

Hemodynamic effects of sufentanil/metocurine versus sufentanil/pancuronium in patients undergoing coronary artery surgery¹

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Thirty-two patients undergoing coronary artery surgery who had coronary artery disease without severe ventricular impairment were studied. Seventeen (Group 1) received sufentanil and pancuronium; 15 (Group 2) received sufentanil and metocurine. Hemodynamic variables were measured before induction (control), 3 minutes after intubation, 3 minutes after incision, 3 minutes after sternotomy, and immediately before cannulation. The heart rate in Group 1 was significantly increased from control values at all points ($p < 0.05$). Pulmonary capillary wedge pressure did not change significantly from control in either group. Cardiac output in Group 1 was significantly higher than control at the postintubation, postincision, and poststernotomy times of measurement ($p < 0.01$), and higher than Group 2 at the postincision and poststernotomy times of measurement. In Group 2, the cardiac output did not change significantly from control. There was no myocardial depression in either group, as evidenced by maintained pulmonary capillary wedge pressure and cardiac output.

Index terms: Anesthesia adjuvants • Anesthetics • Muscle relaxants, central

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Early studies with sufentanil demonstrated that it did not cause an increase in heart rate (HR) or blood pressure (BP); in fact sufentanil decreased the HR.¹ Our preliminary study of sufentanil anesthesia used sufentanil/pancuronium and showed a high incidence of increased HR and increased BP. We postulated the higher incidence of increased HR and increased BP encountered might be related to use of pancuronium bromide.²

This study was designed as a continuation of our initial

Table 1. Patient characteristics

	Treatment			
	Sufentanil/ Metocurine		Sufentanil/ Pancuronium	
	Male	Female	Male	Female
Number of patients	13	2	17	0
Age (years)	47.7 ± 6.6*	47.5 ± 2.1	55.4 ± 6.6*	
Weight (kg)	74.9 ± 9.8	63.0 ± 4.2	84.5 ± 12.3	
ASA Class IV	13	2	17	0

Data presented as mean ± standard deviation.

* The male population was significantly different with respect to age ($p \leq 0.05$).

study in similar groups of patients to determine whether the rise in HR was due to the use of pancuronium bromide or due to an effect of sufentanil. Therefore, we compared the hemodynamic effects of sufentanil/pancuronium with those of sufentanil/metocurine, since metocurine is free from the sympathomimetic and vagolytic effects of pancuronium bromide.

Materials and methods

Following institutional approval, 32 coronary artery revascularization surgery patients were prospectively studied. Preoperatively all patients were informed and consented to the study. All patients fulfilled the following criteria. They were 31 to 65 years of age, with good or mildly impaired ventricular function as diagnosed by ventricular angiography. All patients were A.S.A. Class III or IV. All patients were first-time coronary artery surgery patients and had not undergone other surgical procedures. None of the patients had diabetes or other systemic disease. Patients that were hypertensive preoperatively were excluded, since these patients can react in an exaggerated manner in response to laryngoscopy and endotracheal intubation.³

Patients who received beta-adrenergic blocking agents and nitrates preoperatively continued to receive them, including the morning of sur-

Table 2. Comparison of patients treated preoperatively with propranolol

	Sufentanil/ Metocurine	Sufentanil/ Pancuronium
Number of patients	11	7
Propranolol dosage range (mg) per 24 hours	40-160	80-240
Mean ± S.D. dosage per 24 hours	95 ± 47.5	137 ± 55.9

No statistically significant difference among treatment groups.

gery. Premedication consisted of 0.4 mg scopolamine and 0.15 mg/kg of morphine given intramuscularly and 2 in (5 cm) nitroglycerin paste applied to the chest wall.

Prior to induction of anesthesia, all patients were monitored with electrocardiography, an arterial line, and a pulmonary artery thermistor-tipped catheter. We measured heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), right-side filling pressure (RAP), pulmonary capillary wedge pressure (PCWP), and cardiac output (CO) using thermodilution (the average of three measurements). We calculated the cardiac index (CI) and systemic vascular resistance (SVR).

These measurements were recorded (a) before induction (control), (b) 3 minutes after intubation, (c) 3 minutes after incision, (d) 3 minutes after sternotomy, and (e) immediately before cannulation of the great vessels.

