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Adverse Effects of Pancuronium during High-dose Fentanyl Anesthesia for Coronary Artery Bypass Grafting

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Using a randomized double-blind protocol, the authors prospectively compared three nondepolarizing muscle relaxants with respect to their influence on hemodynamics and on the electrocardiogram. Thirty-three patients undergoing elective coronary artery bypass grafting (CABG) with high-dose (100 μg/kg) fentanyl anesthesia were studied. Patients received 1.5 × ED_{95} of either pancuronium (n = 12), metocurine (n = 9), or a metocurine-pancuronium combination (4:1 ratio by weight) (n = 12) for muscle relaxation. Heart rate and rate pressure product (RPP) were significantly higher postinduction in the pancuronium group. Myocardial ischemia, indicated by new ECG ST-segment depression occurred significantly more frequently, and exclusively, in the pancuronium group. The authors' data suggest that since pancuronium is associated with tachycardia and an increased incidence of myocardial ischemia, it is best avoided in patients with severe coronary artery disease undergoing CABG with high-dose fentanyl. Either metocurine or the metocurine–pancuronium combination provides greater hemodynamic stability, without precipitating myocardial ischemia, and can be safely and effectively substituted for pancuronium. (Key words: Anesthetics: intravenous, fentanyl. Heart: electrocardiography. Neuromuscular relaxants: pancuronium; metocurine. Surgery: cardiac.)

PANCURONIUM BROMIDE is commonly used as the sole muscle relaxant during high-dose fentanyl anesthesia for coronary artery bypass grafting (CABG).[1–4] The popularity of pancuronium may be related to its positive chronotropic effects,[5,6] which tend to antagonize any vagally mediated bradycardia resulting from fentanyl administration.[7] However, bradycardia during fentanyl administration may occur less consistently in humans than in dogs,[8] and high-dose fentanyl anesthesia has been successfully administered without using antimuscarinic agents.[9] The antimuscarinic and sympathomimetic effects of pancuronium[10–12] may increase heart rate (HR) and myocardial contractility. In patients with severe coronary artery disease (CAD), myocardial ischemia may be precipitated by the associated deterioration in myocardial oxygen balance.[13] Sonntag *et al.* reported myocardial lactate production in seven of nine patients undergoing CABG with high-dose fentanyl and pancuronium.[2] In a previous study, we noted a 50% incidence of ischemic electrocardiographic (ECG) changes in a group of 20 patients undergoing CABG with high-dose fentanyl–pancuronium anesthesia.[14] We found a strong positive correlation between HR, rate-pressure product (RPP), and ECG changes of ischemia. We postulated that increases in HR induced by pancuronium were partly responsible for the high incidence of ischemic ECG changes we observed. The present study was designed to test the hypothesis that, compared with other nondepolarizing muscle relaxants, pancuronium bromide is associated with relatively adverse hemodynamic and electrocardiographic responses during high-dose fentanyl anesthesia for CABG.

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Methods

The study received institutional approval, and patients gave informed consent. Thirty-three patients scheduled for elective CABG were studied. All patients had stable angina and normal complexes in lead V_5 of their preoperative 12-lead ECG. All preoperative antianginal medications (nitrates, beta-adrenergic blockers, calcium-entry blockers) were continued until the time of surgery. Patients were randomly assigned to one of three groups, according to which muscle relaxant they received. Relaxant dosage was fixed at one and one-half times the mean dose, causing 95% twitch height depression (1.5 × ED_{95}) in humans.[15] Group 1 (n = 12) received pancuronium bromide 0.105 mg/kg; Group 2 (n = 9) received metocurine iodide 0.420 mg/kg; Group 3 (n = 12) received a combination of metocurine 0.108 mg/kg and pancuronium 0.027 mg/kg. A double-blind protocol was followed. Equipotent concentrations of the three muscle relaxants were prepared in our Hospital Pharmacy and arrived in the operating room in identical coded vials.

