

Comparison of Sufentanil-O₂ and Fentanyl-O₂ for Coronary Artery Surgery

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The cardiovascular responses, speed of anesthetic induction, incidence of chest wall rigidity, need for anesthetic supplements (phenolamine, N₂O, and nitroprusside) to control intraoperative hypertension and speed of postoperative recovery were measured and compared in 37 patients undergoing coronary artery bypass grafting (CABG) operations with fentanyl-O₂ (Group I) or sufentanil-O₂ (Group II) anesthesia. After lorazepam-atropine premedication and pancuronium pretreatment, fentanyl was administered intravenously at 400 µg/min and sufentanil at 300 µg/min until patients were unconscious; at this time they were given succinylcholine and their tracheas were intubated. After intubation an amount of fentanyl or sufentanil equal to the dose producing unconsciousness was infused over the next 30 min, at which time the operation began. Additional fentanyl or sufentanil was given whenever systolic arterial blood pressure (SBP) increased more than 15 per cent of preanesthetic values. When three successive supplemental doses of the narcotic failed to effectively decrease SBP, phenolamine was used to control pressure before and during bypass; after bypass N₂O (25-50 per cent) or, if N₂O was ineffective, nitroprusside was used. Average time of induction was 4.6 ± 0.5 and 1.3 ± 0.3 min (mean ± SD) for fentanyl and sufentanil, respectively. Chest wall rigidity occurred in 22 per cent of patients receiving fentanyl and 28 per cent of those receiving sufentanil. Total doses of fentanyl and sufentanil required for the entire operation were 122 ± 15 and 12.9 ± 0.5 (mean ± SD) µg/kg, respectively. Heart rate, cardiac output, and mean right atrial pressure remained unchanged throughout the study in both groups. SBP was reduced slightly in both groups during induction but returned to control values prior to incision. Group II patients experienced no significant change in SBP after incision, sternotomy, or sternal spread, whereas SBP became significantly increased following sternal spread in patients given fentanyl. Phenolamine was required in 42 and 47 per cent of Group I patients before and during bypass, respectively, but in only 6 and 11 per cent of Group II patients. Fifty-three per cent of Group I patients required N₂O, and 21 per cent required nitroprusside after bypass for blood pressure control. Only 11 per cent of Group II required N₂O and 6 per cent required nitroprusside post-bypass. Hypertension requiring supplementation with phenolamine, N₂O, or nitroprusside occurred more frequently in patients not taking preoperative beta-adrenergic blockers than in

those taking these drugs in Group I. Hypertension requiring supplementation never occurred in patients in Group II taking beta-blockers. The results of this study demonstrate that sufentanil may be a superior narcotic to fentanyl for use in patients undergoing CABG operations. The authors' data also indicate that preoperative use of beta-adrenergic blocking drugs reduces intraoperative hypertension with narcotic-oxygen anesthesia. (Key words: Anesthesia: cardiovascular. Anesthetics, intravenous: fentanyl; sufentanil. Blood pressure: drug effects; hypertension. Surgery: coronary artery bypass.)

FENTANYL (50-100 µg/kg, iv) plus oxygen has been shown to produce profound analgesia and cardiovascular stability in patients with coronary artery disease (CAD) and, therefore, has been advocated as an anesthetic for coronary arterial bypass grafting (CABG) operation.¹⁻⁴ Others have reported a high incidence of chest wall rigidity and hypertension (especially during sternal spread and aortic dissection) with this technique in patients with CAD.⁵ Sufentanil, a new synthetic narcotic (5-10 times as potent as fentanyl but with the same duration of action and a much greater margin of safety in animals)⁶ has been suggested as a better anesthetic than fentanyl in patients likely to experience hypertension or tachycardia ("hemodynamic stress responses") with surgical stimulus.⁷ Sufentanil (N-[4-methoxymethyl]-1-[2-(2-thienyl)ethyl]-4-piperidinyl]-N-phenylpropanamide) is related chemically to fentanyl and is supplied as the aqueous solution of the citrate salt. One of the objectives of this study was to measure and compare the cardiovascular responses after sufentanil-O₂ and fentanyl-O₂ anesthesia during anesthetic induction, endotracheal intubation, and at other key intervals during operation (when surgical-induced "stress responses" were likely to be greatest) in patients with CAD undergoing CABG operation. In addition, we measured and compared anesthetic induction times, doses of the two drugs required for unconsciousness and for the entire operation, the incidence of chest wall rigidity, requirements for additional anesthetic or vasodilator supplements, and recovery time.

