.5 ± 1.6
Peripheral vascular resistance (PRU)	219 ± 39	214 ± 47	220 ± 49	226 ± 54
Mean blood pressure (torr)	99 ± 13	100 ± 12	99 ± 12	96 ± 14
Central venous (torr)	7 ± 2	6 ± 2	6 ± 2	7 ± 2

* $P < .05$, Student's t test for paired data, compared with control values.

In this study, scopolamine, 0.5 mg, iv, differed in the cardiovascular alterations it produced when employed during morphine–nitrous oxide–oxygen anesthesia and during morphine–oxygen anesthesia. During morphine–nitrous oxide anesthesia, scopolamine increased heart rate, stroke volume, cardiac output, and arterial blood pressure, and decreased central venous pressure and peripheral vascular resistance. During morphine–oxygen anesthesia a transient increase in heart rate and a transient decrease in stroke volume were the only changes produced by scopolamine.

The reason for these differences is not entirely clear, but they may be related to effects of scopolamine and morphine on arterial resistance, venous capacitance, and central and peripheral venous blood volumes. Large doses of morphine produce arterial and venous dilation.[6–10] Venodilation after morphine appears to be dose-related and can result in significant venous pooling and decreases in venous return, central (cardio-pulmonary) blood volume, and cardiac output in man.[8–10] Scopolamine may increase cardiac output in morphine–nitrous oxide–oxygen-anesthetized patients and not in those receiving morphine–oxygen, in spite of similar changes in heart rate, because venous pooling is greater in the latter group and thus there is no increase in venous return and cardiac output when heart rate is elevated. A significant decrease in stroke volume after scopolamine in patients anesthetized with morphine–oxygen but not in patients anesthetized with morphine–nitrous oxide–oxygen supports this possibility. However, the inotropic responses to scopolamine may differ in patients anesthetized with morphine–nitrous oxide–oxygen and in those given morphine–oxygen.

Morphine–oxygen anesthesia is frequently used in critically ill patients because it has little effect on cardiovascular dynamics.[7] This investigation demonstrates that scopolamine does not dramatically alter hemodynamics after large doses of morphine. Since even low concentrations (10–30 per cent) of nitrous oxide produce marked reductions in stroke volume, cardiac output, and arterial blood pressure when added to the inspired mixtures of patients anesthetized with 2 mg/kg or more of morphine plus oxygen,[11] our findings suggest that scopolamine may be a better supplement than nitrous oxide during high-dose morphine anesthesia.

In conclusion, our data demonstrate that scopolamine results in different cardiovascular alterations when employed during morphine–nitrous oxide–oxygen anesthesia and during morphine–oxygen anesthesia. The findings also indicate that the drug has only minimal and transient effects on the cardiovascular system during anesthesia with either technique and, therefore, may have a place as an amnesic supplement in management of patients anesthetized with these agents.

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Cardiovascular Responses to Nitrous Oxide during Enflurane and Oxygen Anesthesia

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For many years nitrous oxide was thought to have little influence on cardiovascular dynamics.[1,2] A number of recent reports[3–10] have demonstrated that, contrary to previous belief, nitrous oxide has significant cardiovascular effects, which may be depressant or stimulatory depending on the agent and concentration with which the gas is mixed, and possibly also a host of other factors. The influence of nitrous oxide on cardiovascular dynamics during enflurane and oxygen anesthesia and operation has not been determined. In this study we investigated the dose–response effects of nitrous oxide on cardiovascular dynamics during anesthesia and operation with constant 2–3 per cent inflow concentrations of enflurane in oxygen.

METHODS

Twenty patients (12 male and 8 female) with an average age of 50 ± 8 years (range 23 to 57 years) and mean weight of 169 ± 17 pounds, scheduled to undergo elective lower-extremity orthopedic or abdominal surgical operations, served as the experimental subjects. The study was approved by the Medical Center Human Study Committee. Informed, written consent was obtained from every patient at the preoperative visit.

No patient was receiving alpha- or beta-adrenergic receptor blockers or stimulators or diuretic medications preoperatively. Premedications included meperidine (50–75 mg), diazepam (5–10 mg) and atropine (0.4–0.5 mg) intramuscularly 90 minutes before the scheduled operation. Prior to anesthesia an intravenous infusion was started in an upper extremity, a central venous pressure catheter was placed percutaneously into the superior vena cava or right atrium from the cephalic vein in the antecubital fossa or internal jugular vein in the neck, and a radial or brachial artery catheter was inserted percutaneously and threaded 30–72 cm into the central aorta. The aortic pressure catheter was attached via an arterial pressure transducer to a computer module terminal in the operating room. Warner's method[11] of analyzing the central aortic pulse-pressure curve was used to determine cardiac output, stroke volume, arterial blood pressure, and peripheral arterial resistance.

All patients were allowed to breathe 100 per cent oxygen for 5 minutes. Anesthesia was then induced with thiopental, 4 mg/kg, and the patient was paralyzed with pancuronium bromide, 0.1 mg/kg. Tracheal intubation was performed with a disposable endotracheal tube. Respiration was controlled with a volume-limited respirator at volumes of 10–15 ml/kg and rates of 8–12/min in order to maintain Pa_{CO_2} measured in aortic blood every 15–30 minutes between 30 and 35 torr. Anesthesia was maintained with an inflow concentration of 2–3 per cent enflurane in oxygen issuing from a calibrated Ohio enflurane vaporizer so that systolic arterial blood pressure was kept between 110 and 140 torr. A semiclosed circle system provided CO_2 absorption and a total fresh gas inflow of 5–6 l/min. Continuous monitoring of the electrocardiogram and recording of arterial and central venous pressures were performed.

Data were obtained after a minimum equilibration period of 45 minutes following each change in enflurane concentration. Periods chosen for data collection included those during which there was minimal and consistent surgical stimulation. Recordings were made during ventilation with 97–98 per cent oxygen and after nitrous oxide (10, 20, 30, 40, 50 and then 60 per cent) had been progressively added to the inspired mixture. Enflurane inflow concentration was maintained constant during changes in nitrous oxide. After each change

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