After premedication 1 h preoperatively with morphine 0.1 mg/kg im and scopolamine 0.006 mg/kg im, nasal oxygen (3 l/min) was administered. In the operating room, intravenous, radial artery, and thermodilution

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Swan–Ganz® catheters were inserted under local anesthesia. Electrocardiographic leads II and CS_5 were continuously recorded by a battery-operated Holter Monitor (Del-Mar Avionics). One hundred per cent oxygen (O_2) was then administered by mask and patients allowed to stabilize for 5 min. Two minutes after a small initial dose of iv relaxant ($0.2 \times ED_{95}$), anesthesia was induced with fentanyl citrate iv 5 $\mu g \cdot kg^{-1} \cdot min^{-1}$. When patients no longer responded to repeated commands to breathe, we then administered the remaining relaxant ($1.3 \times ED_{95}$) iv over 2 min, commencing with a bolus ($0.6 \times ED_{95}$). End-tidal P_{CO_2} (ET CO_2) was monitored continuously, and respiration was assisted or controlled to maintain ET CO_2 within 5 mmHg of control. Oropharyngeal airways were inserted as required. After fentanyl 50 $\mu g/kg$ the patients were intubated, and after 100 $\mu g/kg$ surgery commenced. Complete hemodynamic measurements were made at the following times: 1) control (pre-induction); 2) fentanyl 50 $\mu g/kg$ (preintubation); 3) one minute postintubation; 4) fentanyl 100 $\mu g/kg$; 5) one minute poststernotomy. Arterial pressure, pulmonary artery pressure (PAP), pulmonary capillary wedge pressure (PCWP), and central venous pressure (CVP) were recorded by a Hewlett–Packard polygraph and transducers. Thermodilution cardiac output determinations were made in triplicate using an Edwards Laboratory Cardiac Output® computer (Model 9520) and injections of 10 ml of iced 5% dextrose in water. Derived hemodynamic variables included heart rate (HR), cardiac index (CI), systemic vascular resistance index (SVRI), and the heart rate by systolic arterial pressure product (RPP). Arterial blood gases were determined at control, immediately prior to intubation, and 5 min following intubation. The study terminated upon initiation of cardiopulmonary bypass.

The Holter Monitor recordings were evaluated using an Avionics Electrocardioscanner. One of us screened the recordings and obtained representative 15-s write-outs of lead CS_5 at the time intervals corresponding to the hemodynamic measurements listed above and at five additional times. These representative ECG strips then were coded and jumbled. Another investigator then evaluated each ECG strip separately for evidence of myocardial ischemia without knowledge of which patient, treatment group, or time interval was being evaluated. The ST-segment was evaluated with respect to the PQ junction at a point 60 ms following the S-wave nadir. Myocardial ischemia was diagnosed when persistent ST-segment depression ≥ 1 mm at a calibration of 10 mm/mV was observed in lead CS_5. Each ECG recording was then carefully screened for additional ischemic episodes between hemodynamic measurements. Analysis of variance (ANOVA) was used to search for significant hemodynamic differences between treatment groups.

TABLE 1. Preoperative Variables*

	Pancuronium n = 12	Metocurine n = 9	Metocurine–Pancuronium n = 12
Age (±SD) (yr)	57.9 ± 6.6	61.6 ± 7.0	59.2 ± 9.2
Sex			
Male	7	8	7
Female	5	1	5
Ejection fraction (±SD)	64.0 ± 8.7	63.0 ± 9.4	66.0 ± 17.9
LVEDP† (mmHg) (±SD)	13.5 ± 2.7	18.0 ± 7.7	14.0 ± 4.6

* The groups differ significantly only with respect to sex distribution ($P < 0.05$, Fischer's Exact Test).
† Left ventricular end-diastolic pressure at heart cateterization.

Fischer's Exact Test was used for contingency table analysis. The Wilcoxon–Mann–Whitney rank-sums test was used to make intergroup comparisons of ordinal data. Null hypotheses were rejected when P values were less than or equal to 0.05.

