

## Clinical Reports

BURNELL R. BROWN, JR., M.D., Ph.D., *Editor*

### Pancuronium-induced Tachycardia in Relation to Alveolar Halothane, Dose of Pancuronium, and Prior Atropine

RONALD D. MILLER, M.D.,\* EDMOND I. EGER, II, M.D.,† WENDELL C. STEVENS, M.D.,\*  
ROBERT GIBBONS, M.D.‡

Pancuronium produces tachycardia and slightly increases arterial blood pressure during halothane anesthesia.<sup>1,2</sup> Hypotension following *d*-tubocurarine administration depends on the dose of *d*-tubocurarine and on the concentration of halothane at the time of administration.<sup>3</sup> Although Foldes<sup>4</sup> has speculated that pancuronium-induced tachycardia is dependent on the dose of pancuronium, no specific evidence confirming this impression exists. Accordingly, we determined whether heart rate and blood pressure changes following pancuronium depend either on the alveolar concentration of halothane or on the dose of pancuronium. Our results indicate that no such correlation exists.

#### METHODS

Thirty-three unpremedicated adult surgical patients, ASA Classification I and II, were assigned to six groups of five patients each and studied intraoperatively (table 1). Following induction of anesthesia with

halothane and 60 per cent nitrous oxide, the trachea was intubated and ventilation controlled. No other drug was administered. A catheter was inserted into the radial artery for continuous recording of blood pressure and pulse rate. Lead II of the electrocardiogram was monitored continuously. End-tidal halothane, as determined by ultraviolet analysis, was maintained within 0.08 per cent of the desired concentration. Sixty per cent nitrous oxide was continued in all patients. At least 45 minutes after induction of anesthesia and after at least 20 minutes at the desired halothane concentration, pancuronium was administered as an intravenous bolus.

Groups I, II, and III were maintained at 0.30, 0.55 and 0.80 per cent halothane, respectively, and all received 2.4 mg/m<sup>2</sup> of pancuronium (table 1). Groups IV, V, and VI all were maintained at 0.55 per cent halothane and received 1.2, 4.8, and 2.4 mg/m<sup>2</sup> pancuronium, respectively. Thirty minutes prior to administration of pancuronium to Group VI, 0.33 mg/m<sup>2</sup> of atropine was given intravenously. Analysis of variance and the studentized range test were used for part of the statistical analyses. Linear regression, correlation coefficient analysis, and unpaired *t* test were carried out for the remaining results.<sup>5</sup>

#### RESULTS

Pancuronium administration increased heart rate by 20 to 50 per cent, but this increase was unrelated to the concentration

\* Associate Professor.

† Professor.

‡ Research Trainee.

Received from the Departments of Anesthesia and Pharmacology, University of California, San Francisco, California 94143. Accepted for publication September 3, 1974. Supported in part by USPHS Research Grant 5P01 GM15571-06, USPHS Research Training Grant 5T1 GM00063-16, and Organon, Inc. Presented in part at the Annual Meeting of the American Society of Anesthesiologists, Washington, D.C., October 14, 1974.

Address reprint requests to: Ronald D. Miller, M.D., Department of Anesthesia, 436S, University of California, San Francisco, California 94143.

FIG. 1. Relationship between percentage increase in heart rate, systolic blood pressure, and time after pancuronium, 2.4 mg/m<sup>2</sup>, administration during three alveolar concentrations of halothane and 60 per cent nitrous oxide. Each symbol represents the mean  $\pm$  1 SE for five patients.

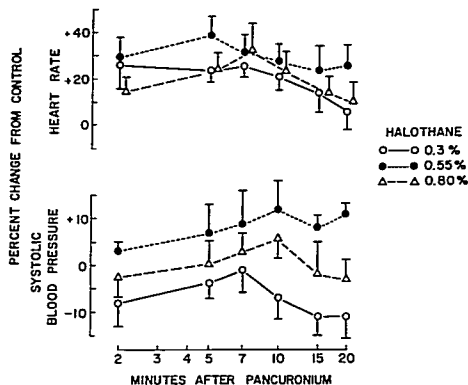


FIG. 2. Relationship between percentage increase in heart rate, systolic blood pressure, and time after pancuronium, 1.2, 2.4, or 4.8 mg/m<sup>2</sup>, administration. One group of patients received 0.33 mg/m<sup>2</sup> atropine prior to pancuronium administration. Each symbol represents the mean  $\pm$  1 SE for five patients.