Sufentanil/pancuronium (Group 1)

While the patient was breathing 100% O₂ by face mask, 1.5–2 mg of pancuronium was administered intravenously (IV). Immediately thereafter, sufentanil infusion was started at a rate of 4–5 µg/kg/minute to a total dose of 15–20 µg/kg. Respiration was assisted when the patient failed to respond to verbal command. Pancuronium bromide, to a total dose of 0.12–0.15 mg/kg IV, was administered to facilitate intubation. For maintenance of anesthesia, additional sufentanil (0.025–0.05 mg) was administered every 45 minutes following the first dose and repeated when there were signs of lightening of anesthesia, such as “sweating” and/or tachycardia.

Sufentanil/metocurine (Group 2)

We followed the same protocol used in Group 1, except that metocurine was used instead of pancuronium bromide. Five to 6 mg of metocurine was administered IV before the start of sufentanil administration, and an additional dose of metocurine to a total of 0.35–0.5 mg/kg was administered to facilitate tracheal intubation.

In both groups if BP increased by more than 20% of control, systolic or diastolic, 0.2 mg nitroglycerin was given IV and repeated after one minute if BP remained elevated. If BP remained elevated, a sodium nitroprusside infusion was started to adjust the BP to close to the control value.

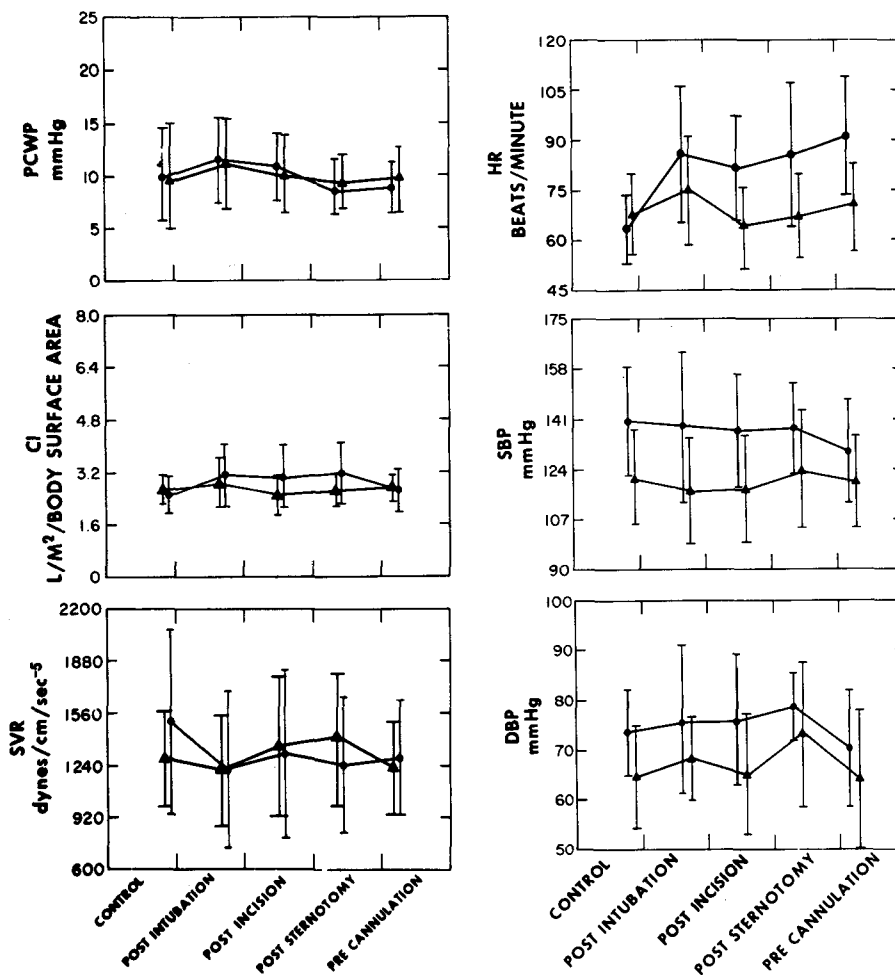


Figure. Changes during sufentanil/metocurine (triangles) versus sufentanil/pancuronium (circles) anesthesia in patients with coronary artery disease. PCWP = pulmonary capillary wedge pressure; CI = cardiac index; SVR = systemic vascular resistance; HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure.

A decrease in systolic pressure to < 90 mmHg or diastolic pressure to < 60 mmHg was treated by rapid volume infusion of 100–200 ml of lactated Ringer’s solution, and if the BP remained decreased, 100 µg Neo-synephrine (phenylephrine hydrochloride) was administered and repeated if necessary.

