Cardiovascular effects of non-depolarizing neuromuscular blockers in patients with aortic valve disease

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To compare haemodynamic responses associated with equipotent doses of neuromuscular blockers and high-dose fentanyl ($50 \mu\text{g}\cdot\text{kg}^{-1}$), 40 patients with aortic valve stenosis (AS) and 20 patients with aortic insufficiency (AI) were randomized to four study groups to receive the following: (1) pancuronium $0.12 \text{ mg}\cdot\text{kg}^{-1}$, (2) vecuronium $0.12 \text{ mg}\cdot\text{kg}^{-1}$, (3) atracurium $0.4 \text{ mg}\cdot\text{kg}^{-1}$, or (4) pancuronium-metocurine mixture ($0.4 \text{ mg} + 1.6 \text{ mg/ml}$; 1 ml/10 kg). Neuromuscular blockers were injected at the same time with the fentanyl; haemodynamics were recorded with the patients awake (baseline), at two minutes post-induction, and at two and five minutes after intubation.

In patients with AS, pancuronium increased heart rate more than vecuronium or atracurium; heart rates were also higher with the pancuronium-metocurine mixture than with vecuronium. Although there were no ECG signs of ischaemia, one patient given pancuronium developed severe hypotension associated with tachycardia. Reductions in SVR after atracurium allowed small but significant ($p < 0.01$) decreases in MAP which were well tolerated; one patient, however, did develop severe hypotension. Intubation resulted in significant ($p < 0.01$) increases in MAP in the pancuronium-metocurine mixture group. Vecuronium permitted the most stable overall haemodynamic course at all measurement times.

In contrast, patients with AI showed stable haemodynamics after vecuronium, pancuronium and the pancuronium-metocurine mixture; one patient became tachycardic following vecuronium. Atracurium caused unexplained elevations in diastolic and mean arterial pressures which were significant when compared to vecuronium ($p < 0.01$). These resulted in increases in PCWP; mean PA pressures and CVP were also increased. These effects of atracurium in patients with AI need further evaluation.

Key words

NEUROMUSCULAR RELAXANTS: pancuronium, vecuronium, atracurium, metocurine; ANAESTHETICS INTRAVENOUS: fentanyl; ANAESTHESIA: cardiovascular.

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Cardiovascular effects of non-depolarizing neuromuscular blocking drugs related to histamine release or to effects on the autonomic nervous system^{1,2} may be especially important in the anaesthetic management of patients with aortic stenosis or aortic insufficiency. Hypotension and tachycardia are poorly tolerated in aortic stenosis, with early development of myocardial ischaemia, while elevations in blood pressure can increase the regurgitant fraction in aortic insufficiency. Recently, combinations of neuromuscular blockers have been examined permitting use of lower doses with reduction of dose-dependent cardiovascular effects.³ The two new competitive blocking agents, atracurium and vecuronium, have been shown to provide adequate muscular relaxation without significant haemodynamic changes in healthy subjects and patients with coronary artery disease.⁴ The present study was undertaken to compare the cardiovascular responses associated with vecuronium, atracurium and a pancuronium-metocurine mixture with those of pancuronium, when used with high-dose fentanyl anesthesia in patients with aortic valvular stenosis or aortic insufficiency.

Methods

Forty patients with aortic stenosis and 20 patients with aortic insufficiency were studied with informed consent, according to a protocol approved by the Human Subjects Committee. All patients had significant aortic valve disease and were scheduled for elective aortic valve replacement surgery. Thirteen patients with aortic stenosis and five patients with aortic insufficiency had associated coronary artery disease (>75 per cent diameter narrowing in at least one coronary artery). Twenty-four patients with aortic stenosis, and ten with aortic insufficiency were in sinus rhythm; the remaining patients had atrial fibrillation on the baseline ECG. Excluded from the study were patients with significant liver and kidney disease (defined as serum bilirubin and creatinine levels greater than twice normal), other valvular heart disease and those who were clinically unstable (NYHA Class IV). Digitalis, beta adrenergic blocker and calcium channel blocker therapies were continued up to the morning of surgery.

