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Cardiovascular Effects of Metocurine in Patients with Aortic Stenosis

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Muscle relaxants are an integral part of the anesthetic management of patients undergoing corrective surgery for aortic stenosis. Because of the pathophysiology of aortic stenosis, use of a muscle relaxant with minimal cardiovascular effects is desirable. Metocurine has been shown to cause minimal hemodynamic changes in ASA class I patients,¹⁻⁴ and in patients with coronary artery disease.⁵ Patients with aortic stenosis, however, have not been studied. The purpose of this study was to determine if the minimal cardiovascular effects of metocurine found in other types of patients would preclude its use in patients with critical aortic stenosis.

MATERIALS AND METHODS

This study was approved by the Emory University Human Investigations Committee. Thirteen patients

gave written informed consent. Seven of these patients were included in the metocurine group and had a mean aortic valve gradient of 91 ± 27 mmHg. The remaining six patients were used as controls and had a mean gradient of 103 ± 13 mmHg. The ages ranged from 46 to 74 years, with a mean of 60 years in the study group and 63 years in the control group. Digoxin was being taken by all but one patient in each group up to the day before surgery. None of the patients were taking beta-adrenergic blocking drugs. Preoperatively, all patients had normal serum electrolyte concentrations and normal arterial blood gases.

Radial artery and pulmonary artery catheters were inserted one hour after the patients had been premedicated with 0.1 mg/kg morphine, im, and 0.3-0.4 mg scopolamine, im. The electrocardiogram was monitored using leads II and V₅. Neuromuscular blockade was evaluated by using a train-of-four nerve stimulator with the skin surface electrodes positioned over the ulnar nerve.

The patients received 100 per cent oxygen via face mask starting five minutes before the preinduction measurement and continuing throughout the study. Ventilation was initially spontaneous and then controlled as necessary to maintain a normal PaCO₂. After the preinduction measurement was performed, anesthesia was induced with a combination of morphine and diazepam at a rate of 5 mg/min. Measurements were performed again ten minutes after the patients lost their lid reflex and no longer responded to verbal stimuli. Then, in the study

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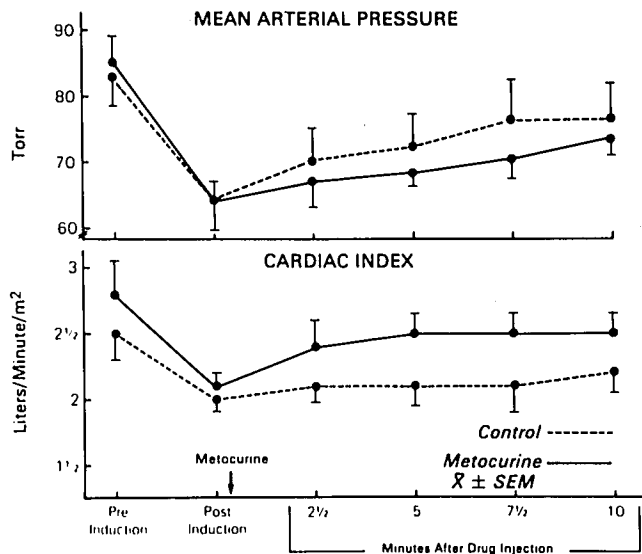


FIG. 1. Effects of induction and addition of metocurine on mean arterial pressure and cardiac index.

group, 0.4 mg/kg metocurine was infused over 2 minutes and measurements were made at 2.5, 5, 7.5, and 10 minutes after the relaxant had been administered. The control group had measurements performed at exactly the same times, but did not receive metocurine. Analyses of arterial blood gases were performed preinduction, postinduction, and 5 and 10 minutes after metocurine. Each set of measurements included: mean arterial blood pressure, mean pulmonary artery pressure, mean pulmonary capillary wedge pressure, mean central venous pressure, heart rate, and cardiac output. Cardiac index,

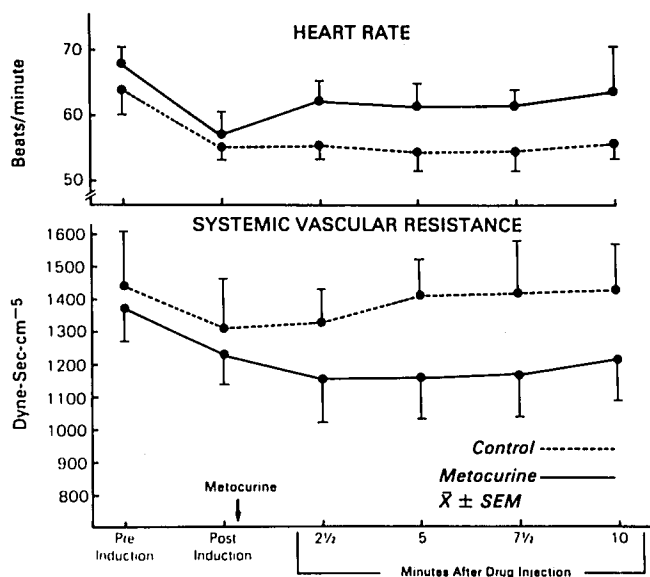


FIG. 2. Effects of induction and addition of metocurine on heart rate and systemic vascular resistance.

stroke index, and systemic vascular resistance were calculated by the standard formulae.