Materials and Methods

The protocol was approved by the Leiden University Human Experimentation Committee. Informed consent to do the study was obtained from each patient at the time of the preoperative visit.

Forty patients scheduled to undergo CABG operations requiring two or more bypass grafts were randomly as-

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signed to receive fentanyl (Group I) or sufentanil (Group II) at the time of the preoperative visit. Thirteen of 20 patients in Group I were taking propranolol or some other beta-adrenergic blocking compound, and 17 were taking nitroglycerin or some other oral vasodilator preoperatively. Twelve of 20 patients in Group II were taking beta-adrenergic blockers and 18 were taking an oral vasodilator. All patients were premedicated with lorazepam (0.08 mg/kg, po) two hours preoperatively, and atropine (0.1 mg/15 kg, im) 30 min before arrival in the operating room. Patients taking a beta-blocking drug received their usual dose of the compound at the time of the oral premedication. Upon arrival in the operating room catheters were placed in a hand vein and a radial artery and a bipolar lead II electrocardiogram was recorded continuously. Prior to induction of anesthesia, 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 5-min stabilization period and while breathing oxygen, control measurements of heart rate (beats/min), cardiac output (l/min),[†] systolic and mean arterial (mmHg), mean pulmonary artery (mmHg) and mean right atrial (mmHg) pressures were made. Two minutes later pancuronium (0.02 mg/kg) was administered intravenously. Three minutes after pancuronium, Group I patients were given fentanyl at 400 µg/min and Group II patients were given sufentanil at 300 µg/min intravenously. Respirations were spontaneous at first, then assisted, and finally controlled using a face mask and semi-closed system to maintain PaCO₂ at 35–40 mmHg as measured in radial arterial blood every 15–45 min. During infusion of fentanyl and sufentanil, patients were requested to open their eyes and/or take a deep breath every 5–10 s. Failure to respond to three consecutive requests was equated with unconsciousness. When unconscious, the patients were paralyzed with intravenous succinylcholine (1.5 mg/kg) and their tracheas were intubated with a cuffed Portex endotracheal tube. After intubation, an amount of fentanyl or sufentanil equal to the dose producing unconsciousness was infused over the next 30 min; thereafter, the operation began. Additional fentanyl (250-µg boluses) or sufentanil (50-µg boluses) was given intravenously throughout the operation whenever systolic arterial blood pressure increased to greater than 15 per cent over preanesthetic (control) values. When three successive supplemental doses of the narcotic failed to decrease systolic blood pressures to within 15

per cent of control values within five minutes before or during bypass, the patients were given intravenous phentolamine (1–3 mg bolus in divided doses) until blood pressure decreased to control values. After bypass N₂O** (25–50 per cent) was added to the inspired mixture of gases to treat hypertension not responding to supplemental doses of fentanyl or sufentanil. If N₂O was ineffective in decreasing postbypass hypertension to within 15 per cent of control systolic arterial blood pressure within 10 min, a sodium nitroprusside infusion (0.5–2.0 µg·kg⁻¹·min⁻¹) was started. The incidence of increases in systolic arterial blood pressure above 20 per cent of control values during endotracheal intubation, chest incision, sternotomy, and maximal sternal spread were recorded for both groups.

Patients were paralyzed with pancuronium (0.08 mg/kg, slowly, intravenously) 15 min after they had received succinylcholine. Paralysis was maintained with 0.02–0.04 mg/kg increments of pancuronium every 45–60 min during cardiopulmonary bypass and in the postbypass period. A balanced saline-glucose solution of (4.5 per cent glucose and 0.1 per cent normal saline in water) was administered at a rate of 1000 ml/h during preanesthetic 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 at preanesthetic values. The extracorporeal system was primed with a Ringer's solution (1500 ml) and glucose 5 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 25–28° C during extracorporeal support and rewarmed to 37° C at its conclusion.

