Catecholamine and cortisol responses to sufentanil-O₂ and alfentanil-O₂ anaesthesia during coronary artery surgery

Simon de Lange MB BS FFARCS,
Theodore H. Stanley MD,
Michael J. Boscoe MB BS FFARCS,
Norbert de Bruijn MD,
Lawrence Berman MD, Orville Green MD,
David Robertson MD

The effects of alfentanil-O₂ and sufentanil-O₂ anaesthesia on plasma catecholamines and cortisol were investigated in 32 patients undergoing coronary artery bypass grafting operations. After lorazepam-atropine premedication and pancuronium pretreatment, alfentanil was given to 16 patients at a rate of 3 mg·min⁻¹ and sufentanil was given to 16 patients at 300 µg·min⁻¹ until the patients were unconscious; at this time they were given succinylcholine and were intubated. After intubation an amount of alfentanil or sufentanil equal to the dose producing unconsciousness was infused over the next 30 min, at which time the operation began. Additional alfentanil or sufentanil were given whenever systolic arterial blood pressure increased more than 15 per cent of preanaesthetic values. Arterial blood samples were obtained for epinephrine, norepinephrine and cortisol assay and cardiovascular dynamics were recorded prior to anaesthetic induction, 5 min after tracheal intubation, immediately prior to and five min after incision, ten min after maximal sternal

spread, just prior to beginning and after 30 and 60 min of bypass and at the end of operation. Cardiovascular dynamics were little changed throughout anaesthesia and operation. Plasma epinephrine and norepinephrine were not significantly changed until bypass. During bypass both hormones became increased and remained increased at the end of operation. Plasma cortisol decreased after incision and remained decreased until the end of operation. These data indicate that alfentanil-O₂ and sufentanil-O₂ anaesthesia produce similar changes in plasma catecholamines and cortisol as does fentanyl-O₂ anaesthesia and hormonal effects are, therefore, not an explanation for any advantages the newer narcotics may have over fentanyl.

Key words

ANALGESICS: sufentanil, alfentanil, fentanyl;

ANAESTHESIA: cardiovascular; HORMONES: corticosteroid, catecholamine.

From the Departments of Anesthesiology, The University Hospital of Leiden, the Netherlands, The University of Utah School of Medicine, Salt Lake City, Utah, Vanderbilt University Medical School, Nashville, Tennessee, Department of Medicine, Vanderbilt University Medical School, Nashville, Tennessee, and Department of Pediatrics, Northwestern University, Evanston, Illinois.

Address correspondence to: Dr. Theodore H. Stanley, Department of Anesthesiology, The University of Utah School of Medicine, 50 North Medical Drive, Salt Lake City, Utah 84132.

Supported in part by Stanley Research Foundation, Salt Lake City, Utah and Janssen Pharmaceutica, New Brunswick, New Jersey.

Sufentanil-O₂ and alfentanil-O₂ anaesthesia have been suggested as alternatives to high dose fentanyl-O₂ for patients undergoing coronary-artery bypass open-heart operations.¹⁻⁵ The major advantages of alfentanil are its rapid onset of action, allowing a fast curtailment of an evoked cardiovascular stress response, and its short duration (fast recovery).^{3,6,7} The advantages of sufentanil are its higher potency and tighter binding to central nervous system opiate receptors than fentanyl. Both of the latter have been suggested as reasons why sufentanil results in a greater blockade of cardiovascular stress responses during operation and an enhancement of cardiovascular stability than comparable doses of fentanyl.^{1,2,6,7}