Results

Table 1 compares the three treatment groups with respect to age, sex, ejection fraction, and left-ventricular end-diastolic pressure (LVEDP) at heart catheterization. Table 2 compares the three groups with respect to the number of coronary bypass grafts received. The groups were identical with respect to the above variables, with the exception of sex distribution. The metocurine group contained a preponderance of men. Patients in the study were receiving a wide variety of antianginal medications preoperatively (table 3). This heterogeneity of medical regimes precluded statistical comparison, but no obvious intergroup differences were apparent. Table 4 summarizes the arterial P_{CO_2} data for the three groups. The groups did not differ significantly with respect to this variable.

Table 5 summarizes the hemodynamic data. Analysis of variance revealed no significant hemodynamic differences between groups at the control period. However, when all five time intervals were considered, the groups

TABLE 2. Number of Coronary Artery Bypass Grafts*

Group	No. of Grafts 1	2	3	4	5	Total
Pancuronium	0	1	4	5	2	12
Metocurine	0	2	4	2	1	9
Metocurine: pancuronium	1	2	4	5	0	12

* The groups do not differ significantly with respect to the number of grafts received (Wilcoxon–Mann–Whitney rank-sums test).

TABLE 3. Preoperative Antianginal Medications and Change in Hemodynamics on Induction

Patient Number	β Blocker Daily Dose	Ca^{++} Entry Blocker Daily Dose	Per cent RPP	Per cent HR
Pancuronium group				
1a	—	Verapamil 480 mg	96*	57*
2a	Propranolol 160 mg	—	78*	28*
3a	Propranolol 160 mg	Nifedipine 60 mg	73	52
4a	Metoprolol 300 mg	—	72*	54*
5a	Propranolol 40 mg	—	71	37
6a	Timolol 15 mg	—	58	31
7a	Oxyprenolol 160 mg	—	50	60
8a	—	Nifedipine 40 mg	14	20
9a	Propranolol 240 mg	Nifedipine 30 mg	0	10
10a	Propranolol 80 mg	Nifedipine 40 mg	−12	14
11a	Propranolol 160 mg	Nifedipine 60 mg	−15	8
12a	Propranolol 200 mg	Nifedipine 60 mg	−18	−6
Metocurine group				
1b	Metoprolol 200 mg	Nifedipine 30 mg	29	29
2b	Metopolol 150 mg	Nifedipine 40 mg	8	8
3b	Propranolol 160 mg	—	4	−7
4b	Pindolol 20 mg	—	0	16
5b	—	Diltiazem 240 mg	0	5
6b	Timolol 20 mg	—	−5	6
7b	Propranolol 160 mg	—	−9	15
8b	Metoprolol 200 mg	Nifedipine 30 mg	−19	0
9b	Propranolol 160 mg	—	−27	0
Metocurine–pancuronium group				
1c	Propranolol 80 mg	Nifedipine 40 mg	64	19
2c	Propranolol 160 mg	—	30	12
3c	Timolol 20 mg	Verapamil 360 mg	22	15
4c	Propranolol 60 mg	—	17	23
5c	Timolol 20 mg	—	11	4
6c	—	—	1	3
7c	Propranolol 160 mg	—	−7	4
8c	—	Verapamil 480 mg	−8	5
9c	Propranolol 160 mg	Nifedipine 60 mg	−12	0
10c	Propranolol 160 mg	Nifedipine 30 mg	−23	4
11c	Timolol 20 mg	—	−24	4
12c	Propranolol 80 mg	—	−24	5

* Ischemic ECG changes postinduction.

differed significantly with regard to HR and RPP ($P < 0.001$, $P < 0.05$ respectively, ANOVA for repeated measures). Heart rate and RPP were significantly higher in the pancuronium group. The groups did not differ significantly with respect to the other hemodynamic variables. However, the ANOVA approached statistical significance for MAP ($P = 0.051$). The MAP tended to be highest in the pancuronium group and lowest in the metocurine group.