TABLE 1 Preoperative data. Mean $\pm$ SD or number of patients

	Atracurium		Vecuronium		Pancuronium		Pancuronium-metocurine mixture	
	AS	AR	AS	AR	AS	AR	AS	AR
Age (yr)	61 $\pm$ 7	49 $\pm$ 16	58 $\pm$ 7	53 $\pm$ 14	62 $\pm$ 5	54 $\pm$ 14	55 $\pm$ 10	58 $\pm$ 5
Male	5	5	6	4	9	4	8	4
Weight (kg)	78 $\pm$ 14	69 $\pm$ 34	77 $\pm$ 14	78 $\pm$ 14	75 $\pm$ 27	86 $\pm$ 6	79 $\pm$ 10	87 $\pm$ 24
Ao gradient	78 $\pm$ 23		77 $\pm$ 40		67 $\pm$ 31		80 $\pm$ 19	
CAD	4	1	2	2	4	0	3	2
Digitalis	2	2	1	3	3	3	2	4
Beta-blocker	2	1	1	0	4	1	1	2
Ca-antagonist	1	0	2	1	2	1	0	1
Sinus rhythm	5	2	5	4	6	1	8	3

n = 10 for AS; n = 5 for AR. Ao = aortic valve; AS = aortic stenosis; AR = aortic regurgitation; CAD = associated coronary artery disease.

Patients were premedicated with morphine 0.1 mg·kg⁻¹ IM and scopolamine 0.4 mg IM. In each patient, a 20-gauge cannula was inserted in a radial artery, and a triple lumen flow-directed pulmonary artery catheter was introduced into the pulmonary artery. Patients were randomly allocated to one of four study groups as follows: (1) pancuronium 0.12 mg·kg⁻¹ IV; (2) vecuronium 0.12 mg·kg⁻¹ IV; (3) atracurium 0.4 mg·kg⁻¹ IV; (4) pancuronium-metocurine mixture (0.4 mg + 1.6 mg·kg⁻¹); 1 ml/10 kg IV. Anaesthesia was induced with fentanyl 50 µg·kg⁻¹ during administration of 100 per cent O₂. Twenty per cent of the calculated neuromuscular blocker dose was given initially to avoid fentanyl rigidity; immediately thereafter, the remaining drug and fentanyl were given by simultaneous injection. The mean duration of fentanyl and remainder of neuromuscular blocker injection was three minutes. All patients were intubated at the first attempt, without difficulty, after the post-induction measurements were completed.

Baseline (awake) haemodynamic measurements were made when heart rate and blood pressure had stabilized after insertion of intravascular catheters (about five minutes). Measurements at end expiration were repeated at two minutes after induction, and at two and five minutes following intubation. Pressures were measured with transducers zeroed to the mid-axillary line. Systemic, pulmonary arterial and central venous pressures, electrocardiogram lead V₅ and the patient's clinical condition was monitored continually, and electrocardiogram limb leads intermittently.

Haemodynamic measurements were obtained using a computer programmed to record pressures and heart rate at specific times. Cardiac outputs were measured by thermodilution and expressed as the mean from two well-formed curves agreeing within ten per cent. Haemodynamic indices were calculated from pressure and cardiac output measurements according to standard formulae.

Myocardial ischaemia on the ECG was defined as >1 mm ST segment depression occurring in at least three consecutive heartbeats when measured at 80 msec after the J point, using the PR interval of each complex as baseline. The ECG was standardized as 1 mV = 10 mm. Patients were specifically treated if mean arterial pressure fell below 60 mmHg ("severe hypotension"), or heart rates exceeded baseline values by 30 per cent. No other drugs or fluids were given during the study.

Ventilation was assisted manually using 100 per cent oxygen and a mask and, following intubation, controlled with 100 per cent oxygen using the non-rebreathing circuit of an Engstrom ventilator. Respiratory rate and tidal volume were adjusted to maintain PaCO₂ about 40 mmHg. Statistical evaluation was by analysis of variance. Differences between the four neuromuscular blocker groups at the same measurement time were examined by a one-way ANOVA followed by t tests when F was significant. For differences in haemodynamic parameters between sequential measurements and baseline values within the same drug group, a one-way repeated measures ANOVA was performed, followed by paired t tests when F was significant. The significance level used for analysis of variance was the traditional 0.05. Since multiple t tests were performed, a more conservative nominal significant level of 0.01 was used for these pairwise comparisons to adjust in part for the problem of simultaneous statistical inference.^{5,6}

Results

Patients in the four study groups were comparable for age, sex, body weight, aortic valve gradient (in patients with aortic stenosis), presence of coronary artery disease, and preoperative digitalis, beta adrenergic and calcium channel blocker therapy (Table 1). Also, there were no significant differences in baseline haemodynamics be-

FIGURE 1 Induction with fentanyl-atracurium in five patients with chronic aortic regurgitation. Individual patient responses are shown; mean changes in haemodynamic parameters are indicated. (---). SAP = systolic arterial pressure; DAP = diastolic arterial pressure; PA = mean pulmonary artery pressure; other abbreviations as in Table II.

tween groups in patients with aortic stenosis (Table II) or aortic regurgitation (Figures 1 and 2).