High dose fentanyl- O_2 anaesthesia decreases or does not change plasma catecholamines, cortisol and anti-diuretic hormone (ADH) in patients undergoing coronary artery bypass graft (CABG) operations up until cardiopulmonary bypass.⁸⁻¹¹ During bypass plasma catecholamines and ADH are usually markedly elevated⁸⁻¹⁰ and this is occasionally associated with severe hypertension (de Lange S., unpublished data). Recent studies suggest that alfentanil- O_2 and sufentanil- O_2 anaesthesia may be superior to high-dose fentanyl- O_2 because hypertension occurs less frequently.^{1,5} In an attempt to explain why anaesthesia with the new synthetic opioids is more effective in preventing intraoperative hypertension we measured plasma ADH and growth hormone in patients undergoing coronary artery surgery. These particular hormones were chosen because they are usually elevated when the other "stress responding hormones," e.g. the catecholamines, cortisol, are increased during anaesthesia and/or surgery and they require smaller blood samples and are cheaper and easier to analyze. Our data indicated that in contrast to fentanyl- O_2 anaesthesia alfentanil- O_2 and sufentanil- O_2 blocked increases in plasma ADH and growth hormone during and after cardiopulmonary bypass, indeed throughout the entire operation.¹²

As a result of these and our previous findings and because the effects of anaesthetic doses of alfentanil and sufentanil on plasma catecholamines and cortisol in patients undergoing CABG operations have not been reported they were investigated in 32 patients in this study.

Methods

Institutional approval was obtained* and all patients provided informed consent at the preoperative visit. Thirty-two patients (16 in each group) were randomly selected to receive alfentanil- O_2 (Group I) or sufentanil- O_2 (Group II) as the sole anaesthetic agent. Patients were ASA Class III and were scheduled to undergo multiple-vessel elective coronary-artery bypass operations. All patients were receiving propranolol (80–120 mg, PO, in divided doses) and all but four (two in each group) were taking nitroglycerin or some other orally administered vasodilator, on occasion, for angina.

All patients were premedicated with lorazepam

(0.08 mg·kg⁻¹, PO) and their usual morning dose of propranolol two hours preoperatively and atropine* (0.1 mg·15 kg⁻¹, IM) 30 min before arrival in the operating room. Upon arrival in the induction room, catheters were placed in a hand vein and a radial artery and a bipolar lead II electrocardiogram was continuously recorded. Prior to induction of anaesthesia, a flow-directed balloon tipped thermodilution pulmonary artery catheter (Instrumentation Laboratories triple lumen 110 cm model 44166 7F) was introduced into the pulmonary artery through an antecubital vein in an upper extremity using a 7 Fr Cordis Introducer.

After a five-minute stabilization period (or somewhat longer if haemodynamics had not returned to pre-pulmonary artery insertion values), and during oxygen breathing, control measurements of heart rate (beats/min), cardiac output (l/min)†, systolic and mean arterial (kPa) and mean pulmonary artery (kPa) pressures were made‡ and a control arterial blood sample obtained for hormonal analysis. Two minutes later pancuronium (1.5 mg/70 kg) was administered intravenously. Three minutes after pancuronium, Group I patients were given alfentanil at 3.0 mg/min and Group II patients sufentanil at 300 µg/min, intravenously.§ Respirations were first spontaneous, then assisted and finally controlled (using a face mask and semi-closed system),

*Atropine is a routine premedication in all our patients about to receive a high dose narcotic anaesthetic because in these intra-muscular doses it does not increase heart rate but does minimize vagal-induced decreases in heart rate which can significantly decrease cardiac output both in man and (using comparable doses of atropine) in animals.

†Measured via thermodilution with 10 ml of 10–15°C dextrose, five per cent in water, as the injectate.

‡Mean pulmonary artery capillary wedge pressures were measured and recorded but are not presented because in four patients it was not possible to clearly wedge the catheter prior to inducing anaesthesia and in four other patients reliable wedge pressures could not be obtained at all of the study prescribed intervals. However, in patients in which pulmonary wedge pressures were obtained throughout the study, there appeared to be few changes at the measuring periods.

§These infusion rates were chosen on the basis of previous experience which suggested they were optimal in terms of minimizing muscle rigidity and maximizing speed of induction.