TABLE 4. Arterial P_{CO_2} in mmHg (mean ± SD)*

	Control	Preintubation	Postintubation
Pancuronium (n = 12)	41 ± 3	40 ± 3	38 ± 3
Metocurine (n = 9)	40 ± 3	42 ± 6	36 ± 3
Metocurine:pancuronium (n = 12)	41 ± 5	38 ± 4	38 ± 4

* The groups do not differ significantly with respect to P_{CO_2} (ANOVA).

Electrocardiographic changes of myocardial ischemia were noted significantly more frequently in the pancuronium group (table 6). Three of 12 patients in Group 1 had episodes of ST-segment depression, compared with zero episodes in the other two groups ($P < 0.05$, Fischer's Exact Test). Patients who developed myocardial ischemia showed increases in both HR (28–57%) and systolic arterial pressure (SAP) (12–39%) in response to induction with fentanyl and pancuronium. The three highest RPP values recorded in this study were noted during induction in the patients who had ECG changes of myocardial ischemia develop. No further hemodynamic changes were apparent when the trachea was subsequently intubated. Ischemia was first apparent during induction in two of the three ischemic patients and after intubation in the third. However, in the latter patient ischemia appeared related to substantial increases in HR and SAP occurring during induction, as no further changes occurred in response to intubation.

TABLE 5. Hemodynamic Variables (mean ± SD)

Variable ± SD	Drug Group	Control	50 μg·kg⁻¹	1 Min Postintubation	100 μg·kg⁻¹	1 Min Poststernotomy	ANOVA
HR (beats/min)	P	58 ± 14	76 ± 24	74 ± 17	68 ± 15	65 ± 12	*
	M	52 ± 7	56 ± 8	56 ± 8	51 ± 7	50 ± 7	†
	M:P	52 ± 8	57 ± 8	57 ± 9	51 ± 7	50 ± 9	‡
SAP (mmHg)	P	152 ± 20	155 ± 25	152 ±17	143 ± 20	149 ± 13	
	M	153 ± 17	135 ± 21	133 ± 13	126 ± 14	138 ± 15	
	M:P	153 ± 23	144 ± 34	143 ± 26	137 ± 24	148 ± 24	
DAP (mmHg)	P	73 ± 5	80 ± 11	79 ± 13	75 ± 13	78 ± 11	
	M	77 ± 17	68 ± 14	66 ± 10	64 ± 13	72 ± 12	
	M:P	73 ± 11	76 ± 18	74 ± 12	70 ± 12	79 ± 13	
MAP (mmHg)	P	102 ± 11	107 ± 17	106 ± 17	99 ± 15	106 ± 13	
	M	99 ± 17	90 ± 16	89 ± 8	84 ± 12	92 ± 12	
	M:P	102 ± 12	99 ± 22	96 ± 16	90 ± 14	101 ± 13	
MPAP (mmHg)	P	22.5 ± 4.4	21.9 ± 7.0	20.0 ± 4.9	18.3 ± 4.9	18.6 ± 4.7	
	M	19.2 ± 3.8	19.4 ± 4.3	19.2 ± 5.6	17.2 ± 4.2	17.0 ± 4.0	
	M:P	18.9 ± 4.2	19.8 ± 4.7	17.6 ± 3.8	17.5 ± 4.4	17.6 ± 4.9	
PCWP (mmHg)	P	16.2 ± 3.3	14.3 ± 4.2	12.3 ± 3.1	11.7 ± 3.1	12.3 ± 2.7	
	M	14.6 ± 4.2	12.6 ± 4.0	11.7 ± 4.6	11.8 ± 3.4	12.0 ± 4.2	
	M:P	12.5 ± 4.4	13.4 ± 4.1	11.4 ± 4.2	11.1 ± 4.5	11.7 ± 4.7	
CVP (mmHg)	P	7.5 ± 2.5	7.6 ± 2.9	6.6 ± 1.8	6.5 ± 2.0	6.5 ± 2.2	
	M	6.1 ± 3.0	6.9 ± 3.2	6.6 ± 3.5	6.0 ± 3.0	7.3 ± 3.4	
	M:P	5.7 ± 2.9	6.2 ± 2.5	5.4 ± 2.6	5.0 ± 2.0	5.6 ± 2.3	
CI ($l \cdot min^{-1} \cdot m^{-2}$)	P	2.52 ± 0.64	3.21 ± 1.85	2.90 ± 0.98	2.72 ± 0.85	2.46 ± 0.78	
	M	2.44 ± 0.48	2.42 ± 0.56	2.44 ± 0.44	2.15 ± 0.29	2.12 ± 0.31	
	M:P	2.32 ± 0.43	2.33 ± 0.58	2.25 ± 0.43	2.06 ± 0.39	2.03 ± 0.40	
SVRI ($dyn \cdot s \cdot cm^{-5} \cdot m^2$)	P	3170 ± 781	2871 ± 958	2922 ± 778	2899 ± 817	3468 ± 973	
	M	3163 ± 916	2850 ± 733	2755 ± 557	2975 ± 700	3269 ± 793	
	M:P	3395 ± 621	3256 ± 724	3305 ± 771	3382 ± 730	3887 ± 1005	
RPP ($mmHg \cdot beats \cdot min^{-1} \cdot 10^{-3}$)	P	8.95 ± 2.34	12.23 ± 5.41	11.35 ± 3.58	9.81 ± 3.38	9.71 ± 2.37	*
	M	7.98 ± 1.56	7.63 ± 1.84	7.53 ± 1.58	6.40 ± 1.18	6.85 ± 1.45	†
	M:P	8.03 ± 1.88	8.29 ± 2.56	8.26 ± 2.81	7.01 ± 1.80	7.44 ± 1.88	‡

