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Hemodynamic evaluation of pancuronium and vecuronium by transesophageal echocardiography

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Introduction

Several studies have demonstrated that pancuronium bromide (PB) usually produces an increase in heart rate (HR) and blood pressure, a response that has been explained in terms of vagolytic and sympathicomimetic effects [1–3]. Vecuronium bromide (VB) has become one of the most frequently used non-depolarizing muscle relaxants because it has a relatively short duration of action, minimal cardiovascular effects, and no histamine-releasing effect.

Transesophageal echocardiography (TEE) is a non-invasive tool to evaluate left ventricular function under clinical conditions. However, there have been no reports on TEE evaluation of the hemodynamic response to PB and VB in patients. We evaluated the effects of PB and VB on the left ventricular function of surgical patients using TEE under clinical conditions.

Patients and Methods

Twenty adult patients [American Society of Anesthesiologists (ASA) physical status I or II] undergoing low-risk surgical procedures were investigated. This study was approved by the Protection of Human Subjects Committee of Jikei University Hospital, and written informed consent was obtained from each patient prior to surgery. Patients with known disorders of the renal or hepatic system, neuromuscular disease, or cardiac disease were excluded. No patient received aminoglycoside antibiotics, antihistamines, or narcotics within a 48-h period preceding the study.

Atropine ($0.02\,mg \cdot kg^{-1}$ PO) and diazepam ($0.2\,mg \cdot kg^{-1}$ PO) were given orally as premedication 1.5 h before the induction of anesthesia. Patients were randomly assigned to two groups ($n = 10$ per group) to receive either PB ($0.1\,mg \cdot kg^{-1}$ IV) or VB ($0.08\,mg \cdot kg^{-1}$ IV) in equipotent doses [4].

The trachea was intubated with thiamylal ($4\,mg \cdot kg^{-1}$ IV), fentanyl ($4\,\mu g \cdot kg^{-1}$ IV), and succinylcholine ($1\,mg \cdot kg^{-1}$ IV); and anesthesia was maintained with isoflurane (0.4–0.8%), nitrous oxide, and 50% oxygen. Ventilation was controlled mechanically to maintain the end-tidal CO_2 in the range of 30–40 mmHg using capnography. Ringer's lactate was infused at $3–5\,ml \cdot kg^{-1} \cdot h^{-1}$. Rectal temperature was monitored and maintained within 1°C of the baseline value. The ulnar nerve was stimulated supramaximally with repetitive trains-of-four using surface electrodes by DigiStim III (P/N 100211, Neuro Technology, Houston, TX, USA).

After the induction of anesthesia, air was removed from the stomach with a nasogastric tube to prevent reverberation of ultrasound by air. The TEE probe was inserted orally, and a TEE view was obtained using an ultrasonograph (model SSA-260A; Toshiba, Tokyo, Japan) with a 5-MHz phased-array biplane two-dimensional TEE probe (PEF-507SB, Toshiba). All echocardiograms were stored on S-VHS videotapes.

Approximately 15 min after the hemodynamics returned to baseline values, we measured the end-diastolic and end-systolic diameters and calculated the stroke volume index (SVI), cardiac index (CI), left

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ventricular ejection fraction (LVEF), and left ventricular fractional shortening (LVFS) using the Teichholz method. Fractional area change (FAC) was calculated from the end-diastolic area (EDA) and end-systolic area (ESA) in the transgastric short-axis view at the midpapillary level, in accordance with the formula:

$$FAC(\%) = (EDA - ESA)/EDA \times 100$$

Heart rate (HR) and systolic (SAP), diastolic (DAP), and mean (MAP) arterial pressures were measured with an automated noninvasive measurement device (BP-203i, Nippon Colin, Tokyo, Japan). All data were obtained during stable anesthesia just before the administration of PB or VB (control) and 3, 5, and 10 min after the injection of PB or VB. Surgical incision was performed after obtaining all of the data.

The TEE data were analyzed by two independent observers to determine interobserver variability, which was expressed as a linear regression between the two observers ($r = 0.78–0.92$). Therefore measurements by the two observers were averaged to the final data. All data were expressed as the mean ± standard deviation (SD). The differences between the various measurement times within one group were analyzed by two-factor repeated-measures analysis of variance (ANOVA), followed by a Bonferroni t-test when the F-ratio resulted in a P value <0.05. Differences between the two groups with the same measurement time and physical characteristics were analyzed by unpaired Student's t-test. $P < 0.05$ was considered statistically significant.

Results

The physical characteristics show that there were no significant differences among the groups for age (PB 39.6 ± 12.6 years; VB 40.0 ± 9.2 years), body weight (PB 54.5 ± 5.9 kg; VB 51.3 ± 11.8 kg), and body surface area (PB 1.58 ± 0.12 m^2; VB 1.52 ± 0.18 m^2). The CI increased significantly after PB administration versus the control, but VB did not lead to any statistically significant change in CI versus the control. Comparison between the two groups revealed that the CI was higher with PB than with VB at 10 min after administration of the muscle relaxants.