Cardiovascular dynamics were recorded before anesthetic induction (control) at the time patients became unconscious, one minute after intubation, immediately before and 5 min after chest incision, after sternotomy, and 5 and 10 min after sternal spread.

The presence of chest wall rigidity during anesthetic induction was evaluated by the following scoring system: none = no apparent change in pulmonary compliance and no difficulty with ventilation during manual positive pressure ventilation; mild = can ventilate but with some

[†] Measured via thermodilution with 10 ml of 10–15° C dextrose, 5 per cent, in water as the injectate.

** N₂O was not used before cardiopulmonary bypass because it reduces cardiac output and increases peripheral vascular resistance during narcotic based anesthesia. We believe these are undesirable changes, especially since hypertension before bypass usually is associated with no change in cardiac output and with an increase in peripheral resistance. While N₂O produces similar changes after bypass, our patients usually had cardiac outputs that were significantly elevated above preoperative controls and peripheral resistances that were unchanged and sometimes decreased at these times, in spite of systolic hypertension. We have not had difficulties with air bubbles in our coronary bypass grafts and therefore have utilized N₂O after bypass in many of our anesthetic techniques.

TABLE 1. Cardiovascular Responses during Fentanyl-Oxygen and Sufentanil-Oxygen Anesthesia and Operation (Mean \pm SD)

	Anesthetic	Control	Unconscious	Intubation	Before Incision	5 min After Incision	After Sternotomy	5 min After Sternal Spread	10 min After Sternal Spread
Heart rate (beats/min)	Fentanyl Sufentanil	68 \pm 9 66 \pm 8	61 \pm 7 60 \pm 6	66 \pm 8 69 \pm 9	70 \pm 9 72 \pm 8	70 \pm 9 70 \pm 9	66 \pm 9 55 \pm 8	68 \pm 8 69 \pm 9	72 \pm 10 71 \pm 1
Cardiac output (l/min)	Fentanyl Sufentanil	5.2 \pm 1.1 5.3 \pm 0.9	5.0 \pm 0.7 4.9 \pm 0.8	5.0 \pm 0.9 5.6 \pm 1.0	5.3 \pm 1.0 5.2 \pm 0.7	5.4 \pm 1.2 5.4 \pm 0.9	5.0 \pm 1.0 5.3 \pm 1.0	5.8 \pm 1.2 5.6 \pm 1.1	5.7 \pm 1.2 5.7 \pm 1.1
Systolic arterial pressure (mmHg)	Fentanyl Sufentanil	119 \pm 13 115 \pm 11	104 \pm 11* 102 \pm 14*	110 \pm 14 105 \pm 13	111 \pm 14 108 \pm 9	119 \pm 15 107 \pm 10	129 \pm 18 119 \pm 16	135 \pm 19 125 \pm 17	136 \pm 20* 124 \pm 19
Mean arterial pressure (mmHg)	Fentanyl Sufentanil	86 \pm 7 84 \pm 6	75 \pm 6* 74 \pm 5*	81 \pm 7 77 \pm 7	84 \pm 7 76 \pm 7	87 \pm 8 77 \pm 7	90 \pm 9 84 \pm 8	99 \pm 8* 86 \pm 7	98 \pm 7* 88 \pm 6
Mean right atrial pressure (mmHg)	Fentanyl Sufentanil	9 \pm 1 8 \pm 1	8 \pm 1 9 \pm 2	9 \pm 2 9 \pm 1	9 \pm 1 8 \pm 1	10 \pm 1 9 \pm 1	8 \pm 1 8 \pm 1	9 \pm 2 8 \pm 1	9 \pm 2 9 \pm 1
Mean pulmonary artery pressure (mmHg)	Fentanyl Sufentanil	14 \pm 2 14 \pm 2	19 \pm 2* 18 \pm 1*	18 \pm 1* 18 \pm 2*	17 \pm 2 17 \pm 2	17 \pm 2 16 \pm 2	16 \pm 2 16 \pm 2	15 \pm 2 17 \pm 2	16 \pm 2 16 \pm 2

* $P < 0.05$, Student's paired t test when compared to control values.

difficulty due to some chest wall rigidity; and severe = virtually impossible to ventilate prior to succinylcholine administration due to marked rigidity.

