Haemodynamic interactions of muscle relaxants and sufentanil in coronary artery surgery

Dany Côté MD FRCPC, R. Martin MD FRCPC,
J.P. Tétrault MD FRCPC

The haemodynamic interactions between sufentanil (S) and muscle relaxants (MR) were studied in 40 ASA physical status III or IV patients (four groups of ten) scheduled for coronary artery bypass grafting (ABG). Group I received pancuronium (P) 0.08 mg · kg⁻¹, Group II received vecuronium (V) 0.1 mg · kg⁻¹, Group III received atracurium (A) 0.5 mg · kg⁻¹ and Group IV metocurine 0.1 mg · kg⁻¹ plus pancuronium 0.02 mg · kg⁻¹ (M-P). Sufentanil, 20 µg · kg⁻¹ was administered before sternotomy, 10 µg · kg⁻¹ being injected before tracheal intubation and 10 µg · kg⁻¹ afterwards. Heart rate (HR), ECG lead_{II} and V₅, systolic, diastolic and mean arterial and pulmonary blood pressures, central venous pressure (CVP) and pulmonary capillary wedge pressure (W) were measured and recorded at the time of seven strategic events between the pre-induction of anaesthesia period and sternotomy. Cardiac output (CO) and systemic vascular resistances (SVR) were also measured before induction of anaesthesia and after the administration of S 10 µg · kg⁻¹ plus the MR. The HR decreased from baseline values in the post-tracheal intubation period in all groups except in P group. The mean arterial pressure also decreased significantly in all groups except in the P group. The CO did not change from baseline values but SVR decreased in all groups. There was no evidence of new myocardial ischaemia according to the ECG monitoring and there was no significant difference in the HR changes between patients who had or who had not received β-blockers in any group. We conclude that within the present study conditions and design, HR and blood pressure changed least with pancuronium.

Key words

ANAESTHETICS, INTRAVENOUS: sufentanil;
NEUROMUSCULAR RELAXANTS: atracurium, metocurine,
pancuronium, vecuronium;
SURGERY: cardiac.

From the Department of Anaesthesia, University of Sherbrooke.

Address correspondence to: Dr. René Martin, Department of Anesthesia, Centre Hospitalier Universitaire de Sherbrooke, 3001, 12ième Avenue nord, Fleurimont (Québec) J1H 5N4.

Accepted for publication 30th November, 1990.

Les interactions hémodynamiques entre le sufentanil (S) et certains relaxants neuromusculaires (MR) ont été étudiées chez 40 patients (quatre groupes de dix) d'état physique ASA III ou IV, opérés pour un pontage aorto-coronarien. Les patients du groupe I ont reçu du pancuronium (P) à raison de 0,08 mg · kg⁻¹, ceux du groupe II du vecuronium (V) 0,1 mg · kg⁻¹, ceux du groupe III de l'atracurium (A) 0,5 mg · kg⁻¹ et ceux du groupe IV un mélange de métocurine 0,1 mg · kg⁻¹ et de pancuronium 0,02 mg · kg⁻¹ (MP). Une dose totale de 20 µg · kg⁻¹ de S a été donnée avant la sternotomie, 10 µg · kg⁻¹ avant l'intubation endotrachéale et l'autre 10 µg · kg⁻¹ après. La fréquence cardiaque (HR), l'électrocardiogramme (ECG) à deux dérivations (DII et V₅), les tensions artérielles systoliques, diastoliques et moyennes et pulmonaires, la pression veineuse centrale (CVP) et la pression capillaire bloquée (W) ont été mesurées et enregistrées à sept périodes stratégiques à partir de la période pré-induction de l'anesthésie jusqu'à la sternotomie. Le débit cardiaque (CO) et les résistances vasculaires systémiques (SVR) ont également été mesurées avant l'induction et après l'injection de 10 µg · kg⁻¹ de S et du MR. La fréquence cardiaque a diminué par rapport aux valeurs pré-induction de l'anesthésie dans tous les groupes excepté dans le groupe P. La tension artérielle moyenne a également diminué significativement dans tous les groupes excepté dans le groupe P. Le CO n'a pas changé significativement par rapport aux valeurs pré-induction, mais la SVR a diminué dans tous les groupes. Il n'y a pas eu d'évidence d'ischémie myocardique nouvelle à l'analyse de l'ECG. Les patients qui recevaient des β-blocants n'ont pas présenté de fréquence cardiaque statistiquement différente par rapport à ceux qui n'en recevaient pas et ce quelque soit le bloqueur neuromusculaire utilisé. Nous concluons que dans les conditions expérimentales de la présente étude, les patients de groupe pancuronium ont présenté une plus grande stabilité de la fréquence cardiaque et de tension artérielle.