Aortic stenosis

Cardiovascular responses to induction and intubation are summarized in Table II. After fentanyl-pancuronium, heart rate increased by 24 per cent which was statistically insignificant compared with a 17 per cent change in the pancuronium-metocurine group. One patient developed tachycardia and severe hypotension after pancuronium and required vasopressor therapy. Intubation resulted in further increases in mean heart rates which were higher than baseline values and, in the pancuronium-metocurine group, were accompanied by significant elevations ($p < 0.01$) in mean arterial pressure. Patients given fentanyl-atracurium showed, on average, an 11 mmHg fall in mean arterial pressure after induction ($p < 0.01$), with a return to baseline values following intubation. One patient de-

TABLE II Haemodynamic measurements (Mean $\pm$ SE) awake, after induction and after intubation in the four muscle relaxant groups in patients with aortic stenosis. All patients were induced with high-dose fentanyl

	Baseline (Awake)	Induction +2 min	Intubation +2 min	Intubation +5 min
HR				
V	73 $\pm$ 5	73 $\pm$ 4	72 $\pm$ 5	66 $\pm$ 6
P	76 $\pm$ 9	94 $\pm$ 10	96 $\pm$ 10	87 $\pm$ 8
A	78 $\pm$ 5	72 $\pm$ 7	75 $\pm$ 7	70 $\pm$ 6
PM	77 $\pm$ 4	90 $\pm$ 4	94 $\pm$ 5	86 $\pm$ 5
MAP				
V	93 $\pm$ 7	97 $\pm$ 6	104 $\pm$ 6	96 $\pm$ 5
P	92 $\pm$ 5	93 $\pm$ 5	97 $\pm$ 6	94 $\pm$ 6
A	90 $\pm$ 2	79 $\pm$ 5*	90 $\pm$ 4	87 $\pm$ 4
PM	95 $\pm$ 5	94 $\pm$ 5	107 $\pm$ 5*	101 $\pm$ 5
PCWP				
V	14 $\pm$ 2	17 $\pm$ 4	21 $\pm$ 5	16 $\pm$ 2
P	16 $\pm$ 3	16 $\pm$ 4	15 $\pm$ 3	9 $\pm$ 1
A	18 $\pm$ 4	15 $\pm$ 2	17 $\pm$ 3	17 $\pm$ 4
PM	13 $\pm$ 2	16 $\pm$ 3	18 $\pm$ 3	17 $\pm$ 3
CVP				
V	6 $\pm$ 1	9 $\pm$ 1	10 $\pm$ 1	10 $\pm$ 1
P	7 $\pm$ 1	10 $\pm$ 1	9 $\pm$ 1	15 $\pm$ 3
A	7 $\pm$ 1	10 $\pm$ 2	10 $\pm$ 1	10 $\pm$ 1
PM	7 $\pm$ 1	10 $\pm$ 1	10 $\pm$ 1	9 $\pm$ 1
CI				
V	3.0 $\pm$ 0.2	2.8 $\pm$ 0.2	2.9 $\pm$ 0.3	2.9 $\pm$ 0.4
P	3.1 $\pm$ 0.2	3.2 $\pm$ 0.2	3.5 $\pm$ 0.2	3.3 $\pm$ 0.3
A	3.1 $\pm$ 0.2	2.9 $\pm$ 0.2	2.9 $\pm$ 0.4	2.8 $\pm$ 0.3
PM	3.0 $\pm$ 0.2	3.0 $\pm$ 0.2	3.3 $\pm$ 0.2	3.4 $\pm$ 0.3
SVR				
V	1306 $\pm$ 124	1419 $\pm$ 157	1496 $\pm$ 165	1422 $\pm$ 179
P	1137 $\pm$ 79	1076 $\pm$ 68	1066 $\pm$ 72	1081 $\pm$ 78
A	1176 $\pm$ 63	1095 $\pm$ 88	1298 $\pm$ 106	1310 $\pm$ 108
PM	1259 $\pm$ 104	1219 $\pm$ 71	1265 $\pm$ 88	1208 $\pm$ 85

