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The Cardiovascular Effects of Low Concentrations of Nitrous Oxide during Morphine Anesthesia

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Intravenous administration of morphine (0.5–3.0 mg/kg) plus oxygen has been shown to be a safe method of anesthetizing critically ill patients for open-heart operations. While producing analgesia and amnesia, morphine has minimal effects on cardiac output. When morphine has been used in healthier patients who may not have fixed, low cardiac outputs, analgesia has been excellent, but amnesia has not always been complete.1 To insure amnesia, nitrous oxide in high concentrations (60–70 per cent) has been added. This provides amnesia; however, cardiac outputs and mean arterial pressures are significantly decreased.2 This study was undertaken to determine the hemodynamic effects of low concentrations (10–50 per cent) of nitrous oxide in patients receiving 0.5–3.0 mg/kg morphine for open-heart operations.

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Received from the Division of Anesthesiology, University of Utah Medical Center, 50 North Medical Drive, Salt Lake City, Utah 84112. Accepted for publication March 4, 1974. Presented at the annual meeting of the American Society of Anesthesiologists, San Francisco, October 1973.


METHODS

Sixteen patients, average age 48 ± 7 years, about to undergo mitral or aortic valve replacement or coronary artery—vein bypass procedures were studied. None was receiving beta-blocking drugs, but all were taking digitalis preparations. Premedication included morphine (5–15 mg) and scopolamine (0.2–0.5 mg) 90 minutes before the scheduled operation. Prior to anesthesia an intravenous line was started in an upper extremity; a central venous pressure catheter was placed percutaneously into the right atrium from the antecubital fossa or 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 central digital computer substation in the operating room. Warner's method of analyzing the central aortic pulse-pressure curve was used to determine cardiac output, stroke volume, arterial blood pressure, and peripheral vascular resistance.3

With the patient breathing pure oxygen, morphine sulfate was administered intravenously at a rate of 5–15 mg/min. Respirations were first assisted and later controlled to maintain P_{a_CO₂} as, measured in arterial blood every 15 minutes, between 30 and 35 torr. A semiclosed circle system provided CO₂ absorption and a total fresh gas inflow of 7–8 l/min. When patients became un-
responsive, pancuronium bromide, 0.1 mg/kg, was administered intravenously and the trachea was intubated. Controlled ventilation was initiated using a volume-limited ventilator. Additional pancuronium bromide, 0.05 mg/kg, was administered as necessary. If additional anesthesia was needed, as determined by movement of the patient or increases of blood pressure and pulse rate of 15 per cent or more, additional morphine was given intravenously in 10-mg increments. After each increment of morphine, a 30-minute period of equilibration elapsed before data were collected. Continuous monitoring of the electrocardiogram and recording of the arterial and central venous pressures were performed.

Data were obtained before the operation began, as well as before and after cardiopulmonary bypass. Periods chosen for data collection included those during which there was minimal and consistent surgical stimulation. Recordings were made during ventilation with pure oxygen and after nitrous oxide (in 10–50 per cent concentration increments) had been progressively added. After each change in nitrous oxide concentration, a 10-minute period of equilibration was allowed before initiating measurements of heart rate; stroke volume; cardiac output; systemic vascular resistance; systolic, diastolic, and mean arterial pressures; and central venous pressure. No other supplemental anesthetic drug was used prior to or during periods of data collection.

**RESULTS**

The 16 patients received an average of 1.7 mg/kg morphine (range 0.6–2.8 mg/kg). Nitrous oxide caused significant concentration-related decreases in cardiac output, stroke volume, and systolic, diastolic, and mean arterial blood pressures and an increase in systemic vascular resistance (table 1). These changes were significant \((P < 0.05)\) at all concentrations of nitrous oxide studied. Heart rate and central venous pressure were not significantly changed at any concentration of nitrous oxide.

**DISCUSSION**

During halothane anesthesia, addition of nitrous oxide, 70 per cent, causes peripheral vascular constriction and an increase or no change in cardiac output and stroke volume.\(^4\)

Addition of nitrous oxide, 70 per cent, to morphine–oxygen anesthesia decreases cardiac output and stroke volume, with an increase in total peripheral resistance.\(^1\) Stoelting and Gibbs concluded that in patients undergoing open-heart surgery morphine anesthesia produced peripheral vasodilation and cardiovascular stimulation.\(^2\) Adding nitrous oxide, 60 per cent, caused mean arterial pressure and cardiac index to decrease approximately 17 and 30 per cent, respectively, and systemic vascular resistance to increase by an average of 22 per cent. Eisele and Lappas both found that 40–50 per cent nitrous oxide produced no change or an increase in left ventricular end-diastolic pressures and a decrease in the rate of increase of left ventricular pressure (unpublished observations).

In our study we found depressions of cardiac output, stroke volume, and mean arterial pressure when 50 per cent nitrous oxide was added.
oxide was added to morphine-oxygen anesthesia. Cardiac output decreased 44 per cent, stroke volume 36 per cent, mean arterial pressure 22 per cent, and systemic vascular resistance increased 96 per cent with 50 per cent nitrous oxide. However, we observed changes at 10, 20, 30 and 40 per cent concentrations as well. Systemic vascular resistance increased 11 per cent at 10 per cent nitrous oxide, cardiac output decreased 10 per cent, mean arterial pressure decreased 4 per cent, and stroke volume declined 11 per cent. Each incremental change in nitrous oxide concentration led to further increments of change in the variables such that the extent of cardiovascular response became directly related to the nitrous oxide concentration. Since heart rate did not significantly change in our study, it appears that depression of cardiac output resulted from a decrease in stroke volume. Decreases in cardiac output and stroke volume at a given nitrous oxide concentration were two to three times the amounts of the observed decrease in arterial blood pressure.

These findings demonstrate that nitrous oxide can significantly reduce cardiac output during morphine anesthesia. This occurs even at low concentrations. While measurement of arterial blood pressures is routine during anesthesia, the magnitude of blood pressure changes caused by nitrous oxide is not necessarily as great as the change in cardiac output. This dissociation is not apparent, however, unless cardiac output and stroke volume are being measured. This suggests that when nitrous oxide is to be used in patients with minimal cardiac reserve, cardiac output or some other measure of cardiac function should be followed as a better index of the overall cardiovascular effects of the agent during morphine anesthesia. The advantage of using morphine should then be balanced against the positive contributions nitrous oxide is making to the maintenance of anesthesia.

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Spinal Hypalgnesia and Analgesia by Low-frequency Electrical Stimulation in the Epidural Space

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Electrical stimulation of the brain by electrodes placed over the scalp can produce

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sufficient unresponsiveness to painful stimuli to permit surgical manipulations, and has been used with success in both animals and man. Electrical stimulation of the spinal cord also causes inhibition of cord function and has been employed in management of pain. Various types of current have been used for electrococcision: 100—300-Hz rectangular pulses, direct current, and combinations of these. However, when applied to the spinal cord, these currents often evoke muscular spasm and unpleasant sensations, which have prevented wide clinical use of the technique in management of pain.