Sufentanil, a highly lipid-soluble narcotic five to ten times more potent than fentanyl,¹ is frequently used for coronary artery bypass grafting.²⁻⁴ It is usually combined with a non-depolarizing muscle relaxant to facilitate tracheal intubation and muscle paralysis during surgery. The muscle relaxants that have been used most commonly are

metocurine or pancuronium⁵ but vecuronium is gaining popularity because it has minimal effect on HR and blood pressure when administered with inhaled anaesthetics or narcotics.⁶ Atracurium also has minimal cardiovascular effects particularly if administered slowly,⁵ and the combination of metocurine with pancuronium has also been recommended.^{7,8}

The main goal during induction of anaesthesia for a patient undergoing CABG is to maintain a stable haemodynamic profile to prevent myocardial ischaemia. This study was undertaken to determine which muscle relaxant when given with high-dose sufentanil produces the greatest cardiovascular stability. Also we attempted to identify those variables, such as pretreatment with β -blockers, which could influence the interactions between sufentanil and the muscle relaxants.

Methods

This study protocol was approved by the ethics committee of our institution and signed consent obtained from the patients. Forty ASA physical status III or IV patients scheduled for elective CABG were studied in a double-blind fashion. The exclusion criteria were valvular disease, left ventricular failure (ejection fraction <50%) or the presence of an obstructed common trunk.

All cardiac medications (β -blockers, calcium channel blocker and nitrates) were continued up to the time of surgery. Patients received premedication with diazepam $0.2 \text{ mg} \cdot \text{kg}^{-1}$ *po* and morphine $0.1 \text{ mg} \cdot \text{kg}^{-1}$ *im* one to five hours before surgery. No *iv* medication was given during the insertion of invasive monitors. Upon arrival in the operating room, ECG monitoring of leads II and V₅ was established, a large caliber *iv* catheter and an arterial radial canula were inserted. A pulmonary artery catheter was placed under local anaesthesia. All baseline values were measured and recorded before induction of anaesthesia. The values recorded were the HR plus a 15 sec recording of ECG V₅, systolic, diastolic and mean arterial pressures, systolic, diastolic and mean pulmonary artery pressures, pulmonary capillary wedge pressure (W), central venous pressure (CVP), cardiac output (CO) and systemic vascular resistances (SVR). The CO was measured in triplicate by thermodilution using injection of 10 ml of room-temperature injectate. All values were measured in the expiratory phase. New myocardial ischaemia was diagnosed when new ST-T segment depression of $\geq 1 \text{ mm}$ at a calibration of $10 \text{ mm} \cdot \text{mv}^{-1}$ was observed.

The 40 patients were randomly divided into four groups according to the muscle relaxant (MR) used. The study was double-blinded and Group I received pancuronium $0.08 \text{ mg} \cdot \text{kg}^{-1}$ (P), Group II received vecuronium $0.1 \text{ mg} \cdot \text{kg}^{-1}$ (V), Group III received atracurium $0.5 \text{ mg} \cdot \text{kg}^{-1}$

(A) and Group IV received metocurine $0.1 \text{ mg} \cdot \text{kg}^{-1}$ plus pancuronium $0.02 \text{ mg} \cdot \text{kg}^{-1}$ (M-P).