V = vecuronium; A = atracurium; P = pancuronium; PM = pancuronium-metocurine mixture; HR = heart rate (beats·min⁻¹); MAP = mean arterial pressure (mmHg); PCWP = pulmonary capillary wedge pressure (mmHg); CVP = central venous pressure (mmHg); CI = cardiac index (L·min⁻¹·m⁻²); SVR = systemic vascular resistance (dyne·sec·cm⁻⁵). * $p < 0.01$ when compared to baseline for the same drug.

veloped severe hypotension requiring vasopressor treatment. Vecuronium, in general, permitted the most stable cardiovascular course in patients with aortic stenosis, with no significant haemodynamic changes being observed at any measurement time.

The per cent increases in heart rate over basal values were higher after induction in patients who had received fentanyl-pancuronium than in those who were given fentanyl-vecuronium (24 per cent vs 0 per cent; $p = 0.04$) or fentanyl-atracurium (24 per cent vs -8 per cent; $p =$

FIGURE 2 Cardiovascular effects (mean $\pm$ SE) of vecuronium ($0.12 \text{ mg} \cdot \text{kg}^{-1}$), pancuronium ($0.12 \text{ mg} \cdot \text{kg}^{-1}$) and pancuronium-metocurine mixture ($0.4 \text{ mg} + 1.6 \text{ mg/ml}$; $1 \text{ ml}/10 \text{ kg}$) in patients with chronic aortic regurgitation. $\circ-\circ$ = vecuronium; $\bullet-\bullet$ = pancuronium; $\triangle-\triangle$ = pancuronium-metocurine mixture. Abbreviations as in Table II.

0.02); the difference persisted at 2 minutes after intubation between the fentanyl-pancuronium and fentanyl-vecuronium groups (26 per cent vs -0.1 per cent). Heart rates also increased more at two minutes after intubation in the pancuronium-metocurine group when compared with those who were given vecuronium (22 per cent vs -0.1 per cent).

Aortic insufficiency

Cardiovascular responses to induction and intubation are summarized in Figures 1 and 2. Significant, unexplained cardiovascular changes occurred in the fentanyl-atracurium group when compared to baseline values. Atracurium was associated with increases in diastolic and mean arterial pressures in four of five patients, along with elevations in left ventricular filling pressures (Figure 1). SVR and cardiac index were unchanged. Mean pulmonary artery pressures also increased resulting in elevations in CVP. These changes were clinically well tolerated. In contrast to patients with aortic stenosis, pancuronium and the pancuronium-metocurine mixture allowed only minimal cardiovascular changes to occur in those with aortic insufficiency (Figure 2). One patient in the fentanyl-vecuronium group showed a tachycardia after induction,

requiring treatment with propranolol; haemodynamics remained stable in the remaining patients in this group.

Comparison between the four neuromuscular blocker groups showed that patients given fentanyl-atracurium had increases in systolic, diastolic and mean arterial pressures with elevations in pulmonary capillary wedge pressures indicating responses that were different ($p = 0.04$) to those who had received fentanyl-pancuronium, in whom systemic pressures fell after induction, with small decreases in left ventricular filling pressures. Similarly, increases in mean arterial pressures in the fentanyl-atracurium group showed a trend that was different ($p = 0.04$) to those who had received fentanyl-vecuronium in whom blood pressures fell minimally. These differences were also clinically well tolerated.

Aortic stenosis vs aortic insufficiency

Atracurium was the only drug associated with significant circulatory differences between the two groups. Thus, increases in systolic, diastolic and mean arterial pressures occurred in aortic insufficiency patients, whereas those with aortic stenosis showed a fall in systemic pressures on induction of anaesthesia.

Satisfactory muscle relaxation for intubation was present in all patients. Fentanyl rigidity was successfully avoided. Continued electrocardiographic monitoring showed no alterations in cardiac rhythm, ST segments or T waves except in one patient with aortic insufficiency who developed frequent PVC's after induction with fentanyl-atracurium.