Patients were all electively mechanically ventilated until the morning after surgery. During the first eight postoperative hours they were evaluated for return of consciousness every 15 min. Once conscious, the ability to sustain adequate spontaneous respirations was assessed every 30 min. Patients were considered conscious when they could give correct affirmative or negative responses to three consecutive questions. Patients were considered ready for extubation when they had stable cardiovascular dynamics for two hours and a spontaneous respiratory rate of 10–12 or more breaths/min, and when they could generate a negative inspiratory pressure of 20 mmHg and sustain a PaCO_2 of less than 45 mmHg and a PaO_2 of 100 mmHg or more while spontaneously breathing (without verbal encouragement) 40 per cent oxygen via a T-piece apparatus for 30 min.

Data were analyzed for statistical significance using Student's paired and unpaired t tests, the chi-square test, and the Mantel-Haenszel chi-square test ($\text{MH}\chi^2$). The latter test was used to analyze $2 \times K$ contingency tables which were controlled for possible confounding variables. $P < 0.05$ was considered statistically significant.

Results

In three of the 40 patients (one in Group I and two in Group II) it was impossible to thread the balloon-tipped catheter into the pulmonary artery. Therefore, data were analyzed for statistical significance in only 37 of the 40 patients entered into the study.

The ages (55 ± 10 years, mean \pm SD) and weights (73 ± 11 kg) of the two groups were similar. Preoperative heart rates, cardiac output, and blood pressures of the two groups were also similar (table 1). Patients in Group I required an average of 28 ± 9 $\mu\text{g}/\text{kg}$ of fentanyl for unconsciousness, while those in Group II needed 4.2 ± 0.8 $\mu\text{g}/\text{kg}$ sufentanil. For the entire operation, doses of the two drugs used were 122 ± 15 $\mu\text{g}/\text{kg}$ fentanyl and 12.9 ± 0.5 $\mu\text{g}/\text{kg}$ sufentanil.

Average time for induction was 4.6 ± 0.5 and 1.3 ± 0.3 min for fentanyl and sufentanil, respectively (table 2). The difference in induction time was significant. Twenty-two per cent of the patients receiving fentanyl and 28 per cent of those getting sufentanil experienced some chest wall rigidity at the end of induction (table 2).

Induction doses of both narcotics produced small but significant decreases in systolic and mean arterial blood pressures and an increase in mean pulmonary artery pressure (table 1). These changes were transient and all pressures were similar to control values at the time of

TABLE 2. Responses to Anesthetic Induction with Fentanyl and Sufentanil in 37 Patients Undergoing CABG Operations

	Patients	Induction Time* (min)	Rigidity (Per Cent)			
			None	Mild	Severe	Total
Fentanyl (Group I)	19	4.6 ± 0.5†	78	16	5	21
Sufentanil (Group II)	18	1.3 ± 0.3	72	22	6	28

* Values are means ± SD.

† $P < 0.01$, Student's unpaired t tests when compared to Group II.

incision. Heart rate, cardiac output, and mean right atrial pressure remained unchanged throughout the study period in both groups. While patients receiving sufentanil experienced no significant changes in systolic or mean arterial blood pressures after chest wall incision, sternotomy and sternal spread, patients receiving fentanyl experienced significant increases in both these variables (in spite of additional fentanyl) 5 and 10 min after sternal spread (table 1).

Increases in systolic blood pressure > 20 per cent of preoperative control values after sternal spread†† and hypertension requiring supplementation with phentolamine and N₂O‡‡ occurred more frequently in patients not taking preoperative beta-adrenergic blockers than in those taking these drugs, considering all patients in one group (tables 3 and 4). Increases in systolic blood pressure > 20 per cent of preoperative values and hypertension requiring supplementation never occurred in patients in Group II taking beta-adrenergic blocking drugs preoperatively.