*From the University Hospital of Leiden Ethics Committee.

to maintain PaCO_2 at 35–40 torr (as measured in radial arterial blood every 15–30 minutes or estimated via continuous end tidal PCO_2 analysis). During infusion of alfentanil and sufentanil patients were requested to open their eyes and/or take a deep breath every five to ten sec. Failure to respond to three consecutive requests was equated with unconsciousness. When unconscious, the patients were paralyzed with intravenous succinylcholine ($1.5 \text{ mg} \cdot \text{kg}^{-1}$) and their tracheas intubated with a cuffed Portex tracheal tube. After intubation an amount of alfentanil or sufentanil equal to the dose producing unconsciousness was infused over the next 30 min. Additional alfentanil (2.5 mg bolus doses) or sufentanil ($50 \mu\text{g}$ bolus doses) was given intravenously throughout operation whenever systolic arterial blood pressure increased 15 per cent or more of control values. During bypass additional alfentanil and sufentanil were given when mean arterial blood pressure increased 10 per cent or more above control values.

Patients were paralyzed with pancuronium ($0.08 \text{ mg} \cdot \text{kg}^{-1}$ slowly intravenously) 15 minutes after they had received succinylcholine. Paralysis was maintained with $0.04 \text{ mg} \cdot \text{kg}^{-1}$ increments of pancuronium every 45–60 minutes, until cardiopulmonary bypass. A saline-glucose solution (4.5 per cent glucose and one per cent normal saline in water) was administered at a rate of 1000 ml/h during preanaesthetic preparations and 200–250 ml/h throughout the remainder of the operation. Whole blood was given after cardiopulmonary bypass and in the postoperative period to maintain right atrial pressure and/or pulmonary artery diastolic pressure at preanaesthetic values. The extracorporeal system was primed with Ringer's solution (1500 ml) and glucose five per cent in water (500 ml) and 500 ml of a solution containing 100 g of albumin and 5000 units of heparin. Patients were cooled to 26–28° during extracorporeal support and rewarmed to 37° C at its conclusion. Extra-corporeal perfusion was maintained at flows necessary to keep mixed venous PO_2 (obtained at the common venous inlet to the oxygenator) at normal (37–43 torr, 4.9–5.7 kPa, corrected for temperature) values.

The surgical procedure began 30 minutes after anaesthetic induction and intubation. Arterial blood samples were obtained for catecholamine and cortisol assay and cardiovascular dynamics were recorded prior to anaesthetic induction (while the pa-

tients were breathing oxygen), five minutes after tracheal intubation, immediately prior to incision, five minutes after incision, ten minutes after maximal sternal spread, just prior to beginning cardiopulmonary bypass, after 30 and 60 minutes of bypass and at the end of operation when the patient was still unconscious prior to movement from the operating table. A 9.5 ml blood sample was obtained from the radial artery catheter via a 10-ml syringe filled with 0.5 ml heparin (1000 units/ml) at each sampling period. The 10-ml blood sample was divided into 4- and 6-ml subsamples. The 6-ml sample (for catecholamine assay) was injected into a special Vacutainer tube containing glutathione and EGTA (EGTA = ethylene-glycol-bis[β -aminoethyl] - N, N' tetraacetic acid). Both samples were then placed in an ice-water bath for ten min and centrifuged in a refrigerated centrifuge to separate plasma from cells. The plasma was removed with a Pasteur pipette, placed in a screw-topped vial, and frozen at -20° until analyzed. Blood samples were analyzed for plasma cortisol using radioimmunoassay¹³ (coefficient of variation = eight per cent; sensitivity = $0.1 \mu\text{g} \cdot 100 \text{ ml}$) and for epinephrine and norepinephrine with radioenzymatic assay^{14,15} (coefficients of variation = ten and nine per cent; sensitivity = 25 and $30 \text{ pg} \cdot \text{ml}$, respectively). No corticosteroids or catecholamines were given to patients during anaesthesia or operation (the study period); however, phentolamine or nitroprusside was occasionally used for short periods to treat hypertension not responsive to additional sufentanil and alfentanil.¹

Data were analyzed for statistical significance utilizing analysis of variance, and Student's unpaired t test. $P < 0.05$ was considered statistically significant.