In this study, if HR increased above 110 beats/minute propranolol (1 mg IV) was given and repeated if necessary after two minutes if HR remained above 110 beats/min.

Statistical analysis of the data was performed in the following manner. Differences between the treatment groups with respect to the variables ASA class and preoperative propranolol usage

were tested by Fisher’s exact test. The variables age, weight, and hemodynamic variables at entry to the operating room (control) were analyzed by analysis of variance followed by a least significant difference test to make pairwise group comparisons. The percent change from control values of hemodynamic variables was calculated for all post-control measurements and then was analyzed with analysis of variance followed by the least significant difference test. The influence of preoperative propranolol treatment on the magnitude of change in measured hemodynamic variables was analyzed by t test.

Tests were considered significant if the *p* value was less than or equal to 0.05.

Table 3. Changes in hemodynamic variables

Variable	Intubation ± 3 min			Postincision			Sternotomy ± 3 min			Precannulation			
	Control	Value	Mean % change	Value	Mean % change	Value	Mean % change	Value	Mean % change	Value	Mean % change	Value	Mean % change
Heart rate	63.5 ± 10.5	85.8 ± 20.3	36.82 ± 33.37 ^{b†}	81.4 ± 15.6	29.79 ± 26.03 ^{b†}	85.4 ± 21.5	35.90 ± 32.49 ^{b†}	90.9 ± 17.7	45.32 ± 29.77 ^{b†}	90.9 ± 17.7	45.32 ± 29.77 ^{b†}	90.9 ± 17.7	45.32 ± 29.77 ^{b†}
SP	67.5 ± 12.5	74.5 ± 16.9	11.17 ± 21.69 ^a	63.2 ± 12.8	-5.61 ± 17.17 ^a	67.3 ± 12.8	0.90 ± 19.31 ^a	69.7 ± 12.7	4.70 ± 22.14 ^a	69.7 ± 12.7	4.70 ± 22.14 ^a	69.7 ± 12.7	4.70 ± 22.14 ^a
Systolic blood pressure	140.7 ± 18.7	138.8 ± 25.2	-0.23 ± 19.44	136.9 ± 18.8	-1.84 ± 12.59	137.8 ± 15.5	-1.24 ± 11.27	129.9 ± 17.8	-6.34 ± 15.46	129.9 ± 17.8	-6.34 ± 15.46	129.9 ± 17.8	-6.34 ± 15.46
SM	121.2 ± 16.1	115.7 ± 17.6	-4.07 ± 11.94	116.1 ± 17.6	-3.40 ± 14.84	122.8 ± 19.9	1.89 ± 14.90	118.4 ± 14.9	-1.56 ± 11.98	118.4 ± 14.9	-1.56 ± 11.98	118.4 ± 14.9	-1.56 ± 11.98
Diastolic blood pressure	73.6 ± 8.5	75.8 ± 14.6	3.06 ± 17.33	75.8 ± 13.1	3.21 ± 15.39	78.6 ± 6.9	7.94 ± 13.53 [*]	70.0 ± 12.0	-3.60 ± 19.67	70.0 ± 12.0	-3.60 ± 19.67	70.0 ± 12.0	-3.60 ± 19.67