There were no statistically significant changes in SVI, LVEF, LVFS, or FAC in the two groups (Table 1). PB caused significant increases in HR and MAP versus the control, but VB caused no significant changes. The comparison between the two groups revealed that HR and MAP were higher in the PB group than the VB group after administration. The muscle relaxant led to complete blockade in both groups 3, 5, and 10 min after administration.

Discussion

Pancuronium bromide caused a significant increase in CI, which was probably due to an enhanced HR, because there was no statistically significant increase in SVI. In contrast, VB did not cause any significant changes in hemodynamic performance. We confirmed that VB had hemodynamic stability.

Previous studies demonstrated that pancuronium increased the HR by two mechanisms: It released norepinephrine (NE) from the pre- and postganglion, and it inhibited NE reuptake [2,5]. The second mechanism was a vagolytic effect [6].

There were no statistically significant increases in LVEF, LVFS, or FAC in the PB group, suggesting that PB had no effect on left ventricular systolic function under clinical conditions. Iwatsuki et al. demonstrated that PB has a positive inotropic effect mediated by β-adrenergic stimulation in isolated canine heart muscle [7]. Our results were not consistent with that report. This discrepancy might have been because our study was an in vivo investigation, and inhalation anesthetics or fentanyl might have inhibited the β-adrenergic effect. Our study demonstrated that any β-adrenergic effect of PB is likely to be trivial

Table 1. Hemodynamic variables

	Control		3 min		5 min		10 min	
Variable	PB	VB	PB	VB	PB	VB	PB	VB
CI ($L \cdot min^{-1} \cdot m^{2-1}$)	1.92 ± 0.39	2.00 ± 0.34	2.27 ± 0.58#	1.98 ± 0.40	2.32 ± 0.47#	1.91 ± 0.47	2.46 ± 0.58#*	1.89 ± 0.47
SVI ($ml \cdot m^{2-1}$)	26.90 ± 3.36	31.30 ± 8.40	27.50 ± 6.01	31.90 ± 8.08	27.40 ± 3.67	31.00 ± 8.29	28.20 ± 5.53	30.80 ± 8.18
HR ($beats \cdot min^{-1}$)	71.30 ± 11.70	64.80 ± 12.90	82.60 ± 10.40#*	63.50 ± 11.80	84.00 ± 9.14#*	62.80 ± 12.20	84.40 ± 9.29#*	62.70 ± 13.00
MAP (mmHg)	66.70 ± 7.29	64.80 ± 8.16	77.30 ± 8.49#*	66.20 ± 10.10	77.90 ± 9.48#*	68.50 ± 6.75	77.40 ± 7.60#*	67.80 ± 8.64
LVEF (%)	56.10 ± 7.96	60.30 ± 7.95	56.60 ± 8.90	62.00 ± 8.19	56.80 ± 8.95	60.70 ± 8.73	56.70 ± 9.12	59.50 ± 7.75
LVFS (%)	29.00 ± 5.03	32.40 ± 6.35	30.20 ± 5.75	32.80 ± 7.24	29.80 ± 5.69	31.10 ± 6.52	29.60 ± 5.68	30.10 ± 5.97
FAC (%)	62.20 ± 11.10	68.20 ± 9.57	63.50 ± 12.40	67.30 ± 8.23	65.40 ± 12.10	68.00 ± 8.76	63.50 ± 11.00	67.10 ± 8.43

PB, pancuronium bromide; VB, vecuronium bromide; CI, cardiac index; SVI, stroke volume index; HR, heart rate; MAP, mean arterial pressure; LVEF, left ventricular ejection fraction; LVFS, left ventricular fractional shortening; FAC, fractional area change.
Results are means ± SD.
# $P < 0.05$ *vs* control; * = $P < 0.05$ between groups.

following administration of the usual dose of PB; the vagolytic effect of PB was emphasized under clinical conditions.

We did not measure central venous pressure because the patients underwent only low-risk surgical procedures. Therefore we did not measure the systemic vascular resistance. We did not compare the CI obtained by TEE with that seen by the thermodilution method using a pulmonary artery catheter because a close correlation between echocardiographic and angiographic volumes has been reported, and several methods for deriving ventricular volumes from single M-mode dimensions have been developed [8]. We measured stroke volume noninvasively using the Teichholz formula.

In conclusion, the study showed that PB caused significant increases in HR, MAP, and CI. The enhanced HR probably caused the increase in CI, because there was no statistically significant increase in SVI. PB had no effect on left ventricular contractility under clinical conditions. In contrast, VB did not cause significant changes in hemodynamic performance.

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