Results

The ages (53 ± 9)*, weights ($72 \pm 7 \text{ kg}$)*, preoperative cardiovascular dynamics,* preoperative plasma epinephrine,* norepinephrine* and cortisol concentrations* and the duration of operation ($6 \pm 0.2 \text{ hrs}$, mean $\pm$ SD)* were similar in the two groups (Table I). Unconsciousness was provided by an average of $42 \pm 9 \mu\text{g} \cdot \text{kg}^{-1}$ of alfentanil and $4.0 \pm 0.6 \mu\text{g} \cdot \text{kg}^{-1}$ of sufentanil. Narcotic requirements for

*Student's unpaired t test.

TABLE I Cardiovascular and hormonal responses to sufentanil-O₂ and alfentanil-O₂ anaesthesia during coronary artery surgery (Mean $\pm$ SD)

		Control	Intubation	Prior to Incision	After Incision	Maximal Sternal Spread	Bypass		End of Operation
							30 min.	60 min.	
Heart Rate (beats/min)	Sufentanil	65 $\pm$ 7	63 $\pm$ 6	61 $\pm$ 6	64 $\pm$ 6	66 $\pm$ 7	65 $\pm$ 7	—	73 $\pm$ 8
	Alfentanil	64 $\pm$ 7	63 $\pm$ 7	61 $\pm$ 6	65 $\pm$ 6	67 $\pm$ 7	68 $\pm$ 8	—	73 $\pm$ 8
Cardiac Output (l/min)	Sufentanil	5.3 $\pm$ 0.8	5.2 $\pm$ 0.7	5.2 $\pm$ 0.8	5.3 $\pm$ 0.8	5.4 $\pm$ 0.7	5.4 $\pm$ 0.7	4.3 $\pm$ 0.4	5.8 $\pm$ 0.9
	Alfentanil	5.2 $\pm$ 0.7	5.1 $\pm$ 0.7	5.0 $\pm$ 0.8	5.2 $\pm$ 0.7	5.3 $\pm$ 0.7	5.4 $\pm$ 0.7	4.2 $\pm$ 0.5	5.8 $\pm$ 0.8
Systolic Arterial Blood Pressure (kPa)	Sufentanil	16.6 $\pm$ 1.6	16.1 $\pm$ 1.7	16.2 $\pm$ 1.5	16.5 $\pm$ 2.0	16.8 $\pm$ 1.3	17.0 $\pm$ 1.5	—	17.4 $\pm$ 1.9
	Alfentanil	16.4 $\pm$ 1.5	16.0 $\pm$ 1.6	15.8 $\pm$ 1.6	16.8 $\pm$ 1.5	18.4 $\pm$ 1.7#	17.3 $\pm$ 1.2	—	17.6 $\pm$ 1.7
Mean Arterial Blood Pressure (kPa)	Sufentanil	11.6 $\pm$ 1.1	11.2 $\pm$ 1.2	11.2 $\pm$ 1.1	11.4 $\pm$ 1.2	11.6 $\pm$ 1.2	11.7 $\pm$ 1.2	9.4 $\pm$ 1.2#	11.8 $\pm$ 1.1
	Alfentanil	11.2 $\pm$ 0.9	11.2 $\pm$ 1.1	11.2 $\pm$ 1.2	11.8 $\pm$ 1.3	12.1 $\pm$ 1.2	11.7 $\pm$ 1.1	9.3 $\pm$ 1.1#	12.0 $\pm$ 1.2
Mean Pulmonary Artery Pressure	Sufentanil	2.1 $\pm$ 0.3	2.0 $\pm$ 0.3	1.9 $\pm$ 0.3	2.0 $\pm$ 0.3	2.1 $\pm$ 0.4	2.0 $\pm$ 0.3	—	2.1 $\pm$ 0.3
	Alfentanil	2.0 $\pm$ 0.3	2.0 $\pm$ 0.3	1.9 $\pm$ 0.3	1.9 $\pm$ 0.3	2.0 $\pm$ 0.3	1.7 $\pm$ 0.4	—	2.1 $\pm$ 0.3
Epinephrine (pg/ml)	Sufentanil	51 $\pm$ 9	53 $\pm$ 9	46 $\pm$ 8	42 $\pm$ 9	43 $\pm$ 9	42 $\pm$ 8	225 $\pm$ 30*	178 $\pm$ 27*
	Alfentanil	48 $\pm$ 8	49 $\pm$ 8	44 $\pm$ 7	39 $\pm$ 8	44 $\pm$ 9	41 $\pm$ 8	179 $\pm$ 28*	161 $\pm$ 26*
Norepinephrine (pg/ml)	Sufentanil	181 $\pm$ 17	178 $\pm$ 16	170 $\pm$ 17	174 $\pm$ 17	167 $\pm$ 17	164 $\pm$ 17	395 $\pm$ 39*	537 $\pm$ 37*
	Alfentanil	168 $\pm$ 19	164 $\pm$ 18	161 $\pm$ 16	159 $\pm$ 17	158 $\pm$ 16	155 $\pm$ 17	386 $\pm$ 36*	524 $\pm$ 34*
Cortisol (μ g/dl)	Sufentanil	15 $\pm$ 2	12 $\pm$ 2	12 $\pm$ 2	7 $\pm$ 2*	6 $\pm$ 1*	7 $\pm$ 2*	5 $\pm$ 1*	16 $\pm$ 3
	Alfentanil	13 $\pm$ 2	9 $\pm$ 3	10 $\pm$ 2	7 $\pm$ 2*	7 $\pm$ 1*	7 $\pm$ 2*	5 $\pm$ 1*	15 $\pm$ 3