SP	64.3 ± 10.4	67.8 ± 8.3	6.72 ± 12.78	64.9 ± 12.1	2.29 ± 20.78	73.1 ± 14.8	15.58 ± 26.50 [*]	63.7 ± 14.3	0.35 ± 24.85	63.7 ± 14.3	0.35 ± 24.85	63.7 ± 14.3	0.35 ± 24.85
SM	94.5 ± 9.6	95.5 ± 16.9	1.06 ± 14.87	95.9 ± 14.2	1.52 ± 11.56	97.1 ± 8.5	3.22 ± 8.88	86.2 ± 8.1	-7.76 ± 13.63 [*]	86.2 ± 8.1	-7.76 ± 13.63 [*]	86.2 ± 8.1	-7.76 ± 13.63 [*]
Mean arterial pressure	82.1 ± 11.0	82.9 ± 9.9	1.52 ± 10.20	81.0 ± 13.3	-0.59 ± 16.34	89.1 ± 15.5	9.19 ± 18.58	81.1 ± 12.7	-0.48 ± 15.91	81.1 ± 12.7	-0.48 ± 15.91	81.1 ± 12.7	-0.48 ± 15.91
Right-side filling pressure	6.2 ± 3.2	9.4 ± 3.7	111.27 ± 204.55 [*]	7.9 ± 2.5	70.20 ± 126.68 [*]	7.5 ± 3.0	62.68 ± 125.44	6.7 ± 2.8	40.63 ± 107.64	6.7 ± 2.8	40.63 ± 107.64	6.7 ± 2.8	40.63 ± 107.64
SP	6.5 ± 3.8	8.4 ± 3.0	115.06 ± 214.00	7.3 ± 3.0	68.54 ± 143.98	7.1 ± 2.4	73.67 ± 155.62	6.2 ± 2.0	72.32 ± 196.85	6.2 ± 2.0	72.32 ± 196.85	6.2 ± 2.0	72.32 ± 196.85
Pulmonary capillary wedge pressure	9.8 ± 4.6	11.5 ± 4.0	65.51 ± 145.30	10.8 ± 3.1	48.98 ± 116.01	8.5 ± 2.9	22.42 ± 116.03	8.7 ± 2.3	29.65 ± 133.52	8.7 ± 2.3	29.65 ± 133.52	8.7 ± 2.3	29.65 ± 133.52
SM	9.7 ± 5.3	11.0 ± 4.3	65.37 ± 147.95	9.9 ± 3.8	40.89 ± 104.03	9.2 ± 2.6	28.58 ± 86.43	9.4 ± 3.0	42.05 ± 118.73	9.4 ± 3.0	42.05 ± 118.73	9.4 ± 3.0	42.05 ± 118.73
Cardiac output	5.05 ± 1.25	6.21 ± 1.76	26.06 ± 30.96 [†]	6.04 ± 1.94	22.27 ± 25.87 [†]	6.20 ± 1.70	28.28 ± 34.14 [†]	5.26 ± 1.32	8.44 ± 29.08	5.26 ± 1.32	8.44 ± 29.08	5.26 ± 1.32	8.44 ± 29.08
SP	4.85 ± 0.87	5.16 ± 1.23	8.19 ± 26.62	4.53 ± 0.86	-4.70 ± 20.77 ^b	5.22 ± 0.96	2.60 ± 27.47 ^b	4.88 ± 0.68	2.73 ± 16.98	4.88 ± 0.68	2.73 ± 16.98	4.88 ± 0.68	2.73 ± 16.98
SM	2.51 ± 0.54	3.12 ± 0.90	26.06 ± 30.96 [†]	3.03 ± 0.95	22.27 ± 25.87 [†]	3.16 ± 0.90	28.28 ± 34.14 [†]	2.63 ± 0.62	2.73 ± 16.98	2.63 ± 0.62	2.73 ± 16.98	2.63 ± 0.62	2.73 ± 16.98
Cardiac index	2.63 ± 0.43	2.83 ± 0.79	8.19 ± 26.62	2.48 ± 0.58	-4.70 ± 20.77 ^b	2.62 ± 0.49	2.60 ± 27.47 ^b	2.68 ± 0.42	8.44 ± 29.08	2.68 ± 0.42	8.44 ± 29.08	2.68 ± 0.42	8.44 ± 29.08
Systemic vascular resistance	1507 ± 554	1207 ± 468	-16.00 ± 32.48	1307 ± 376	-9.18 ± 43.45	1238 ± 407	-12.56 ± 34.12	1282 ± 341	-0.28 ± 23.85	1282 ± 341	-0.28 ± 23.85	1282 ± 341	-0.28 ± 23.85
SP	1287 ± 294	1215 ± 340	-1.86 ± 30.77	1357 ± 425	8.36 ± 31.76	1414 ± 406	15.25 ± 41.10	1230 ± 278	-7.14 ± 41.63	1230 ± 278	-7.14 ± 41.63	1230 ± 278	-7.14 ± 41.63
SM													