P = pancuronium; M = metocurine; M:P = metocurine:pancuronium; ANOVA = analysis of variance for repeated measures; HR = heart rate; SAP = systolic arterial pressure; DAP = diastolic arterial pressure; MAP = mean arterial pressure; MPAP = mean pulmonary arterial pressure; PCWP = pulmonary capillary wedge pressure; CVP = central venous pressure; CI = cardiac index; SVRI = systemic vascular resistance index; RPP = heart rate × systolic arterial pressure.

* $P < 0.05$ P *versus* M *versus* M:P.

† $P < 0.05$ P *versus* M (tested only when $P < 0.05$ for P *vs.* M *vs.* M:P).

‡ $P < 0.05$ P *versus* M:P (tested only when $P < 0.05$ for P *vs.* M *vs.* M:P).

Ischemic ST-segment changes persisted for several minutes in all patients. All patients who developed ischemia were male and were receiving antianginal medications preoperatively (table 3).

Bradycardia and/or hypotension were not major problems in the patients who received a muscle relaxant other than pancuronium. None of these patients required atropine or a pacemaker in the prebypass period. One patient in the metocurine group required a brief phenylephrine infusion during induction, when systolic arterial pressure fell to 58 mmHg.

Discussion

Our results demonstrate that during induction of high-dose fentanyl anesthesia for CABG, the use of pancuronium bromide as the sole muscle relaxant results in a comparatively unfavorable hemodynamic response. Of greatest importance is the fact that HR is significantly elevated with pancuronium, compared with either me-

TABLE 6. Incidence of ST-Depression*

	ST Depression	No ST Depression	Totals
Pancuronium	3	9	12
Metocurine	0	9	9
Metocurine:pancuronium	0	12	12
Totals	3	30	33

* The groups differ significantly with respect to the incidence of ischemic ST-segment changes, $P < 0.05$, Fischer's Exact Test.

tocurine or a metocurine–pancuronium combination. By increasing myocardial oxygen demand and decreasing diastolic perfusion time, increases in heart rate may precipitate myocardial ischemia in patients with CAD. In this study ECG changes of ischemia were indeed significantly more common in the pancuronium group.