T tests for paired data were used to compare preinduction and postinduction measurements within the groups, and *t* tests for unpaired data to compare preinduction and postinduction measurements between the two groups. The metocurine and control groups also were compared with a two-way analysis of variance (AOV).

RESULTS

The two groups were similar ($P > 0.05$) with respect to patient characteristics, preinduction hemodynamic measurements, and doses of morphine and diazepam. *T* tests for unpaired data revealed no differences between the two groups for the preinduction ($P > 0.05$) and the postinduction measurements ($P > 0.05$) indicating that the two groups had similar hemodynamic responses to the induction of anesthesia.

In each group, morphine and diazepam administration was associated with decreases in mean arterial blood pressure, cardiac index (fig. 1), systemic vascular resistance, and heart rate (fig. 2) ($P < 0.05$ paired data). Filling pressures, stroke index, and pulmonary vascular resistance did not change.

The dose of metocurine was 26 ± 2.6 mg in the study group. Both the study and the control groups had gradual and statistically similar ($P > 0.05$) increases in mean arterial pressure and cardiac index throughout the remainder of the study. Mean heart rate increased within 2.5 minutes after metocurine, but was stable thereafter. The heart rates in the two groups were different ($P < 0.05$), although the absolute difference was small. Systemic vascular resistance returned to the preinduction level in the control group. The systemic vascular resistance in the study group, however, remained lower and was different from the controls ($P < 0.05$). As during induction of anesthesia, filling pressures and stroke index did not change significantly. $PaCO_2$ was stable throughout the study in both groups.

The train-of-four indicated an 80 per cent neuromuscular blockade measured 10 minutes after the administration of metocurine.⁶

DISCUSSION

The morphine/diazepam induction of anesthesia in patients with aortic stenosis caused a bradycardia and a mild vasodilation with secondary decreases in cardiac index and arterial pressure.

Increased intraventricular pressure associated with aortic stenosis reduces subendocardial blood flow.⁸ Tachycardia compromises coronary artery flow by decreasing diastolic perfusion time. Hypotension further reduces coronary artery blood flow. The overall result

of tachycardia and hypotension is a reduced myocardial oxygen supply and, if the oxygen supply cannot balance the oxygen demand, myocardial ischemia, especially in the presence of increased intraventricular pressure. For these reasons, tachycardia and hypotension probably should be avoided in patients with aortic stenosis.

Studies with metocurine combined with enflurane,¹ halothane,² and narcotic^{3,4} techniques have demonstrated only slight cardiovascular changes in ASA class I and II patients. Also, metocurine has been shown to be associated with mild vasodilation and increased cardiac index in patients with coronary artery disease taking propranolol.⁵

We found that the administration of metocurine maintained the vasodilation caused by the morphine and diazepam induction of anesthesia. This vasodilation was associated with a return of the heart rate toward the preinduction measurement, but it did not result in a tachycardia.

Metocurine, therefore, appears to offer an advantage over muscle relaxants that have vagolytic actions, such as gallamine and pancuronium,⁹ which could cause the heart rate to increase above the preoperative levels. *d*-Tubocurarine is known to cause not only vasodilation, and therefore hypotension, secondary to histamine release and ganglionic blockade, but also a reflex tachycardia.¹⁰ Metocurine causes less histamine release and ganglionic blockade,¹¹ and therefore would have an advantage over *d*-tubocurarine as well.

Metocurine was infused over two minutes. While histamine release was not clinically evident, we cannot rule out the possibility that 0.4 mg/kg metocurine given very rapidly could cause a significant release of histamine with secondary hypotension.

One disadvantage of metocurine concerns its route of elimination.¹² Unlike pancuronium and *d*-tubocurarine, only approximately 2 per cent of the administered dose of metocurine is excreted by the liver. Although from a theoretical viewpoint, metocurine should not be used in patients with renal failure, it was recently evaluated in anephric patients undergoing renal transplant.¹³ In these patients the neuromuscular blockades were reversed without apparent complication at the end of the proce-

dures, so that metocurine appears reasonable as a neuromuscular blocking drug in the presence of decreased renal function.

In summary, the administration of metocurine to patients with aortic stenosis after a morphine-diazepam anesthetic induction is associated with very slight vasodilation and minimal increases in heart rate. These effects are different from the hemodynamic changes caused by the other nondepolarizing relaxants. For this reason, metocurine is a better choice than gallamine and *d*-tubocurarine and a reasonable alternative to pancuronium in patients with aortic stenosis after the induction of anesthesia with morphine and diazepam.

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