Discussion

In this study pancuronium, which is a drug commonly used in patients undergoing aortic valve surgery, was compared with atracurium, vecuronium and a pancuronium-metocurine mixture. Doses in excess of ED_{50} were given to provide satisfactory neuromuscular blockade for endotracheal intubation. The potency of vecuronium is equal to or slightly greater than pancuronium ($1-1.74:1$), whereas atracurium is less potent than pancuronium ($0.25-0.33:1$).⁴ Under narcotic-nitrous oxide anaesthesia, vecuronium has been shown to be as potent as pancuronium in producing 95 per cent twitch depression;⁷ hence, equal doses ($0.12 \text{ mg} \cdot \text{kg}^{-1}$) of pancuronium and vecuronium were chosen.⁸ A $1:4$ ratio ($0.4 + 1.6 \text{ mg} \cdot \text{kg}^{-1}$) was used in the pancuronium-metocurine mixture as described by Lebowitz *et al.*³

The contributions of preoperative medication and fentanyl to the observed haemodynamics cannot be distinguished from the cardiovascular effects of the neuromuscular blocker alone, as the latter was given during induction with fentanyl. However, since patient selection, preoperative medications, background anaes-

thetia (fentanyl dose), and times of measurement were standardized, and since the four study groups were comparable regarding preoperative data and baseline haemodynamics, differences in observed haemodynamic responses following induction can be reasonably attributed to the different neuromuscular blockers used. Observations following intubation reflect the cardiovascular differences between the neuromuscular blocker-fentanyl groups when associated with the potent stimulation of laryngoscopy.

Aortic stenosis

Since coronary vascular reserve is limited in the presence of left ventricular hypertrophy,⁹ patients with severe aortic stenosis are more predisposed to myocardial ischaemia when MVO_2 (myocardial oxygen demand) is increased or coronary blood flow (myocardial oxygen supply) is reduced. Tachycardia, which increases MVO_2 and compromises coronary flow by reducing diastolic perfusion time, and hypotension that may further reduce coronary flow, may be expected to cause myocardial ischaemia earlier in patients with aortic stenosis, and hence should be avoided during anaesthesia.

The most striking haemodynamic difference appeared in the HR responses in the fentanyl-pancuronium and the fentanyl pancuronium-metocurine mixture groups when compared to those who had received fentanyl-vecuronium or fentanyl-atracurium. This may be due to the fact that pancuronium, unlike vecuronium or atracurium, has vagolytic effects on cardiac muscarinic receptors,¹⁰ facilitates norepinephrine release,¹¹ and blocks norepinephrine reuptake by sympathetic nerve terminals.¹² In contrast to previous reports,^{1,3} pancuronium-metocurine mixtures did not attenuate HR responses when compared to pancuronium alone. The mean maximum heart rate in our study was 96 beats·min⁻¹ (26 per cent increase over baseline) with pancuronium, and 94 beats·min⁻¹ (22 per cent increase over baseline) with pancuronium-metocurine, unassociated with dysrhythmias or ECG signs of ischaemia. In one patient given pancuronium, tachycardia did result in severe hypotension requiring treatment with propranolol and a vasopressor.

Atracurium has been reported to have minimal haemodynamic effects in both healthy patients¹³ and those with coronary artery disease,¹⁴ although an occasional patient can unpredictably develop hypotension usually ascribed to histamine release.¹⁴ Reductions in SVR following atracurium in our study allowed mean arterial pressures to fall which were clinically well tolerated with one exception.

The greatest haemodynamic stability to induction and intubation was shown in patients given vecuronium with

high-dose fentanyl. This is consistent with previous reports of minimal cardiovascular effects with 0.28 mg·kg⁻¹ vecuronium ($12 \times ED_{50}$) with halothane anaesthesia in patients with coronary artery disease¹⁵ and 0.3 mg·kg⁻¹ vecuronium in healthy, anaesthetized patients.¹⁶

Aortic insufficiency

The magnitude of regurgitant blood flow through an incompetent aortic valve is principally determined by the diastolic pressure gradient between the aorta and left ventricle and the duration of diastole.¹⁷ Increasing the diastolic gradient would increase regurgitation and this should be avoided in the anaesthetized patient. Abridgment of diastole by increasing heart rate usually has little effect on the severity of regurgitation, since only the last part of diastole in which least regurgitant flow occurs would be eliminated.^{17,18}

