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Hemodynamic and Gas Exchange Effects of Pancuronium Bromide in Sedated Patients with Respiratory Failure

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Pancuronium bromide often is used in patients with acute respiratory failure to facilitate controlled ventilation.¹ Light *et al.*² concluded that because the heart rates and blood pressures decreased after pancuronium in six patients, their hypoxia probably had improved. However, they published neither analysis of arterial blood gases nor hemodynamic data.

Studies of patients with the infant respiratory distress syndrome have produced conflicting findings.³⁻⁶ Some authors note an improvement in arterial oxygenation,^{3,4} while others caution that worsening hypoxia may occur after pancuronium.^{5,6} However, because of the absence of pulmonary artery pressures or analysis of mixed venous blood for gas tensions, the actual physiologic changes that took place are difficult to ascertain.

This study was undertaken to determine whether pancuronium improves gas exchange in unanesthetized (but sedated) patients with respiratory failure.

METHODS

This study was approved by the Human Subjects Committee of the University of Washington. The decision to paralyze the patients studied was in all cases made by the primary staff physicians. The author examined the patient only after the decision to proceed with paralysis had been reached.

Patients' ages ranged from 17 to 75 years, with a mean age of 40 ± 6 years. Five patients had adult respiratory distress syndrome, three had bacterial pneumonias, and one had chest trauma with paradoxical inspiratory movement ("flail chest"). The FI_{O_2} ranged from 0.4 to 1.0 (mean 0.4 ± 0.1), resulting in a Pa_{O_2} ranging from 39-106 mmHg (mean, 72 ± 7 SEM).

Immediately prior to the administration of the pancuronium, motor activity was evaluated on a 1 to 4 scoring basis (table 1). Only one of the nine patients responded appropriately to command prior to paralysis. That patient received additional sedation prior to the initial measurements.

All patients had arterial lines and pulmonary arterial catheters in place prior to drug administration. Baseline arterial, pulmonary arterial (PAP), and pulmonary arterial wedge pressures (PAWP) were determined and arterial and mixed venous blood samples drawn. Triplicate determinations of cardiac output (\dot{Q}_t) were made using a thermodilution technique. Then pancuronium was given in a dose ranging from 0.07-0.1 mg/kg, as ordered by the patient's physician, and in all cases was sufficient to entirely abolish spontaneous motor activity. Patients who had been initiating breaths either in an intermittent mandatory ventilation mode or an assisted ventilation mode were returned to controlled ventilation. Ten minutes after the administration of the pancuronium, all measurements were repeated.

All blood-gas samples were placed in an ice bath and determinations performed within 15 min. Oxygen consumption (\dot{V}_{O_2}) was determined from the Fick equation, $\dot{V}_{O_2} = \dot{Q}_t \times (Ca_{O_2} - Cv_{O_2})$, where Ca_{O_2} and Cv_{O_2} are arterial and mixed venous oxygen contents, respectively. Oxygen contents were calculated from gas tensions, temperature, hemoglobin, and pH. Venous admixture (\dot{Q}_{VA}/\dot{Q}_t) was determined using the standard Berggren equation⁷ for the FI_{O_2} in use at the time of pancuronium administration. FI_{O_2} was not changed between the two sets of measurements. Values after pancuronium administration were compared with pre-drug values using Student's *t* test for paired data.

RESULTS

The hemodynamic changes after pancuronium are summarized in table 2. All patients had pre-existing tachycardias which accelerated in eight of the nine patients and remained unchanged in only one. Although cardiac output remained unchanged, arterial blood pressure tended to increase. Calculated systemic resistance rose 30%.

PAP, which, consistent with the respiratory failure present in these patients, was elevated significantly, in-

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TABLE 1. Motor Activity Score

Constant thrashing or seizing	1
Frequent but not continuous movement	2
Rare spontaneous movement other than ventilatory effort	3
Movement absent	4

creased still further after pancuronium administration. Since PAWP and \dot{Q}_t were unchanged, calculated pulmonary vascular resistance (PVR) increased 25%. Arterial oxygen tension and calculated venous admixture remained unchanged after paralysis (fig. 1).

\dot{V}_{O_2} decreased in eight of nine patients and remained unchanged in one patient, declining from 435 to 367 ml/min. When the change in oxygen consumption was examined on a case-by-case basis, the three most active patients (activity score 1 or 2) showed a mean decrease of 22%, whereas those in the less active groups showed a mean decrease of 15% in oxygen consumption ($P = 0.06$ for patients with scores of 1 and 2 vs. those with scores of 3 and 4).

DISCUSSION

Clinical wisdom that terminating "bucking" improves ventilation/perfusion (V_A/Q) mismatch, was not substantiated by this study. The lack of improvement may well represent a combination of several effects. While a decrease in bucking might better expand unventilated or poorly ventilated alveoli, paralysis of the diaphragm in the supine patient may worsen V_A/Q matching.⁸ This results from greater movement of the anterior portions of the relaxed diaphragm, whereas perfusion, as a result

TABLE 2. Hemodynamic Changes after Pancuronium

Control	Before Pancuronium	After Pancuronium	<i>p</i>
Heart rate (beats/m)	118 ± 5	132 ± 17	0.006
Cardiac output (l/m)	6.56 ± 0.67	6.60 ± 0.90	>0.1
Blood pressure (mmHg)	76 ± 8	90 ± 9	0.06
Pulmonary artery pressure (mmHg)	28 ± 4	31 ± 4	0.01
Pulmonary artery wedge pressure (mmHg)	16 ± 2	16 ± 2	>0.1
Stroke volume (ml/beat)	56 ± 6	50 ± 7	0.004
Systemic resistance (dyne · s · cm ⁻⁵)	987 ± 106	1221 ± 164	0.04
Pulmonary vascular resistance (dyne · s · cm ⁻⁵)	163 ± 33	205 ± 38	0.004

Values are means ± SEM.