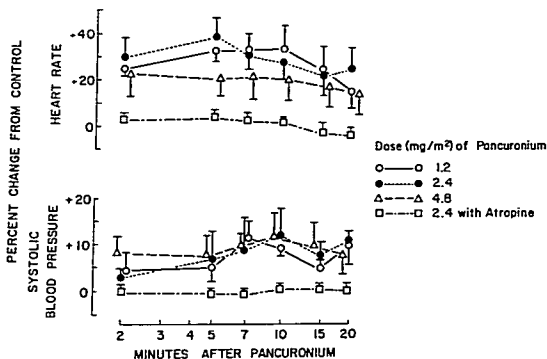


TABLE 1. Alveolar Concentration of Halothane, Dose of Pancuronium, and Atropine

	Number	Alveolar Concentration of Halothane (Per Cent)	Pancuronium (mg/m <sup>2</sup> )	P <sub>ACO<sub>2</sub></sub> (torr)	Atropine	Control Heart Rate (Beats/Min)
Group I	6	0.30	2.4	36 $\pm$ 3*	None	79 $\pm$ 8*
Group II	5	0.55	2.4	39 $\pm$ 1	None	76 $\pm$ 6
Group III	7	0.80	2.4	35 $\pm$ 2	None	94 $\pm$ 12
Group IV	5	0.55	1.2	36 $\pm$ 2	None	82 $\pm$ 5
Group V	5	0.55	4.8	35 $\pm$ 3	None	81 $\pm$ 7
Group VI	5	0.55	2.4	34 $\pm$ 2	0.33 mg/m <sup>2</sup> †	110 $\pm$ 4

\* Mean  $\pm$  1 SE.

† Atropine was given 30 minutes prior to pancuronium administration.

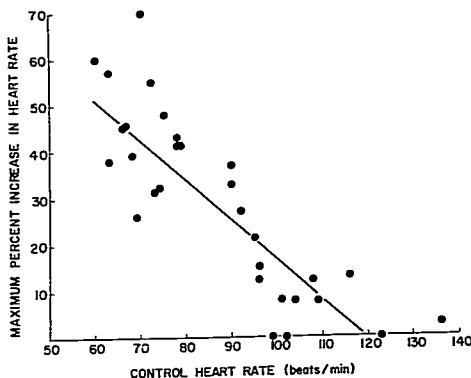


FIG. 3. Correlation of heart rate before pancuronium (control heart rate) with maximum percentage increase in heart rate following pancuronium. The line represents analysis of linear regression ( $r = 0.85$ ).

of halothane or the dose of pancuronium (figs. 1 and 2). No significant increase in pulse rate followed pancuronium in patients who first received atropine,  $0.33 \text{ mg/m}^2$  (fig. 2). For all the data, the maximum increase in heart rate was related inversely to the heart rate immediately before administration of pancuronium ( $r = 0.85$ ) (fig. 3).

Systolic blood pressures increased slightly but not significantly following pancuronium. These changes also were not related to the alveolar concentration of halothane or the dose of pancuronium (figs. 1 and 2).

In two patients anesthetized with 0.8 per cent halothane (Group III) heart rates increased by 70 and 82 beats/min and ventricular extrasystoles appeared. This occurred 5 minutes and ceased 15 minutes after pancuronium administration. The heart rate in one patient in Group I increased by 61 beats/min 5 minutes after pancuronium; this increase persisted for 4 minutes; A-V dissociation occurred intermittently during this time. These three patients were not included with the other data in all figures because their increases in heart rate were more than two standard deviations from the mean. Their arterial blood-gas values were not different from those of the remaining patients in their respective groups.