Phentolamine was required to control arterial blood pressure in 42 per cent of patients in Group I before bypass (almost always during sternal spread or dissection of the aorta prior to aortic cannulation) and 47 per cent of this group during bypass (table 4). Only 6 and 11 per cent, respectively, of Group II patients required phentolamine for blood pressure control before and during

cardiopulmonary bypass. Fifty-three per cent of Group I patients required N₂O and 21 per cent required sodium nitroprusside after bypass for blood pressure control. Only two patients (11 per cent) of Group II required N₂O and only one (6 per cent) needed nitroprusside post-bypass.

Even when controlled for the presence or absence of preoperative beta-adrenergic-blockade, there was a significant difference in the need for supplementation between the fentanyl and sufentanil groups. In particular, there was a greater need for supplementation in the fentanyl group with phentolamine before bypass; ($MH\chi^2 = 5.748, P = 0.017$) and during bypass; ($MH\chi^2 = 5.873, P = 0.015$). Also, there was a greater need for supplementation with N₂O after bypass in the fentanyl group; ($MH\chi^2 = 6.963, P = 0.008$). There was no difference in the need for supplementation with SNP after bypass; ($MH\chi^2 = 0.001, P = 0.980$).

When controlled for the presence or absence of preoperative beta-adrenergic-blockade, there was no difference in the incidence of hypertension at endotracheal intubation, skin incision, and sternotomy between the fentanyl and sufentanil groups (table 3). However, at the time of sternal spread, there was a greater incidence of hypertension in the fentanyl group even when controlled for beta-adrenergic blockade ($MH\chi^2 = 4.043, P = 0.044$).

All patients were conscious within six hours of the end of operation and all but seven (four in Group I and three in Group II) fulfilled the criteria for endotracheal ex-

†† $P < 0.01$, chi-square test.

‡‡ $P < 0.05$, chi-square test.

TABLE 3. Per Cent of Patients with Increases in Systolic Arterial Blood Pressure Greater than 20 Per Cent of Control Values during Stressful Stimulation

	Intubation	Incision	Sternotomy	Sternal Spread
Fentanyl				
All Patients (19)	0	5 (1)	32 (6)	53 (10)
Patients taking beta-adrenergic blockers (12)	0	8 (1)	17 (2)	33 (4)
Patients not taking beta-adrenergic blockers (7)	0	0	57 (4)	86 (6)
Sufentanil				
All Patients (18)	0	0	11 (2)	22 (4)
Patients taking beta-adrenergic blockers (10)	0	0	0	0
Patients not taking beta-adrenergic blockers (8)	0	0	25 (2)	50 (4)

TABLE 4. Per Cent of Patients Requiring Supplementation with Phentolamine, N₂O and Nitroprusside During CABG Operations with Fentanyl and Sufentanil

	Phentolamine		N ₂ O After Bypass	Nitroprusside After Bypass
	Before Bypass	During Bypass		
Fentanyl				
All Patients (19)	42 (8)	47 (9)	53 (10)	21 (4)
Patients taking beta-adrenergic blockers (12)	25 (3)	25 (3)	33 (4)	17 (2)
Patients not taking beta-adrenergic blockers (7)	71 (5)	86 (6)	86 (6)	29 (2)
Sufentanil				
All Patients (18)	6 (1)	11 (2)	11 (2)	6 (1)
Patients taking beta-adrenergic blockers (10)	0	0	0	0
Patients not taking beta-adrenergic blockers (8)	13 (1)	25 (1)	25 (2)	13 (1)

tubation by the end of the eighth postoperative hour (table 5). Average time for recovery of consciousness and extubation were similar in the two groups although there was great individual variation among patients in both groups. When interviewed 48 h postoperatively, no patient in either group remembered being rigid or any other aspect of their anesthetic induction, laryngoscopy, endotracheal intubation, or operation.