#P < 0.05, *P < 0.01, analysis of variance when compared to control values.

the entire operation averaged 1.0 ± 0.2 mg·kg of alfentanil and $12.8 \mu\text{g}\cdot\text{kg}$ of sufentanil.

Cardiovascular dynamics were minimally altered throughout operation in both groups when measured at the pre-set measuring periods (Table I). The only significant changes occurred in the alfentanil group ten minutes after maximal sternal spread when systolic arterial blood pressure became significantly increased and in both groups during bypass when mean arterial blood pressures were significantly decreased when compared to control values.* In spite of relatively similar cardiovascular recordings at prescribed intervals, we found sufentanil easier to use than alfentanil. The reason for this was that bolus doses of alfentanil had to be given much more frequently to treat surgical-manipulation-induced increases in systolic blood pressure than with sufentanil. In addition, sudden increases of arterial blood pressure with maximum surgical stimulation occurred more often during alfentanil anaesthesia. While these increases rapidly responded to additional alfentanil, so that mean readings obtained at most prescribed study intervals were not different from control values, the anaesthetic course was smoother with sufentanil because there were rarely rapid increases in arterial pressure and thus rarely need for additional narcotic at similar stressful periods.

Plasma cortisol, epinephrine and norepinephrine concentrations were unchanged by anaesthetic induction or tracheal intubation in both patient groups (Table I). Plasma concentrations of epinephrine and norepinephrine remained unchanged from control values until cardiopulmonary bypass in both groups, when they were significantly increased. Plasma concentrations of these hormones remained elevated throughout bypass and at the end of operation. Plasma cortisol concentrations became significantly decreased at the time of incision in both groups when compared to control values. Plasma cortisol concentrations remained decreased until the end of operation in both groups when they returned to normal control values.