The induction of anaesthesia was as follows: at time zero, one-fifth of the calculated dose of muscle relaxant was administered and one minute later S, $10 \mu\text{g} \cdot \text{kg}^{-1}$ was injected over five minutes. When the patient lost consciousness, the remainder of the muscle relaxant was given in a bolus. Tracheal intubation was performed at six minutes. Finally S, $10 \mu\text{g} \cdot \text{kg}^{-1}$ was given over five minutes before skin incision.

The haemodynamic data were recorded before anaesthesia, one minute after the beginning of induction of anaesthesia with S; at the end of the administration of S and MR, one and five minutes after tracheal intubation; one minute after skin incision; and one minute after sternotomy. The cardiac output and systemic vascular resistance were measured only before and after the administration of S plus MR but before tracheal intubation.

All values are expressed as means $\pm$ SD. The haemodynamic values were first analysed by a two-way analysis of variance followed by a Dunnett's test for comparisons, within each group, between the values measured at the time of each event and the values measured in the pre-induction period of anaesthesia. X^2 analysis was used to compare demographic data between groups. Unpaired *t* test was utilized to compare the HR of patients who had or had not received β -blockers within each group. A $P < 0.05$ was considered as statistically significant.

Results

Demographic data are shown in Table I. No significant differences were found among the four groups concerning age, sex, and the presence of cardiac medication (β -blockers or calcium channel blockers). Variations in HR with regard to the pre-induction of anaesthesia values showed a slight increase in the group receiving pancuronium and a significant decrease in groups III (atracurium) and IV (metocurine-pancuronium) ($P < 0.05$). The greatest reduction in HR was observed in the atracurium group (Figure 1). These changes in HR occurred at least seven minutes after the administration of the muscle relaxant, at the time of surgical events. Mean arterial pressures decreased significantly in all groups ($P < 0.05$) except in the pancuronium group. These changes in MAP occurred immediately after the injection of S and MR (Figure 2), before any surgical stimulation, and persisted throughout the surgical events. No statistically significant changes in CO were observed but SVR decreased in all groups, the difference being statistically significant in Group II (V) and IV (M-P) (Table II). Pulmonary artery pressures and pulmonary capillary wedge pressures remained stable.

FIGURE 1 Changes in the heart rate at the time of seven important events from the pre-induction of anaesthesia period to the sternotomy. All values are expressed as means $\pm$ SD. *Different from pre-induction of anaesthesia values within a group ($P < 0.05$ with Dunnett's test).

The ECG strips recorded at the time of the seven events and examined by a blinded observer revealed no new ischaemia in any group.

The only potentially critical incident that occurred during the course of the study was a transitory decrease of systolic blood pressure to 40 mmHg in one patient of the atracurium group. The blood pressure rapidly increased without specific treatment and the outcome was uneventful.

Nearly half the patients in each group were receiving β -blockers (Table I). There was no significant difference in the HR changes between patients who had or had not received β -blockers in any group (Figure 3), except that β -blocker patients in Group III (atracurium) had slower HR than non- β -blocked patients in the pre-induction of anaesthesia period and at the event no. 5.

Discussion

The result of this study suggest that pancuronium in the dosage used and under the conditions of the study was probably the most appropriate relaxant. It did not produce any clinically important increase in HR and was associated with the least decrease in MAP.

