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The Cardiovascular Effects of Vecuronium (ORG NC45) and Pancuronium in Patients Undergoing Coronary Artery Bypass Grafting

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Vecuronium is a new nondepolarizing muscle relaxant which has been shown to cause no significant cardiovascular effects. Utilizing invasive monitoring in patients undergoing coronary artery bypass grafting, the authors compared the cardiovascular effects of vecuronium (0.28 mg/kg) in seven anesthetized patients with those of pancuronium (0.1 mg/kg) in five anesthetized patients. This dose of pancuronium represents three times its ED_{90} (dose producing a 90% depression of evoked twitch tension), while the vecuronium dose represents twelve times its ED_{90}. This relatively large dose of vecuronium was chosen deliberately in an attempt to manifest any possible cardiovascular effects. Following administration of vecuronium, cardiac output increased 9% and systemic vascular resistance decreased 12%, while pancuronium produced a significantly greater 17% increase in cardiac output without change in systemic vascular resistance. Heart rate and systemic mean arterial pressure did not change following vecuronium, while increasing 22% and 24%, respectively, following pancuronium. The authors conclude that large doses of vecuronium have minimal cardiovascular effects and thus offer an advantage over pancuronium in patients anesthetized for coronary artery surgery. (Key words: Blood pressure: drug effects. Heart: vascular pressures; cardiac output; rate. Neuromuscular relaxants: pancuronium; vecuronium. Surgery: cardiac.)

VECURONIUM (ORG NC45) is a new muscle relaxant and a monoquaternary analogue of pancuronium. In studies in animals and preliminary studies in humans, no significant changes in heart rate or blood pressure were observed.[1–4] These findings were confirmed recently in patients who received vecuronium while anesthetized with thiopental/nitrous oxide,[5] halothane, or enflurane.[6] Furthermore, vecuronium produced no cardiovascular changes in patients undergoing removal of a pheochromocytoma.[7] In contrast, all the currently available nondepolarizing neuromuscular-blocking agents have significant cardiovascular effects.[8–10] Perhaps the most commonly used of these drugs is pancuronium, which increases heart rate, cardiac output, and systemic arterial blood pressure.[11] We designed this study to compare the cardiovascular effects of vecuronium with those of pancuronium in patients with ischemic heart disease undergoing coronary artery bypass grafting, a group of patients in whom cardiovascular changes may be especially hazardous.

Methods

After obtaining their informed consent, we studied 12 adult patients scheduled for coronary artery bypass grafting. Approval by our Committee on Human Research was granted for this study. At cardiac catheterization, all patients demonstrated multi-vessel disease and ejection fractions greater than 50%. Eight of these patients were receiving beta-adrenergic blocking drugs in doses ranging from the equivalent of 10 to 120 mg q 6 h of propranolol. All patients who received beta blockade therapy were given their last dose within three hours of operation. Of those patients not receiving beta blockade therapy, two subsequently received vecuronium and two received pancuronium. One hour following premedication with 10 to 15 mg morphine, im, and 10 to 15 mg, diazepam po, a catheter was inserted into a radial artery and anesthesia was induced with 1.5 mg/kg thiopental, iv, 60% nitrous oxide, and halothane. Intubation of the trachea was facilitated by 100 mg succinylcholine, iv, after which a pulmonary artery catheter was inserted. During insertion of this catheter, stable end-tidal concentrations of halothane (0.2 to 0.35%) and 60% nitrous oxide were established as measured by mass spectrometry. Control values for heart rate (HR), rhythm, systemic blood pressure, pulmonary artery pressure, central venous pressure (CVP), pulmonary capillary wedge pressure (PCWP), and cardiac output (CO) were obtained. The electrocardiogram was constantly displayed (MCL5) during the study and monitored for ST segment and T wave changes by a cardiac anesthetist. Cardiac output was estimated as the mean of multiple thermodilution determinations utilizing iced saline and the Edward's model 9520A computer. If the second determination differed by more than 10% from the first, a third value was obtained (in five of 36 mea-

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TABLE 1. Cardiovascular Response to Vecuronium