Discussion

The original studies evaluating large doses of fentanyl plus oxygen as an anesthetic technique for patients undergoing open heart surgery reported minimal cardiovascular changes throughout anesthesia and operation and a low incidence or total absence of chest wall rigidity on anesthetic induction.^{1,2,8,9} However, there are reports which document that at least under certain circumstances, chest wall rigidity is common during anesthetic induction with large doses of fentanyl;^{10,11} tachycardia and hypertension can also be problems during operation, especially with sternotomy, in patients with CAD undergoing CABG operations.⁵ In our experience use of a nondepolarizing muscle relaxant prior to anesthetic induction and use of significantly higher doses of fentanyl

TABLE 5. Recovery Times in 37 Patients Anesthetized with Fentanyl and Sufentanil Undergoing CABG Operations (Means \pm SD)

	Conscious (h)	Ready for Extubation* (h)	Per Cent of Patients Not Ready for Extubation 8 h after Operation
Fentanyl (Group I)	2.1 \pm 1.4	4.6 \pm 1.8	21
Sufentanil (Group II)	1.8 \pm 1.1	4.8 \pm 1.6	17

* Data in this column are from 30 patients who were considered ready for endotracheal extubation before the ninth postoperative hour.

than was originally reported by Stanley and co-workers^{1,2,8,9} reduces these problems but is not always foolproof in eliminating rigidity during induction and hypertension with sternotomy. §§

In an attempt to decrease or totally eliminate these problems, yet preserve the other advantages of fentanyl-oxygen anesthesia (*i.e.*, absence of cardiovascular changes during anesthetic induction, absence of histamine release, rapid return of consciousness after surgery, *etc.*), we decided to study sufentanil as a narcotic anesthetic. Sufentanil is a new, more potent chemical relative of fentanyl. Sufentanil was thought to be potentially better than fentanyl as a narcotic anesthetic for patients undergoing open heart surgery because in preliminary animal^{6,12} and human studies^{7,13-15} it has properties similar to fentanyl, but in addition appeared more effective in preventing intraoperative hypertension and tachycardia,^{7,14} reducing myocardial oxygen consumption¹³ and producing less postoperative respiratory depression.¹⁵

Our initial pilot studies with sufentanil (done in a similar fashion as those reported here) in patients undergoing open heart surgery^{¶¶} indicated that when given at an infusion rate of one-tenth to one-half that of fentanyl (40–200 μ g/min, potency of sufentanil—5 to 10 times fentanyl) sufentanil produced unconsciousness in approximately four to five minutes and resulted in an incidence of mild rigidity of 15 per cent and no severe rigidity if preceded by pancuronium (0.02 mg/kg). We found that by increasing the infusion rate of sufentanil to 300 μ g/min, anesthetic induction was faster, but the incidence of rigidity was not increased signifi-

§§ de Lange S, Stanley TH, Boscoe M: Fentanyl-oxygen anesthesia: Comparison of anesthetic requirements and cardiovascular responses in Salt Lake City and Leiden, Holland. Abstracts 7th World Congress of Anesthesiologists, Hamburg, 1980, p 313.

¶¶ de Lange S, Stanley TH: Unpublished data.

cantly. At infusion rates higher than 300 $\mu\text{g}/\text{min}$, sufentanil did not appreciably decrease induction time, but markedly increased the overall frequency of rigidity and resulted in a much higher incidence of severe rigidity. Similar studies done in the United States by Stanley and co-workers (unpublished data) and others¹⁰ have established that when fentanyl is given at infusion rates greater than 400 $\mu\text{g}/\text{min}$ anesthetic induction is faster. However, the incidence of rigidity may be increased, with or without pancuronium pretreatment. The results of this study demonstrate that when infused at a higher relative dose rate, sufentanil produces, as expected, a much shorter induction time than fentanyl, but does not significantly increase the incidence of chest wall rigidity.