SM = sufentanil/metocurine; SP = sufentanil/pancuronium.

^{a,b} Different letters for means at the same observation point indicate a significant between-group difference, *p* < 0.05.

* Significantly different from control, *p* < 0.05.

† Significantly different from control, *p* ≤ 0.01.

Table 4. Influence of preoperative beta-adrenergic blockade on hemodynamic variables

Variable	Sufentanil/Metocurine		Sufentanil/Pancuronium	
	+B (n = 11)	-B (n = 4)	+B (n = 7)	-B (n = 10)
Control				
HR	64.3 ± 3.1	77.3 ± 7.3	58.4 ± 2.6	67.0 ± 3.6
CO	4.71 ± 0.19	5.5 ± 0.62	4.51 ± 0.55	5.43 ± 0.31
MAP	82.9 ± 3.4 ^b	80.0 ± 11.9	100.6 ± 3.8 ^b	90.3 ± 2.2 ^a
PCWP	9.6 ± 1.7	10.0 ± 2.3	12.4 ± 1.6	7.9 ± 1.3 ^c
Postintubation				
HR	75.5 ± 4.9	71.8 ± 10.2	74.3 ± 5.3	93.8 ± 6.5
CO	5.05 ± 0.37	5.5 ± 0.67	4.81 ± 0.30	7.20 ± 0.50
MAP	84.9 ± 3.2	77.3 ± 3.2	99.4 ± 4.4	92.8 ± 6.3
PCWP	10.5 ± 1.3	12.3 ± 2.2	10.6 ± 0.9	12.1 ± 1.5 ^d
Postincision				
HR	62.8 ± 4.0	64.3 ± 6.5	76.6 ± 5.3	84.9 ± 4.2 ^e
CO	4.38 ± 0.20	4.93 ± 0.65	4.74 ± 0.35	7.06 ± 0.65
MAP	83.3 ± 4.4	74.8 ± 3.4	103.6 ± 3.9	90.6 ± 4.6
PCWP	9.7 ± 1.1	10.5 ± 2.3	10.7 ± 1.0	10.8 ± 1.1
Poststernotomy				
HR	67.6 ± 4.0	66.5 ± 6.5	87.1 ± 11.0	84.1 ± 5.0
CO	4.90 ± 0.28	4.58 ± 0.57	5.71 ± 0.64	6.69 ± 0.53
MAP	90.9 ± 5.5	84.0 ± 3.4	100.0 ± 3.5	95.1 ± 2.5
PCWP	9.4 ± 10.8	8.8 ± 1.4	9.3 ± 10.8	8.0 ± 1.0
Pre coronary artery bypass				
HR	68.8 ± 3.8	72.0 ± 7.3	88.0 ± 5.3	93.0 ± 6.4
CO	5.03 ± 0.24	4.52 ± 0.10	4.69 ± 0.35	5.67 ± 0.45
MAP	81.9 ± 3.6	79.8 ± 8.2	89.3 ± 3.6	84.1 ± 2.1
PCWP	9.7 ± 10.9	8.5 ± 1.5	9.6 ± 0.8	8.1 ± 0.8

+B = patients that received beta adrenergic blocking agents preoperatively; -B = patients that did not receive beta adrenergic blocking agents preoperatively; HR = heart rate; CO = cardiac output; MAP = mean arterial pressure; PCWP = pulmonary capillary wedge pressure; SM = sufentanil/metocurine; SP = sufentanil/pancuronium.

* Data presented as mean ± standard error.

^a Control MAP + B(SP) significantly different from control MAP -B(SP), *p* < 0.05.

^b Control MAP +B(SM) significantly different from control MAP +B(SP), *p* < 0.004.

^c Control PCWP +B(SP) significantly different from control PCWP -B(SP), *p* < 0.05.

^d The change in PCWP from control to postintubation in -B(SP) was significantly greater than change in PCWP from control to postintubation in +B(SP), *p* = 0.050.

^e The change in HR from postintubation to postincision in -B(SP) was significantly greater than the change in HR from postintubation to postincision in +B(SP), *p* < 0.05.

Results

Patient characteristics are presented in Table 1.

Table 2 presents the comparison of both treatment groups with reference to preoperative treatment with propranolol.

Hemodynamic changes that occurred in both groups are presented in Table 3 and in the Figure. Significant changes from control and significant differences between groups are noted.

Table 4 compares the influence of preoperative beta-adrenergic blockade on the hemodynamic changes that occurred in each group. Significant differences between and within groups are noted.

In Group 1, following induction of anesthesia, the HR increased significantly above control and was also significantly higher than that in Group

2 (Table 3, Fig.). In Group 2, the HR did not attain any significant difference when compared with control following the initial stages of induction of anesthesia. Throughout the study the incidence of tachycardia that required beta-blocker therapy in Group 1 was significantly higher (9/17 patients versus 1/15 patients in Group 2, *p* < 0.05).

Following endotracheal intubation, the systemic pressures were not statistically different from control, except poststernotomy when the DBP in both groups was significantly higher than control (Table 3, Fig.). The incidence of hypertensive episodes that required treatment throughout the study was 14/17 patients in Group 1 versus 5/15 patients in Group 2 (*p* < 0.05).