Although we did not demonstrate a significant intergroup difference in MAP ($P = 0.051$), increases in arterial pressure appeared to contribute somewhat to the pathogenesis of myocardial ischemia in the patients in the pancuronium group who developed ST-segment depression. Both HR and arterial pressure increased during induction in those patients. The RPP product was also significantly higher in the pancuronium group. Interestingly, the three highest RPP values recorded in this study occurred in the patients who developed myocardial ischemia. These adverse hemodynamic and electrocardiographic events occurred even though conventional antianginal medications were continued until the time of surgery. Neither were these events related to elevated arterial P_{CO_2}, as ET_{CO_2} was carefully monitored and blood gases were checked prior to intubation in all patients.

The hemodynamic and electrocardiographic changes noted in the pancuronium group were probably precipitated by a combination of antimuscarinic and sympathomimetic effects of pancuronium bromide. Our study does not demonstrate which of these mechanisms, if any, is predominant. Our data do not exclude a specific pancuronium–fentanyl interaction as the cause of the changes observed. Further studies should clarify these issues.

Potentially adverse hemodynamic responses to anesthetic induction with fentanyl and pancuronium may be exaggerated in patients with well-preserved ventricular function compared with those with impaired ventricular function.[4] Our selection criteria required a normal ECG complex in lead V5 of the resting ECG. This criterion appears to select a group of patients with relatively well-preserved ventricular function. Mean ejection fraction was 0.64 for the patients in this study. This may, in part, explain the hemodynamic responsiveness to induction with fentanyl and pancuronium in this study, and in our previous experiment.[14]

In the studies of Stanley *et al.*,[16,17] increases in heart rate did not occur during high-dose fentanyl anesthesia, despite the use of pancuronium. In those studies, succinylcholine was administered for intubation, and pancuronium was administered later. Succinylcholine may exert a specific pharmacologic effect that prevents tachycardia in response to pancuronium.[18] Alternatively, simply delaying pancuronium administration may prevent a fentanyl-pancuronium interaction that is confined to the early stages of fentanyl administration. Administration of fentanyl may lead to catecholamine release.[19] To date, two studies have demonstrated increases in serum catecholamines during the early stages of anesthetic induction with fentanyl in patients with CAD.[9,20] Concomitant administration of pancuronium, an agent that blocks reuptake of norepinephrine at sympathetic nerve endings,[12] might lead to an exaggerated sympathomimetic response to fentanyl infusion. This hypothesis may explain why early, but not late, administration of pancuronium is associated with tachycardia. Further investigations are needed.

Our study demonstrates that either metocurine or the combination of metocurine and pancuronium can be effectively substituted for pancuronium during high-dose fentanyl anesthesia for CABG. Hemodynamics were stable with both techniques, and significant bradycardia and/or hypotension were infrequent. More importantly, ischemic ECG changes did not occur with either of these agents.

In summary, in these patients with stable angina and well-preserved ventricular function the use of pancuronium bromide as the sole muscle relaxant during induction of high-dose fentanyl anesthesia for elective CABG resulted in a distinctly different hemodynamic and electrocardiographic response compared with metocurine or a metocurine–pancuronium combination. Most importantly, HR was significantly higher, and ischemic ECG changes were significantly more common with pancuronium. For these reasons we prefer to use either metocurine or the metocurine–pancuronium combination and avoid the use of pancuronium, during high-dose fentanyl anesthesia for CABG in this population.