Previous studies on the haemodynamic effects of relaxants and sufentanil are contradictory. Severe bradycardia or even asystole have been described in patients who received sufentanil and vecuronium.⁹ Meanwhile other authors have reported haemodynamic stability with S and P, A and V.^{10,11} Several factors influence the interactions between relaxants and sufentanil. First, the dose of muscle relaxant is important. We used the intubation doses recommended by Miller.¹² Pancuronium at $0.08 \text{ mg} \cdot \text{kg}^{-1}$ is sufficient to cause complete neuro-

TABLE I Demographic data of the patients

Groups	Age (yr) Mean $\pm$ S.D.	Sex		β -blockers	Calcium channel blockers
		Male	Female		
I (Pancuronium)	56.7 $\pm$ 7.7	9	1	6	7
II (Vecuronium)	66.1 $\pm$ 8.8	7	3	4	10
III (Atracurium)	61.2 $\pm$ 11.6	6	4	4	7
IV (Metocurine-pancuronium)	61 $\pm$ 9.6	6	4	6	10

FIGURE 2 Changes in mean arterial pressure at the time of seven important events from the pre-induction of anaesthesia period to the sternotomy. All values are expressed as means $\pm$ SD. *Different from pre-induction of anaesthesia values within a group ($P < 0.05$ with Dunnett's test).

muscular blockade and no patient offered resistance to tracheal intubation. Larger dosages of pancuronium could produce more side-effects. A second factor is the dose of sufentanil. Sufentanil, by its central effect, may cause bradycardia.¹³ This parasympathomimetic effect is greater at higher dosage. Therefore high doses probably offer a better protection against the vagolytic effect of pancuronium¹⁴ and accentuate the bradycardia caused by other muscle relaxants. A third possible consideration would be the speed of injection of S. Rapid induction of anaesthesia with high-dose fentanyl led to good haemodynamic stability in one study.¹⁴ In the present protocol, induction of anaesthesia was smooth and this could account for the stability of HR and blood pressure.

Patients for CABG are often receiving β -blockers and

calcium channel blockers. Both of these act on the cardiac conduction system and attenuate the effects of sympathetic stimulation. Most of our patients were receiving calcium channel blockers and approximately 50% in each group were on β -blocker therapy. This therapy did not influence haemodynamic stability in our study contrary to the findings of others.¹⁵ In that study patients who received pancuronium and were not receiving β -blockers were not stable at induction of anaesthesia. These differences could be explained by the fact that almost all the patients in the present study were receiving calcium channel blockers, and by the difference of dose of sufentanil ($5 \mu\text{g} \cdot \text{kg}^{-1}$ versus $10 \mu\text{g} \cdot \text{kg}^{-1}$) and because the patients received scopolamine in premedication in the Zahl and Ellison's study. Our patients also received

TABLE II Cardiac output and systemic vascular resistance

Groups	Cardiac index (mean $\pm$ SD)		Systemic vascular resistance $\text{dynes} \cdot \text{s}^{-1} \cdot \text{cm}^{-5}$	
	Pre-induction	Pre-intubation	Pre-induction	Pre-intubation
I Pancuronium	$2.92 \pm .47$	$2.99 \pm .66$	1249 ± 276	1013 ± 237
II Vecuronium	$2.92 \pm .56$	$2.76 \pm .61$	1298 ± 299	$1069 \pm 214^*$
III Atracurium	$2.77 \pm .64$	$2.8 \pm .967$	1421 ± 602	1110 ± 488
IV Metocurinc-panc.	$2.9 \pm .657$	$2.82 \pm .646$	1606 ± 587	$1084 \pm 302^*$

* $P < 0.05$ (Dunnett's test) (pre-induction of anaesthesia vs pre-tracheal intubation values).

FIGURE 3 Influence of β -blockers on heart rate at the time of seven important events from the pre-induction of anaesthesia period to the sternotomy. (See Figures 1 or 2 for the nature of the events.) *Indicates values statistically different between patients within a group who had or had not received β -blockers pre-operatively ($P < 0.05$ with unpaired t test).

diazepam but only *po* premedication. This might also contribute to the cardiovascular stability observed in the present study if we consider that the *iv* administration of diazepam has been reported to contribute to cardiovascular instability in high-dose fentanyl induction.¹⁶