## DISCUSSION

In contrast to the cardiovascular effects of  $d\text{Tc}$ ,<sup>3</sup> those of pancuronium are not related to the alveolar concentration of halothane or the dose of pancuronium. Although pancuronium in certain doses smaller than  $1.2 \text{ mg/m}^2$  probably causes significantly less tachycardia than was observed in this study, such doses would be less than those usually given as an initial paralytic bolus. Thus, our data suggest that clinical use of pancuronium in the presence of halothane will produce tachycardia that will not be influenced by anesthetic or relaxant dose.

When patients received no prior belladonna medication, the mean increase in heart rate following pancuronium administration was consistent with the 25 per cent increase after pancuronium,  $0.07 \text{ mg/kg}$ , observed by Kelman and Kennedy.<sup>6</sup> Twenty and 16 per cent increases in heart rate after 6 and 5.2 mg pancuronium were observed by Gertel *et al.*<sup>1</sup> and Stoelting,<sup>2</sup> respectively, in patients premedicated with 0.4 mg atropine or scopolamine, intramuscularly. No increase in heart rate occurred following pancuronium when patients were given  $0.33 \text{ mg/m}^2$  atropine intravenously in this study or 1.2 mg atropine in the study of Coleman *et al.*<sup>7</sup>

These findings plus the inverse correlation between control heart rate and the increase in pulse rate suggest that pancuronium's cardiovascular actions may be vagolytic. In animals, pancuronium has been shown to suppress both the inhibitory effects of vagal stimulation and the negative inotropic and chronotropic effects of parasympathomimetic drugs.<sup>8</sup>

Three patients developed either ventricular extrasystoles or A-V dissociation. These arrhythmias disappeared spontaneously. In ten patients anesthetized with halothane, Stoelting<sup>2</sup> observed two instances of premature ventricular contractions following pancuronium. Why these patients developed arrhythmias and the remaining 30 did not remains unknown. They were taking no medication preoperatively, nor had they diseases such as pheochromocytoma that might predispose to arrhythmias. Their  $P_{aCO_2}$  values were not different from those in other patients.

If pancuronium affects the cardiovascular system as does atropine, then occasional ventricular extrasystoles from pancuronium should be expected during halothane anesthesia. In 12 patients anesthetized with halothane, Jones *et al.*<sup>9</sup> observed two cases of ventricular extrasystoles and three cases of A-V dissociation following intravenous administration of 0.4 mg atropine. No arrhythmias followed atropine in patients anesthetized with nitrous oxide and thiopental.

This suggests that ventricular arrhythmias from pancuronium are more likely during halothane than during nitrous oxide-thiopental anesthesia.

#### REFERENCES

1. Gertel M, Fox GS, Rabow FI, et al: The cardiovascular effects of pancuronium during halothane anaesthesia. *Can Anesth Soc J* 19:599-606, 1972
2. Stoelting RK: The hemodynamic effects of pancuronium and *d*-tubocurarine in anesthetized patients. *ANESTHESIOLOGY* 36: 612-615, 1972
3. Munger WL, Miller RD, Stevens WC: The dependence of *d*-tubocurarine-induced hypotension on alveolar concentration of halothane, dose of *d*-tubocurarine, and nitrous oxide. *ANESTHESIOLOGY* 40:442-448, 1974
4. Folds FF: Pancuronium bromide side effects. *JAMA* 225:418, 1973
5. Goldstein A: *Biostatistics*, New York, MacMillan, 1964, pp 70-72, 135-154
6. Kelman GR, Kennedy BR: Cardiovascular effects of pancuronium in man. *Br J Anaesth* 43:335-338, 1971
7. Coleman AJ, Downing JW, Leary WP, et al: The immediate cardiovascular effects of pancuronium, alcuronium and tubocurarine in man. *Anaesthesia* 27:415-422, 1972
8. Saxena PR, Bonta IL: Mechanism of selective cardiac vagolytic action of pancuronium bromide: Specific blockade of cardiac muscarinic receptors. *Eur J Pharmacol* 11:332-341, 1970
9. Jones RE, Deutsch S, Turndorf H: Effects of atropine on cardiac rhythm in conscious and anesthetized man. *ANESTHESIOLOGY* 22: 67-73, 1961