Fig. 2. Resolution of atrioventricular block during second operative procedure.

ejection murmur, thought to be a flow murmur related to mild anemia with a hemoglobin of 8.9 g/dl. Holter monitoring revealed no abnormalities over a 24-hour period, and His-bundle electrocardiography was without abnormality. Postoperatively, the patient had an uncomplicated course and was discharged from the hospital on the 15th postoperative day with a good surgical result.

DISCUSSION

Application of MMA has been associated with decreases in blood pressure probably due to absorption of free MMA monomer into the systemic circulation. Some investigators have found little hemodynamic changes when monitoring with arterial and pulmonary artery catheters during MMA use. Wong et al. studied MMA administered to isolated perfused rabbit hearts and found a dose-dependent depression of dp/dT which correlated with a depression of the spontaneous heart rate. However, no cardiac conduction defects have been related to MMA with premature ventricular contractions during profound cardiovascular collapse being the only reported dysrhythmia. The appearance of second-degree atrioventricular block in our patient was temporally related to placement of the acetaldehyde portion of the joint prosthesis during periods of stable hemodynamics on two separate occasions. The occurrence of atrioventricular block only with acetaldehyde prosthesis placement may be related to the greater vascularity of the acetaldehyde site as compared to the femoral head, thus allowing greater access of free monomer to the systemic circulation.

This case documents the temporal association of the appearance of second-degree atrioventricular block with the placement of MMA in the highly vascular acetalbum during hip replacement procedures. This association occurred on two separate occasions in a patient free from cardiac disease. While the dysrhythmia we observed was transient and self-limited in our patient, a similar occurrence in a patient with significant cardiac disease might be of more clinical significance.

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Anesthesiology
56:392–395, 1982

Heart Rate and Blood Pressure Changes after ORG NC45 (Vecuronium) and Pancuronium during Halothane and Enflurane Anesthesia

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The new muscle relaxant Org NC45 is a monooquaternary homologue of pancuronium. It has a shorter duration of action and less cumulative and cardiovascular effects as compared to pancuronium and other currently used competitive neuromuscular blocking agents. To better confirm the cardiovascular effects of Org NC45, we monitored heart rate and arterial blood pressure after administration of an intubating dose of Org NC45 and pancuronium in patients anesthetized with either halothane or enflurane while surgical stimulation was absent.

MATERIALS AND METHODS

Thirty-five patients (20 men and 15 women), 16 to 57 years old, in ASA class I, scheduled for elective ENT procedures, were studied. The mean age was 30.5 (±12.2

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SD) years; the mean body weight was 67.7 (±9.3 SD) kg. All the patients were given 10 mg diazepam, po, one hour before anesthesia. Thiopental, 4-5 mg/kg, was given iv and orotracheal intubation was accomplished after administration of 1 mg/kg succinylcholine, iv. In the first group of 14 patients, halothane with 66 per cent nitrous oxide was administered via a non-rebreathing system at an inhaled concentration of 2 per cent for 3 min, which was decreased stepwise to the maintenance concentration of 0.5 per cent in about 4 min. Ventilation was controlled to maintain normocarbia. ECG (lead II) was monitored continuously and heart rate and blood pressure were measured every minute with a DINAMAP. After approximately 15 min of halothane anesthesia, when heart rate and blood pressure were constant, 0.1 mg/kg of either Org NC45 or pancuronium was administered as a bolus over 10 s. Cardiovascular variables were measured for 10 min after the injection of the relaxant. Analysis of arterial blood gases were performed before relaxant administration and at the end of the study period. Surgery was then allowed to start. In the second group of 14 patients a similar study was performed using enflurane anesthesia. Enflurane was administered with 66 per cent nitrous oxide at an inhaled concentration of 3 per cent for 3 min, which was decreased stepwise to the maintenance concentration of 1 per cent in about 4 min. Another group of seven patients was anesthetized with enflurane in an identical manner as the second group and cardiovascular measurements were made in a similar time course without administration of any muscle relaxant. This observation was needed to assess the nature of the heart rate decrease seen after Org NC45 in the second group. In each group the heart rate and blood pressure after 15 min of anesthesia were used as controls for measurements during the subsequent 10 min, with or without relaxant administration.

The results were analyzed using Student’s t test for paired and unpaired data.