In conclusion, within the present protocol conditions, pancuronium $0.08 \text{ mg} \cdot \text{kg}^{-1}$, when used to facilitate tracheal intubation, was the muscle relaxant which presented the greatest haemodynamic stability, even in the absence of β -blockers. However, the other muscle relaxants used would be acceptable substitutes since minor haemodynamic changes during anaesthesia do not seem to affect the outcome from CABG.¹⁷

References

- 1 Stoelting RK. Pharmacology and Physiology in Anesthetic Practice. Philadelphia: J.B. Lippincott Company 1987; 86-7.
- 2 Thomson I, Rosenbloom M, Meatherall R. A randomized double blind comparison of fentanyl and sufentanil anaesthesia for coronary artery surgery. Can J Anaesth 1987; 34: 227-32.
- 3 Howie M, McSweeney T, Lingam R, Maschke SP. Comparison of fentanyl- O_2 and sufentanil- O_2 for cardiac anaesthesia. Anesth Analg 1985; 64: 877-87.
- 4 Sanford T, Smith N, Dec-Silber H et al. A comparison of morphine, fentanyl, and sufentanil anaesthesia for cardiac surgery: induction, emergence, and extubation. Anesth Analg 1986; 65: 259-66.
- 5 Stoelting RK. Choice of muscle relaxants in patients with heart disease. Seminars in Anesthesia, 1985; IV: 1-8.
- 6 Baraka A, Ghaya L. Haemodynamic effects of vecuronium in patients with coronary artery disease. Acta Anaesthesiol Scand 1986; 30: 28-9.
- 7 Lebowitz PW, Ramsey FM, Savarese JJ. Potentiation of neuromuscular blockade in man produced by combinations of pancuronium and metocurine or pancuronium and d-tubocurarine. Anesth Analg 1980; 59: 604-9.
- 8 Thomson IR, Putnins CL. Adverse effects of pancuronium during high-dose fentanyl anaesthesia for coronary artery bypass grafting. Anesthesiology 1985; 62: 708-13.

- 9 Starr N, Sethna D, Estafanous F. Bradycardia and asystole following the rapid administration of sufentanil with vecuronium. *Anesthesiology* 1986; 64: 521–3.
- 10 Waldmann C, Wark K, Sebel P, Feneck RO. Hemodynamic effects of atracurium, vecuronium and pancuronium during sufentanil anesthesia for coronary artery bypass. *Acta Anaesthesiol Scand* 1986; 30: 351–6.
- 11 Dhamee MS, Olund T, Reynolds AC, Entress J, Kalbfleish J. Cardiovascular effects of pancuronium, vecuronium, and atracurium during induction of anesthesia with sufentanil and lorazepam for myocardial revascularization. *Journal of Cardiothoracic Anesthesia* 1990; 4: 336–9.
- 12 Miller RD, Savarese JJ. Pharmacology of muscle relaxants and their antagonists. In: Miller RD (Ed.). *Anesthesia*, 2nd ed., vol. 2, New York: Churchill Livingstone Inc. 1986: 897.
- 13 Sanford TJ. A review of sufentanil. *Seminars in Anesthesia* 1988; VII: 127–36.
- 14 Murkin J, Moldenhawer C, Hug C. High-dose fentanyl for rapid induction of anesthesia in patients with coronary artery disease. *Can Anaesth Soc J* 1985; 32: 320–5.
- 15 Kahl K, Ellison N. Influence of β -blockers on vecuronium/sufentanil or pancuronium/sufentanil combination for rapid induction and intubation of cardiac surgical patients. *Journal of Cardiothoracic Anesthesia* 1988; 2: 607–14.
- 16 Tomicheck R, Rosow C, Philbin D. Diazepam-fentanyl interaction – hemodynamic and hormonal effects in coronary artery surgery. *Anesth Analg* 1983; 62: 881–4.
- 17 Moffitt EA, Sethna DH. The coronary circulation and myocardial oxygenation in coronary artery disease: effect of anesthesia. *Anesth Analg* 1986; 65: 395–410.