Discussion

The results of this study demonstrate that sufentanil- O_2 and alfentanil- O_2 anaesthesia result in stable cardiovascular dynamics, block increases in plasma

cortisol throughout operation and prevent increases in plasma catecholamines up to but not during or after cardiopulmonary bypass in patients undergoing coronary artery surgery. These findings are similar to those that have been reported by Stanley *et al.*⁹ and Sebel *et al.*¹⁰ with high dose fentanyl ($70\text{--}100 \mu\text{g}\cdot\text{kg}^{-1}$) and oxygen anaesthesia in similar groups of patients and are disappointing because earlier studies¹² had indicated that large (anaesthetic) doses of sufentanil and alfentanil were capable of blocking rises in antidiuretic (ADH) and human growth hormones (HGH) throughout operation, including bypass. No other anaesthetic, including fentanyl, even in massive doses ($200 \mu\text{g}\cdot\text{kg}^{-1}$, Stanley TH, unreported data) has been able to block increases in ADH and HGH during and after bypass. It was reasoned on the basis of the earlier hormonal studies,¹² other data demonstrating less intra-operative hypertension before, during and after bypass with sufentanil- O_2 than fentanyl- O_2 ¹ and similar, recent findings with alfentanil- O_2 ⁵, that the newer narcotics were more effective in blocking hormonal stress responses during periods of severe physiological stress, e.g., bypass, than fentanyl. Furthermore, we thought that the explanation for the greater stability in cardiovascular dynamics with the newer narcotics, as compared to high dose fentanyl, might be related to lower plasma catecholamine concentrations throughout operation. Comparison of the catecholamine data in this study with that obtained in our previous investigation with fentanyl⁹ shows no statistical difference in absolute plasma epinephrine and norepinephrine concentrations nor in changes in concentrations of these hormones at similar intervals during the study period.

The metabolic response to general anaesthesia and surgery with most general anaesthetics is similar to the human physiological response to many kinds of stress and usually consists of marked increases in a number of hormones including the catecholamines, ADH, HGH, cortisol, renin, angiotensin and aldosterone, as well as rises in blood glucose, lactate and pyruvate.^{16,17} Cardiopulmonary bypass has always been considered an even greater physiological stress than operation because all the stress hormones and metabolites are further increased during this period.^{10,18,19} That some anaesthetic techniques (spinal and epidural anaesthesia) can block operative induced hormonal stress

*One way analysis of variance.

responses (at least as long as the anaesthetic is present) is generally considered desirable,^{20,21} for increases in the stress hormones can cause arrhythmias, unwanted cardiovascular stimulation and catabolism (protein and amino acid breakdown).^{20,21} While there are no data which indicate that blockade of intraoperative hormonal stress responses lasts postoperatively when the anaesthetic is gone, it was hoped, especially after large doses of fentanyl were shown to block hormonal stress responses during open-heart operations, that some of this blockade would last postoperatively. Unfortunately, a recent study by Walsh *et al.*²² confirms that it does not.

Although sufentanil and alfentanil do not block increases in plasma catecholamines during and after cardiopulmonary bypass they do result in more stable haemodynamics and less need for vasodilators and other anaesthetic adjuvants throughout operation including bypass than comparable doses of fentanyl in patients undergoing coronary artery bypass operations.^{1,5} Whether the reason for this is related to greater blockade of ADH and HGH responses, greater blockade of the other stress hormones (renin, angiotensin, aldosterone, etc.) which could not be measured during this investigation, to intrinsic properties of the molecules themselves, or other factors, is unknown.

Plasma cortisol was decreased after the operation began and remained so until the end of operation in this study. These data are similar to what we⁹ and others^{10,11} have found during high-dose fentanyl anaesthesia. In patients undergoing open-heart surgery with halothane, plasma cortisol is increased during operation.¹⁰ Similarly, patients anaesthetized with morphine (1–2 mg·kg⁻¹) plus nitrous oxide experience increases of plasma cortisol with operation.²³ However, if the morphine dosage is increased to 4 mg·kg⁻¹ and combined with N₂O, plasma cortisol decreases. These findings, combined with our results in this and our previous study, suggest that cortisol responses to operation are easier to block with narcotics than catecholamine responses. We believe, on the basis of this investigation and our previous studies with fentanyl, sufentanil and alfentanil^{8,9,12} that HGH and ADH responses to surgical stress are more difficult to block with narcotic anaesthesia than cortisol responses but easier than catecholamine responses. If this is true, it indicates that some of the stress

responding hormones are more sensitive to blockade by anaesthetics than others. It also suggests that there may be other narcotics, narcotic administration techniques or anaesthetic compounds capable of completely blocking the metabolic response to all kinds of surgical stress. If and when such compounds are found, it should be possible to determine what, if any, clinical advantages they possess as anaesthetics for patients during and after open-heart surgery.