	Control	2 Min	5 Min	10 Min
HR (beats/min)	46* ± 7.0	46 ± 5.8	47 ± 5.0	47 ± 5.7
SMAP (mmHg)	72 ± 6.4	71 ± 6.7	70 ± 8.6	72 ± 10.0
SVR (dyn·s·cm^{-5})	1,482 ± 451	—‡	1,299† ± 387	1,348† ± 493
CO (l/min)	3.29 ± 0.55	—‡	3.57† ± 0.39	3.57† ± 0.41
PMAP (mmHg)	21.7 ± 9.0	20.4† ± 9.2	20.6 ± 10.1	22.0 ± 10.1
PCWP (mmHg)	16.3 ± 8.1	14.9 ± 8.7	15.3 ± 9.5	16.4 ± 9.7

* Means ± SD, n = 7.
† Significantly different from control ($P < 0.05$).
‡ Value not obtained.

surement periods). Seven patients then received 0.28 mg/kg vecuronium as an iv bolus. Cardiovascular variables were recorded at 2, 5, and 10 min following vecuronium administration, except for cardiac output which was measured only at the 5- and 10-min periods. Five patients received 0.1 mg/kg pancuronium, iv, and their cardiovascular variables were similarly recorded. This dose of pancuronium represents three times its ED_{90} (dose producing a 90% depression of evoked twitch tension), while the dose of vecuronium used is equivalent to twelve times it ED_{90}. The relatively large vecuronium dose was chosen deliberately in an attempt to demonstrate any possible cardiovascular effects. Surgery was not begun until all measurements were completed. Systemic and pulmonary mean arterial pressure (SMAP, PMAP), and systemic and pulmonary vascular resistance (SVR, PVR) were calculated from these data. Statistical analysis was performed by repeated measures analysis of variance. When P values were less than the critical value of 0.05, Bonferroni t tests were used to assess intragroup differences. The relative increases in CO following vecuronium and pancuronium administration were compared by unpaired t test, with significance accepted at $P < 0.05$.

Results

The data are summarized in tables 1 and 2. Following vecuronium administration at both five and ten minutes, a small but significant increase in CO occurred concomitant with a small but significant decrease in SVR ($P < 0.05$). PMAP decreased at two minutes. No significant changes were noted in HR, rhythm, SMAP, CVP, or PCWP.

Following pancuronium administration, a significant increase in HR was observed at two, five, and ten minutes ($P < 0.05$). Similarly, CO increased significantly at both 5- and 10-min intervals. This increase in CO was significantly greater than that following vecuronium. SMAP rose significantly at only the 2- and 5-min intervals. No significant changes were noted in rhythm, SVR, CVP, PMAP, PVR, or PCWP. No ST segment or T wave changes were noted by the cardiac anesthetist monitoring MCL5 following either vecuronium or pancuronium.

Discussion

All the currently available nondepolarizing muscle relaxants produce significant cardiovascular effects. *d*-Tubocurarine produces dose-dependent decreases in SVR and SMAP, with variable increases in HR.[8] Metocurine produces similar effects when the dose exceeds 0.3 mg/kg.[10] Gallamine causes a profound atropine-like response characterized by tachycardia and increases in SMAP and CO.[9] Perhaps the most commonly used nondepolarizing muscle relaxant, pancuronium, produces similar, although less profound, increases in HR, SMAP and CO.[8,11] With the data from our study, we confirm these findings with pancuronium. Interestingly, while the three patients in the pancuronium group receiving beta blockers generally had lower control heart rates, they exhibited a generally greater absolute increase in heart rate following pancuronium than did those pa-

TABLE 2. Cardiovascular Response to Pancuronium

	Control	2 Min	5 Min	10 Min
HR (beats/min)	50* ± 9.7	61† ± 8.5	58† ± 11.3	59† ± 10.1
SMAP (mmHg)	68 ± 13.0	84† ± 7.5	79† ± 9.7	76 ± 9.4
SVR (dyn·s·cm^{-5})	1,217 ± 218	—‡	1,357 ± 253	1,221 ± 178
CO (l/min)	3.84 ± 1.14	—‡	4.25† ± 1.32	4.51† ± 1.17
PMAP (mmHg)	20.6 ± 8.4	20.2 ± 7.6	19.6 ± 7.4	18.6 ± 6.9
PCWP (mmHg)	13.8 ± 5.3	13.0 ± 4.2	12.2 ± 3.4	12.0 ± 3.3

* Means ± SD, n = 5.
† Significantly different from control ($P < 0.05$).
‡ Value not obtained.