In our patients, pancuronium, vecuronium and the pancuronium-metocurine mixture were associated with minimal cardiovascular changes when given with high-dose fentanyl, and these anaesthetic techniques were well tolerated with the single exception of tachycardia following vecuronium. It is not clear why an increase in heart rate was not observed in patients with aortic insufficiency when pancuronium or the pancuronium-metocurine mixture was utilized. It is possible that in the pancuronium group, the high baseline heart rate in patients with aortic insufficiency may have prevented a further significant increase in heart rate. However, in the pancuronium-metocurine group, the baseline heart rate was similar to that in the aortic stenosis group. The elevations in systemic and pulmonary arterial pressures after fentanyl-atracurium were also unexpected and remain unexplained. Raised systemic arterial pressure would have increased the diastolic pressure gradient between the aorta and left ventricle, and most likely worsened the magnitude of regurgitant blood flow, resulting in the observed significant elevations in pulmonary capillary wedge pressure. Although only few patients could be studied, this observation occurred in four of five patients. These elevations in arterial pressures also account for the different trends noted with fentanyl-atracurium in patients with aortic insufficiency when compared to those with aortic stenosis in whom blood pressures fell after atracurium.

In summary, we showed that differences in cardiovascular responses occurred after induction with intubating doses of neuromuscular blockers in patients with aortic stenosis. Pancuronium and the pancuronium-metocurine mixture consistently allowed greater increases in heart rates, and reductions in blood pressure occurred with atracurium. Although these were not accompanied with

ECG signs of ischaemia, one patient did develop severe hypotension from the tachycardia associated with pancuronium, suggesting that other neuromuscular blockers should be considered in preference to pancuronium in patients with critical left ventricular outflow obstruction. In contrast, pancuronium and the pancuronium-metocurine mixture permitted stable haemodynamics in aortic insufficiency patients. Also, in the aortic insufficiency group, atracurium caused unexplained elevations in systemic arterial pressure with possible increases in the aortic regurgitant blood fraction. Vecuronium, which does not release histamine or show autonomic effects, was generally associated with the most stable haemodynamic course in our patients.

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Résumé

Afin de comparer les réponses hémodynamiques associées à des doses équipotentes de bloqueurs neuromusculaires et une à dose élevée de fentanyl ($50 \mu\text{g}\cdot\text{kg}^{-1}$), 40 patients avant une sténose de la valve aortique (SA) et 20 patients souffrant d'insuffisance aortique (IA) ont été répartis, de façon aléatoire, en quatre groupes d'étude, afin de recevoir: (1) $0.12 \text{ mg}\cdot\text{kg}^{-1}$ de pancuronium, (2) $0.12 \text{ mg}\cdot\text{kg}^{-1}$ de vécuronium, (3) $0.4 \text{ mg}\cdot\text{kg}^{-1}$ d'atracurium, ou (4) une mixture de pancuronium-métocurine ($0.4 \text{ mg} + 1.6 \text{ mg/ml}$): $1 \text{ ml}/10 \text{ kg}$. On injectait simultanément le fentanyl et bloqueurs neuromusculaires; les données hémodynamiques étaient enregistrées alors que les patients étaient éveillés (valeur témoin) à deux minutes post induction, et à deux et cinq minutes post intubation.

Chez les patients ayant une SA, l'augmentation de la fréquence cardiaque était plus grande avec le pancuronium qu'avec le vécuronium ou l'atracurium; les fréquences cardiaques étaient aussi plus élevées avec la mixture de pancuronium-métocurine qu'avec le vécuronium. Quoiqu'à l'ECG il n'y avait pas de signe d'ischémie, il s'est produit une hypotension grave associée à une tachycardie chez un patient avant reçu du pancuronium. Après l'injection d'atracurium, des réductions dans la RVS ont donné lieu à des diminutions de PAM, petites mais significatives ($p < 0.01$), qui étaient bien tolérées; cependant, il s'est produit une hypotension importante chez un patient. Dans le groupe recevant la mixture de pancuronium-métocurine, l'intubation a entraîné des augmentations significatives ($p < 0.01$) de la PAM. Le vécuronium a donné, dans l'ensemble, l'état hémodynamique le plus stable à tous les temps de mesure.

Par contre, des états hémodynamiques stables se sont manifestés après l'injection de vécuronium, de pancuronium et de mixture de pancuronium-métocurine, chez les patients souffrant de IA; un patient est devenu tachycarde à la suite de l'injection de vécuronium. L'atracurium a causé des élévations inexplicables des pressions diastoliques et artérielles moyennes qui étaient significatives quand on les comparait à celles produites avec le vécuronium ($p < 0.01$). Ces élévations ont entraîné des augmentations de la PCWP; les pressions PA moyennes et PVC ont aussi augmenté. Il est nécessaire de faire une évaluation plus poussée de ces effets de l'atracurium chez les patients souffrant d'IA.