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References

1. Quinton L, Whalley DG, Wynands JE, Morin JE, Burke J: High dose fentanyl anesthesia with oxygen for aorto-coronary bypass surgery. Can Anaesth Soc J 28:314–320, 1981
2. Sonntag H, Larsen R, Hilfiker O, Kettler D, Brockschnieder B: Myocardial blood flow and oxygen consumption during high-dose fentanyl anesthesia in patients with coronary artery disease. ANESTHESIOLOGY 56:417–422, 1982
3. Sprigge JS, Wynands JE, Whalley DG, Bevan DR, Townsend GE, Nathan H, Patel YC, Srikant CB: Fentanyl infusion anesthesia for aortocoronary bypass surgery: Plasma levels and hemodynamic response. Anesth Analg 61:972–978, 1982
4. Wynands JE, Wong P, Whalley DG, Sprigge JS, Townsend GE, Patel YC: Oxygen-fentanyl anesthesia in patients with poor ventricular function: Hemodynamics and plasma fentanyl concentrations. Anesth Analg 62:476–482, 1983

5. Stoelting RK: The hemodynamic effects of pancuronium and d-tubocurarine in anesthetized patients. ANESTHESIOLOGY 36: 612–615, 1972
6. Stanley TH, Liu WS: Cardiovascular effects of meperidine–N_2O anesthesia before and after pancuronium. Anesth Analg 56: 669–673, 1977
7. Liu W, Bidwai AV, Stanley TH, Isern-Amaral J: Cardiovascular dynamics after large doses of fentanyl and fentanyl plus N_2O in the dog. Anesth Analg 55:168–172, 1976
8. Lowenstein E, Philbin DM: Narcotic "Anesthesia" in the eighties. ANESTHESIOLOGY 55:195–197, 1981
9. Hicks HC, Mowbray AG, Yhap EO: Cardiovascular effects of and catecholamine responses to high dose fentanyl–O_2 for induction of anesthesia in patients with ischemic coronary artery disease. Anesth Analg 60:563–568, 1981
10. Booij LHDJ, Edwards RP, Sohn YJ, Miller RD: Cardiovascular and neuromuscular effects of Org NC 45, pancuronium, metocurine and d-tubocurarine in dogs. Anesth Analg 59: 26–30, 1980
11. Domenech JS, Garcia RC, Sasiain JMR, Loyola AQ, Oroz JS: Pancuronium bromide: An indirect sympathomimetic agent. Br J Anaesth 48:1143–1148, 1976
12. Marshall RJ, McGrath JC, Miller RD, Docherty JR, Lamar JC: Comparison of the cardiovascular actions of Org NC 45 with those produced by other non-depolarizing neuromuscular blocking agents in experimental animals. Br J Anaesth 52: 21S–31S, 1980
13. Waller JL, Kaplan JA, Jones EL: Anesthesia for coronary revascularization, Cardiac Anesthesia. Edited by Kaplan JA. New York, Grune and Stratton, 1979, pp 241–280
14. Thomson IR, Mutch WAC, Culligan JD: Failure of intravenous nitroglycerin to prevent intraoperative myocardial ischemia during fentanyl–pancuronium anesthesia. ANESTHESIOLOGY 61:385–393, 1984
15. Lebowitz PW, Ramsey FM, Savarese JJ, Hassan HA: Potentiation of neuromuscular blockade in man produced by combinations of pancuronium and metocurine or pancuronium and d-tubocurarine. Anesth Analg 59:604–609, 1980
16. Stanley TH, Philbin DM, Coggins CH: Fentanyl–oxygen anesthesia for coronary artery surgery: Cardiovascular and antidiuretic hormone responses. Can Anaesth Soc J 26:168–171, 1979
17. Stanley TH, Berman L, Green O, Robertson D: Plasma catecholamine and cortisol responses to fentanyl–oxygen anesthesia for coronary-artery operations. ANESTHESIOLOGY 53:250–253, 1980
18. Nigrovic V: Succinylcholine, cholinoceptors and catecholamines: Proposed mechanism of early adverse haemodynamic reactions. Can Anaesth Soc J 31:382–394, 1984.
19. Rorie DK, Muldoon SM, Tyce GM: Effects of fentanyl on adrenergic function in canine coronary arteries. Anesth Analg 60:21–27, 1981
20. Tomichek RC, Rosow CE, Philbin DM, Moss J, Teplick RS, Schneider RC. Diazepam–fentanyl interaction—hemodynamic and hormonal effects in coronary artery surgery. Anesth Analg 62:881–884, 1983