Both CO and CI were significantly higher than

control in Group 1 at the postintubation, postincision, and poststernotomy measurements and higher than Group 2 at postintubation, postincision, and poststernotomy measurements (*Table 3, Fig.*).

Preoperative propranolol therapy had no significant effect on the magnitude of change in hemodynamic variables measured from one time point to the next in the group of patients given sufentanil/metocurine for anesthesia. The MAP of the patients who took propranolol preoperatively and were in the sufentanil/metocurine group was significantly less than the MAP in the patients who took propranolol preoperatively and were in the sufentanil/pancuronium group (*Table 4*). There were several hemodynamic responses that were significantly different between the subgroup that took propranolol preoperatively and the one that did not take propranolol preoperatively within the group given sufentanil/pancuronium for anesthesia (*Table 4*).

Discussion

In an earlier study of sufentanil or halothane anesthesia for patients requiring coronary artery surgery we used pancuronium bromide for muscle relaxation and found that the combination of sufentanil/pancuronium caused minimal changes in PCWP and SVR, and no change or increased CO. However, significant increases in HR and BP were noted with the combination sufentanil/pancuronium, and the incidence of occurrence seemed greater than previously noted with the combinations of halothane/pancuronium and fentanyl/pancuronium.⁴⁻⁶

For this study we used large doses of muscle relaxants (1.5–2 times their ED₉₅)* to insure adequate muscle relaxation and accentuate the cardiovascular differences.

The group of patients that received sufentanil and metocurine had no significant change in HR, MAP, CO, or PCWP and required significantly less intraoperative treatment with beta-adrenergic blocking agents and vasodilators ($p < 0.05$) throughout the study period than the group given sufentanil and pancuronium. The fact that pancuronium and metocurine have different cardiovascular effects is well known, however, the differences in cardiovascular effects when com-

bined with sufentanil for anesthesia have not, to our knowledge, previously been reported. The findings in this study highlight the differences in cardiovascular effects seen with metocurine or pancuronium and suggest that sufentanil does not interfere with expression of these cardiovascular differences.

In this study the choice of muscle relaxant resulted in significant hemodynamic differences. Not only were HR and CO significantly higher in the group of patients given pancuronium, this group also required more frequent treatment with beta-adrenergic blocking agents and vasodilators intraoperatively ($p < 0.05$).

The cardiovascular effects of pancuronium as functions of other anesthetic sequences have been well described, especially the tendency to increase HR.⁷⁻⁹ Since sufentanil had been shown in earlier experimental and clinical trials to decrease HR, why did the combination with pancuronium result in an increase in HR in the present study? Two possible mechanisms are: (1) Because of the high specificity for opioid receptors, sufentanil may interfere less with cardiovascular receptors and reflexes and allow more observation of the cardiovascular effects of pancuronium. (2) There may be an unidentified interaction between sufentanil and pancuronium that results in exaggerated cardiovascular effects seen when sufentanil and pancuronium are given for anesthesia. The first mechanism is more probable on the basis of similar (increased HR) cardiovascular effects seen when pancuronium was given with fentanyl for anesthesia.⁴⁻⁶

The significantly higher CO seen in the group of patients given sufentanil/pancuronium at the postintubation, postincision, and poststernotomy measurements (*Table 3*) we believe was a result of the significantly greater incidence of use of vasodilators in this group of patients ($p < 0.05$). However, since SVR was not significantly different and PCWP was not significantly different between groups, the increased CO may also have been the result of administration of pancuronium.⁷⁻⁹

Preoperative beta-adrenergic blockade (*Table 4*) did influence the changes in HR and CO after intubation for patients given sufentanil/pancuronium anesthesia (+B < -B, $p < 0.05$). Preoperative beta-adrenergic blockade did not influence the response to sufentanil/metocurine anesthesia in this study. The use of preoperative beta-adrenergic blockade in this study provided

*ED₉₅ is the dose of muscle relaxant that results in 95% depression of twitch tension. ED₉₅ for metocurine is 0.28 mg/kg and pancuronium is 0.07 mg/kg.

protection against the cardiovascular effects of pancuronium.

In conclusion, the use of pancuronium with sufentanil was associated with significant increases in HR and CO that are amplified when patients are not given beta-adrenergic blockers preoperatively. In contrast, the use of metocurine with sufentanil for anesthesia was associated with no significant hemodynamic changes and reduced requirements for intraoperative use of vasodilators and beta-adrenergic blocking agents.

We recommend the use of metocurine for muscle relaxation with sufentanil anesthesia when no increase in HR is desired.

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