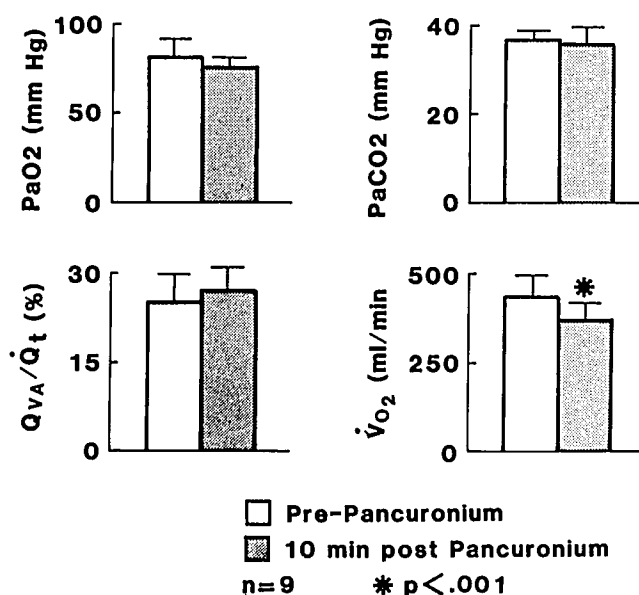


FIG. 1. Gas exchange before and 10 minutes after pancuronium as measured by PaO₂, PaCO₂, venous admixture (\dot{Q}_{VA}/\dot{Q}_t), and oxygen consumption (\dot{V}_{O_2}). All values are means ± SEM.

of gravity continues to be greatest posteriorly. The increase in PAP also may contribute to venous admixture, since high PAP has been shown to inhibit hypoxic pulmonary vasoconstriction,⁹ thus allowing increased perfusion of hypoxic areas of lung.

The consistent decrease in \dot{V}_{O_2} , even in relatively inactive patients, may be due to a combination of removal of existing muscle tone and the abolition of work of breathing in those patients whose ventilation was not controlled completely prior to paralysis. Although nondepolarizing muscle relaxants do not decrease \dot{V}_{O_2} in anesthetized animals,¹⁰ those animals are already in a basal state of activity, whereas our patients were not.

Work of breathing, consisting of only 1 to 2% of \dot{V}_{O_2} in normal patients, can rise to levels of 15–20% in the patient with abnormal lungs.^{11,12} Although all patients in this study were ventilated mechanically, five of nine were by intermittent mandatory ventilation, and the other four were by assisted ventilation with some ventilatory effort present in all but one case. However, no correlation could be made between apparent ventilatory effort and the decline in \dot{V}_{O_2} .

The hemodynamic effects of pancuronium in these patients differed in some respects from reported results in anesthetized patients.^{13–15} In anesthetized patients, heart rate, cardiac output, and blood pressure all increase in the absence of prior medications, while calculated systemic vascular resistance does not change. In the present study, the chronotropic effects of the drug were reconfirmed despite the fact that all the patients had pre-existing

tachycardias. However, cardiac output did not change, while systemic resistance rose substantially.

Several factors may contribute to the differences observed. First, many of these patients were severely ill and were receiving inotropic and vasopressor drugs; they may have been unable to further augment cardiac output. Second, most of them had developed high PAP over a relatively short period of time; the further increase in right heart afterload may have prevented the expected increase in \dot{Q}_t . Third, these patients may develop systemic vasoconstriction, whereas in anesthetized patients, the anesthetic agents may modify or prevent this response. Finally, although these patients generally were heavily sedated and unresponsive to command, there may have been a fright response to paralysis, so that the observed effects may not represent the pure pharmacologic effects of the drug.

The observed hemodynamic changes have several potentially harmful effects for these patients. The tachycardia results both in increased myocardial oxygen consumption as well as a decrease in the length of diastole with consequent decrease in the time of optimal myocardial perfusion. A second adverse consequence of pancuronium was the increase in PAP and PVR. High PAP and PVR have been correlated with a poorer prognosis in patients with respiratory failure and therapeutic intervention to lower these has been advocated.^{16,17}

A potential, long-term benefit of paralysis that cannot be assessed from this study is a decrease in barotrauma. In a mechanically ventilated patient who is not well-coordinated with the ventilator, transient alveolar overdistention might result. However, when this question was examined in infants with respiratory distress, there was no difference in the incidence of pneumothoraces between the paralyzed and unparalyzed patients.³

Measurements are made in our intensive care unit immediately prior to and 10 minutes after the administration of pancuronium. It is possible that the adverse hemodynamic effects may be relatively transient. Ten minutes was chosen as a time limit in order to allow respiratory gas equilibration in the lungs and because in the anesthetized patient, hemodynamic effects are relatively constant over that time period.¹⁴ Measurements including several points may be more useful in determining the benefits of paralysis for any given patient.

Based on our experience with these nine patients, pancuronium seemed most useful for lowering \dot{V}_{O_2} in the patient with a high degree of skeletal muscle activity.

This must be weighed against potentially adverse hemodynamic consequences.

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