RESULTS

Administration of Org NC45 produced minimal changes in the heart rate and blood pressure during the subsequent 10 min in patients anesthetized with halothane or enflurane (figs. 1 and 2). On the other hand, pancuronium always increased the heart rate in both groups. Systolic and diastolic blood pressure increased

<table>
<thead>
<tr>
<th>Anesthetic</th>
<th>Number of Patients</th>
<th>Pre-Induction</th>
<th>After 15 min of Anesthesia (Control Values)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Blood Pressure</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Heart Rate</td>
<td>Heart Rate</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Systolic</td>
<td>Diastolic</td>
</tr>
<tr>
<td>Halothane</td>
<td>14</td>
<td>76 ± 14.1</td>
<td>126 ± 11.8</td>
</tr>
<tr>
<td>Enflurane</td>
<td>21</td>
<td>80 ± 11.9</td>
<td>129 ± 10.2</td>
</tr>
</tbody>
</table>

Values are means ±SD. * Significantly different (P < 0.01) from pre-induction values.
TABLE 2. Time Course of Changes in Heart Rate (beats/min) and Blood Pressure (mmHg) Under Enflurane Anesthesia without Org NC45

<table>
<thead>
<tr>
<th></th>
<th>Control Values</th>
<th>2</th>
<th>4</th>
<th>6</th>
<th>8</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate</td>
<td></td>
<td>78 ± 9.3</td>
<td>75 ± 9.1*</td>
<td>73 ± 9.5*</td>
<td>72 ± 9.9*</td>
<td>71 ± 9.9*</td>
</tr>
<tr>
<td>Blood pressure</td>
<td></td>
<td>103 ± 7.3</td>
<td>103 ± 6.6</td>
<td>101 ± 6.8</td>
<td>98 ± 4.9</td>
<td>99 ± 5.7</td>
</tr>
<tr>
<td>Systolic</td>
<td></td>
<td>53 ± 7.7</td>
<td>52 ± 8.4</td>
<td>52 ± 8.4</td>
<td>54 ± 8.5</td>
<td>54 ± 8.2</td>
</tr>
<tr>
<td>Diastolic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Values are means ±SD; n = 7 patients.

* Significantly different (P < 0.01) from the control values.

constantly but minimally after pancuronium in patients anesthetized with halothane, whereas they did not change in patients anesthetized with enflurane.

The heart rate decreased with induction of anesthesia in patients anesthetized with halothane (P < 0.01), but did not change in those anesthetized with enflurane; blood pressure decreased as expected with both anesthetics (table 1). The groups did not differ significantly in age, sex, and body weight.

Under halothane anesthesia, after 0.1 mg/kg pancuronium the heart rate increased after the first minute by an average of 19 beats/min (33 per cent of control) (fig. 1). Systolic and diastolic blood pressure increased by 3–7 mmHg at different times (P < 0.05). After 0.1 mg/kg Org NC45, neither the heart rate nor blood pressure changed, remaining within ±5 per cent of control.

Under enflurane anesthesia, after pancuronium the heart rate increased by an average of 12 beats/min (16 per cent of control), but blood pressure did not change significantly (fig. 2). After Org NC45 blood pressure did not change, but the heart rate decreased slightly with time, the decrease being by 6 beats/min (8 per cent of control) during the last 3 min (P < 0.01). However, a similar decrease in the heart rate was observed in the time course of the study in the group who received no muscle relaxant (table 2).

No patient developed an arrhythmia after Org NC45. In one patient under halothane anesthesia occasional ventricular ectopic beats were present which did not change after Org NC45. Junctional rhythm was observed after pancuronium in two patients; in two additional patients a similar pre-existent arrhythmia was not modified by pancuronium. $P_{CO_2}$ before relaxation administration was 36 ± 3.7 mmHg, and at the end of the observation 34 ± 3.7 mmHg; in each individual the largest difference between the two values was ±3.7 mmHg.

**DISCUSSION**

We found that in patients without cardiovascular disease who were anesthetized with halothane or enflurane, pancuronium regularly produces tachycardia, whereas Org NC45 produces minimal changes of cardiovascular signs. Sinus tachycardia, A-V dissociation, and a variable rise in blood pressure following pancuronium have been cited in numerous reports. The A-V dissociation, usually of negligible hemodynamic consequence, may seriously decrease the cardiac output and blood pressure in patients with cardiac diseases and/or depressed cardiac contractility.

The cardiovascular effects of pancuronium have been explained to be due to its vagolytic and sympathomimetic properties. Org NC45, being devoid of autonomic neural activities, does not produce any cardiovascular effect and may be safer than pancuronium when an increase in heart rate is contraindicated or when liability to arrhythmia is considered. On the other hand when Org NC45, which has negligible vagolytic activity, is used, drug or reflex-induced bradycardia during anesthesia and surgery may appear more easily.

The authors thank the surgeons and the nurses of the ENT Department for their kind cooperation. The authors also acknowledge the advice of Dr. S. Agoston, Professor D. Langrehr (Department of Anesthesia), and Professor H. Weseloh (Department of Clinical Pharmacology).

**REFERENCES**

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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Received from the Emory University Hospital, Division of Cardiothoracic Anesthesia, Department of Anesthesiology, 1364 Clifton Road, Atlanta, Georgia 30322. Accepted for publication November 4, 1981. Supported by Lilly Research Laboratories grant number 82490. Presented at the annual meeting of the American Society of Anesthesiologists, San Francisco, October 1979.

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Key words: Neuromuscular relaxants: metocurine. Surgery: cardiac. Heart: aortic stenosis; vascular pressures; pulse rate.

0003-3022/82/0500/0395 $00.65 © The American Society of Anesthesiologists, Inc.