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tients not receiving beta blockers. While there is no such comparison of heart rate changes from pancuronium in patients with and without propranolol available in the literature, and the number of patients involved in our study is too small for statistical analysis, this observation supports the thesis that the cardiovascular effects of pancuronium are produced largely through inhibition of vagal tone, rather than a direct or indirect beta-adrenergic effect.[11,12] In contrast to pancuronium, vecuronium produced only minimal cardiovascular effects (table 1). Expressed as per cent change from control, the increase in CO was 9%, the decrease in SVR was 12%, and the decrease in PMAP 6%. The fact that these small changes proved statistically significant underlines the consistency of the experimental setting and response to vecuronium. Furthermore, these changes followed a dose of vecuronium equivalent to three times the dose necessary to intubate the trachea and twelve times the ED_{90}. This relatively large dose of vecuronium was chosen deliberately in an attempt to enhance any possible cardiovascular effects.

Control of the myocardial oxygen supply-demand ratio is important, especially in patients with ischemic heart disease. The mean values for two of the prime determinants of myocardial oxygen supply-demand, HR and SMAP, did not change following vecuronium, while increasing 22% and 24%, respectively, following pancuronium. This represents a mean increase in rate-pressure product of 51%, with a range of 25 to 137%. Furthermore, while the mean values for HR and SMAP did not change following vecuronium, individual patients varied no more than 5 beats/min or 6 mmHg, respectively, from control. We conclude that large doses of vecuronium have minimal cardiovascular effects in patients undergoing coronary artery bypass grafting and thus offer an advantage over currently available nondepolarizing muscle relaxants.

References

1. Booij LHDJ, Edwards RP, Sohn YJ, Miller RD: Cardiovascular and neuromuscular effects of Org NC45, pancuronium, metocurine, and *d*-tubocurarine in dogs. Anesth Analg (Cleve) 59:26–30, 1980
2. Marshall RJ, McGrath JC, Miller RD, Docherty JR, Lamar J-C: Comparison of the cardiovascular actions of Org NC45 with those produced by other non-depolarizing neuromuscular blocking agents in experimental animals. Br J Anaesth 52:21S–32S, 1980
3. Durant NN, Marshall IG, Savage DS, Nelson DJ, Sleigh T, Carlyle IC: The neuromuscular and autonomic blocking activities of pancuronium, Org NC45, and other pancuronium analogues, in the cat. J Pharm Pharmacol 31:831–836, 1979
4. Fahey MR, Morris RB, Miller RD, Sohn YJ, Cronnelly R, Gencarelli P: Clinical pharmacology of ORG NC45 (Norcuron™): A new nondepolarizing muscle relaxant. ANESTHESIOLOGY 55:6–11, 1981
5. Barnes PK, Smith GB, White WD, Tennant R: Comparison of the effects of Org NC45 and pancuronium bromide on heart rate and arterial pressure in anaesthetized man. Br J Anaesth 54:435–439, 1982
6. Gregoretti SM, Sohn YJ, Sia RL: Heart rate and blood pressure changes after ORG NC45 (vecuronium) and pancuronium during halothane and enflurane anesthesia. ANESTHESIOLOGY 56:392–395, 1982
7. Gencarelli PJ, Roizen MF, Miller RD, Joyce J, Hunt TK, Tyrrell JB: ORG NC45 (Norcuron™) and pheochromocytoma: a report of three cases. ANESTHESIOLOGY 55:690–693, 1981
8. Stoelting RK: The hemodynamic effects of pancuronium and *d*-tubocurarine in anesthetized patients. ANESTHESIOLOGY 36:612–615, 1972
9. Longnecker DE, Stoelting RK, Morrow AG: Cardiac and peripheral vascular effects of gallamine in man. Anesth Analg (Cleve) 52:931–935, 1973
10. Savarese JJ, Hassan HA, Antonio RB: The clinical pharmacology of metocurine: dimethyltubocurarine revisited. ANESTHESIOLOGY 47:277–284, 1977
11. Kelman GR, Kennedy BR: Cardiovascular effects of pancuronium in man. Br J Anaesth 48:335–338, 1974
12. Roizen MF, Forbes RA, Miller RD, Lake CR, Stanski DR: Similarity between effects of pancuronium and atropine on plasma norepinephrine levels in man. J Pharmacol Exp Ther 211:419–422, 1979

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