In conclusion, the results of this study demonstrate that sufentanil-O₂ and alfentanil-O₂ result in similar changes in plasma catecholamines and cortisol during coronary artery surgery as does fentanyl-O₂ anaesthesia. Although previous studies had suggested greater cardiovascular stability and blockade of hormonal stress responses with sufentanil-O₂ and alfentanil-O₂ than fentanyl-O₂ anaesthesia, our data do not confirm that the mechanism of greater cardiovascular stability is due to a different action of the newer narcotics on plasma catecholamines or cortisol.

References

- 1 de Lange S, Stanley TH, Bosco MJ. Comparison of sufentanil-O₂ and fentanyl-O₂ for coronary artery surgery. *Anesthesiology* 1982; 56: 112–8.
- 2 Sebel P, Bovill J. Cardiovascular effects of sufentanil. *Anesth Analg* 1982; 61: 115–9.
- 3 de Lange S, Stanley TH, Boscoe MJ. Alfentanil-oxygen anaesthesia for coronary artery surgery. *Br J Anaesth* 1981; 53: 1291–6.
- 4 Nauta J, de Lange S, Koopman D, Spierdijk J, Van Kleef J, Stanley TH. Anesthetic induction with alfentanil: A new short-acting narcotic analgesic. *Anesth Analg* 1982; 61: 267–272.
- 5 de Lange S, de Bruijn N, Stanley TH, Boscoe MD. Alfentanil-oxygen anaesthesia: Comparison of continuous infusion and frequent bolus techniques for coronary artery surgery. *Anesthesiology* 1981; 55: A42.
- 6 de Castro J, Van de Water A, Wouters L, Xhonneux R, Reneman R, Kay B. Comparative study of cardiovascular, neurological and metabolic side effects of eight narcotics in dogs. *Acta Anaesthesiol Belg* 1979; 30: 5–99.
- 7 de Castro J. Practical application and limitation of analgesic anaesthesia. *Acta Anaesthesiol Belg* 1976; 27: 107–28.
- 8 Stanley TH, Philbin DM, Coggins CH. Fentanyl-

- oxygen anaesthesia for coronary artery surgery. Cardiovascular and anti-diuretic hormone responses. *Can Anaesth Soc J* 1979; 26: 168-71.
- 9 Stanley TH, Berman L, Green O, Robertson D. Plasma catecholamine and cortisol responses to fentanyl-oxygen anaesthesia for coronary artery operations. *Anesthesiology* 1980; 53: 250-3.
 - 10 Sebel PS, Bovill JG, Schellekens APM, Hawker CD. Hormonal responses to high-dose fentanyl anaesthesia. A study in patients undergoing cardiac surgery. *Br J Anaesth* 1981; 53: 941-8.
 - 11 Kono K, Philbin DM, Coggins CH, et al. Renal function and stress response during halothane or fentanyl anaesthesia. *Anesth Analg* 1981; 60: 552-7.
 - 12 de Lange S, Stanley TH, Boscoe MJ. Antidiuretic hormone responses during coronary artery surgery with sufentanil-oxygen and alfentanil-oxygen in man. *Anesth Analg* 1982; 61: 434-8.
 - 13 Ruder JH, Guy RW, Lipsitt MB. A radiometric assay for cortisol in plasma and urine. *J Clin Endocrinol Metab* 1972; 35: 219-24.
 - 14 Passon TG, Peuler JD. A simplified radioimmunoassay for plasma norepinephrine and epinephrine. *Anal Biochem* 1973; 51: 618-31.
 - 15 Robertson D, Frolich JC, Carr KK, et al. Effects of caffeine on plasma renin activity, catecholamines and blood pressure. *N Engl J Med* 1978; 298: 181-6.
 - 16 Hall G, Young C, Holdcroft A, Alaugband-Zadek K. Substrate mobilization during surgery: A comparison between halothane and fentanyl anaesthesia. *Anaesthesia* 1978; 33: 924-30.
 - 17 Forence A. Attenuation of stress and haemodynamic stability, *Stress-Free Anaesthesia*. Edited by Wood, C., New York, Grune and Stratton, 1979, pp 23-25.
 - 18 Anton AH, Gravenstein JS, Wheat MW. Extracorporeal circulation and endogenous epinephrine and norepinephrine in plasma, atrium and urine in man. *Anesthesiology* 1964; 25: 262-9.
 - 19 Replogle R, Levy M, De Walt RA, Lillikie RC. Catecholamine and serotonin response to cardiopulmonary bypass. *J Thorac Cardiovasc Surg* 1962; 44: 638-48.
 - 20 Kehlet H, Brandt MR, Hansen AP, Alberti KGMM. Effect of epidural analgesia on metabolic profiles during and after surgery. *Br J Surg* 1979; 66: 543-9.
 - 21 Traynor C, Hall GM. Endocrine and metabolic changes during surgery: anaesthetic complications. *Br J Anaesth* 1981; 53: 153-60.
 - 22 Walsh ES, Paterson JL, O'Riordan JBA, Hall GM. Effect of high dose fentanyl anaesthesia on the metabolic and endocrine responses to cardiac surgery. *Br J Anaesth* 1981; 53: 1155-65.
 - 23 George JV, Reier CE, Lanese RR, Rower JM. Morphine anaesthesia blocks cortisol and growth hormone response to surgical stress in humans. *J Clin Endocrinol Metab* 1974; 38: 736-41.

Résumé

Les effets de l'anesthésie avec de l'alfentanil-O₂ et du sulfentanil-O₂ sur le plasma catécholamine et cortisol ont été étudiés chez 32 patients subissant un pontage aorto-coronarien. Après une prémédication de lorazépam-atropine et un traitement au pancuronium, de l'alfentanil fut administré à seize patients en dose de 3 mg·min⁻¹ et du sulfentanil en dose de 300 µg·min⁻¹ fut administré aux seize autres patients jusqu'à ce qu'ils s'endorment. Ensuite on leur donna de la succinylcholine et on procéda à l'intubation trachéale. Après l'intubation, une dose d'alfentanil ou de sulfentanil égale à la dose utilisée pour les endormir fut injectée pendant les 30 minutes suivantes et on commença l'intervention chirurgicale. Lorsque la tension artérielle augmentait à plus de 15 pour cent des taux préanesthésiques, on ajoutait un supplément d'alfentanil ou de sulfentanil. Des prélèvements de sang artériel furent obtenus pour l'analyse de l'épinéphrine, de la norépinéphrine et du cortisol et la dynamique cardio-vasculaire fut notée avant l'induction de l'anesthésie, cinq minutes après l'intubation trachéale, immédiatement avant et cinq minutes après l'incision, dix minutes après l'extension sternale maximum, juste avant le début et après 30 minutes et 60 minutes du pontage cardio-pulmonaire et à la fin de l'opération. La dynamique cardio-vasculaire changea peu pendant la durée de l'anesthésie et de l'opération. Le plasma épinéphrine et norépinéphrine ne changèrent pas significativement jusqu'au moment du pontage. Pendant le pontage les deux hormones s'accrochèrent et continuèrent ainsi jusqu'à la fin de l'opération. Le plasma cortisol diminua après l'incision et continua ainsi jusqu'à la fin de l'opération. Ces données indiquent que l'alfentanil-O₂ et le sulfentanil-O₂ pour l'anesthésie engendrent des changements dans le plasma catécholamine et cortisol comme l'anesthésie avec le fentanyl-O₂ et ne procure aucune explication sur les avantages que les nouveaux narcotiques peuvent avoir sur le fentanyl.