In this study both fentanyl and sufentanil were associated with similar and minimal mean changes in all cardiovascular variables measured up to sternal spread, when systolic and mean arterial blood pressures became significantly elevated only in the fentanyl group. The differences between the groups at this time were even more marked than are indicated in table 1 if the incidence of the patients with increases in systolic blood pressure greater than 20 per cent and the requirements for phenolamine are compared (tables 3 and 4). A higher incidence of hypertension was also observed in Group I (fentanyl) compared to Group II (sufentanil) during and after bypass, as indicated by the requirements for phenolamine and nitrous oxide (table 4). Similar rises in systolic arterial blood pressure and requirements for supplementation during and after sternotomy, and during and after bypass have been reported by Waller *et al.*⁵ during fentanyl anesthesia. These findings are distinctly different from those previously reported by Stanley and co-workers¹ and are not easily explainable. However, one possible explanation for the difference in the findings with fentanyl in this study and in the report of Stanley *et al.* could be related to the number of patients taking propranolol as well as the dosage and time of the last dose. We now believe that the degree of beta-adrenergic blockade present at operation influences not only the amount of fentanyl required for unconsciousness but also the likelihood of hypertension during laryngoscopy, incision, sternotomy, and sternal spread, irrespective of fentanyl dosage.¹⁶ Although it is unreported, all of the patients of Stanley *et al.* were taking propranolol (approximately the same dosage and the same time of the last dose as patients in this study) whereas only 63 per cent (12 of 19) of Group I patients in this study were taking propranolol or some other beta-adrenergic blockers. Since the degree of preanesthetic beta-adrenergic blockade was not evaluated in this or in the report of Stanley *et al.*,¹ it is difficult to know if this factor could be an explanation for the differences observed. However,

it is interesting to note that in this study, four of the six patients in Group I that experienced an increase in systolic arterial blood pressure greater than 20 per cent of control with sternotomy and six of the ten that sustained a similar change with maximal sternal spread were not taking beta-adrenergic blockers preoperatively. Similarly, all patients in Group II that experienced an increase in systolic arterial blood pressure greater than 20 per cent of control with sternotomy and sternal spread were not taking beta-adrenergic blockers preoperatively. Also, none of Group II patients taking beta-blockers preoperatively required supplementation with phenolamine, N₂O, or nitroprusside. Considering all 37 patients as a single group, only four of 22 patients taking beta-blockers preoperatively experienced hypertension with sternal spread, whereas 10 of 15 not taking these drugs had a similar result. It appears clear then, that one of the explanations for the varying incidence of hypertension during high-dose narcotic anesthesia may be preoperative beta-adrenergic blocker management. The hypertension observed by Waller *et al.*⁵ during operation with fentanyl-oxygen anesthesia may also have been related to the degree of preoperative beta-adrenergic blockade. These investigators did not administer beta-adrenergic blockers on the day of surgery in patients taking these drugs and, therefore, probably had little beta-adrenergic blockade present during operation.

It is difficult to understand why a comparable dose of a more potent narcotic (sufentanil) results in less hypertension and less need for supplementation than one that is less potent (fentanyl). Differences in the number of patients taking preoperative beta-blocking drugs, as well as the dosage and timing of the last dose, are not likely explanations for the findings in this study because these factors were similar in the two groups. On the other hand, sufentanil may have a beta-adrenergic blocking action or cause a greater decrease in circulating catecholamines than does fentanyl.⁹ Unfortunately, there are no data currently available either to prove or disprove these theories.

Time for recovery of unconsciousness, duration of mechanical postoperative respiration, and the per cent of patients who did not fulfill our criteria for extubation eight hours after operation were similar in the two groups in this study. However, there are new data available*** which indicate that sufentanil is cleared from plasma faster than fentanyl. This suggests that if a single massive dose technique of administering fentanyl or sufentanil is adopted,¹⁷ rather than a multiple dose technique as was done in this study, recovery from sufentanil may, indeed, be faster than from fentanyl.

*** Bovill JG, Sebel PS: Unpublished data.

References

1. Stanley TH, Philbin DM, Coggins CH: Fentanyl-oxygen anesthesia for coronary artery surgery: Cardiovascular and anti-diuretic hormone responses. *Can Anaesth Soc J* 26:168-171, 1979
2. Lunn JK, Stanley TH, Eisele J, et al: High dose fentanyl anesthesia for coronary artery surgery: Plasma fentanyl concentrations and influence of nitrous oxide on cardiovascular responses. *Anesth Analg (Cleve)* 58:390-395, 1979
3. Hall GM: Fentanyl and the metabolic responses to surgery. *Br J Anaesth* 52:561-562, 1980
4. Wynands JE: Anesthetic considerations for coronary artery surgery. *Cleve Clin* 48:86-92, 1981
5. Waller J, Hug C, Nagle DM, et al: Hemodynamic changes during fentanyl-oxygen anesthesia for aortocoronary bypass operation. *ANESTHESIOLOGY* 55:212-217, 1981
6. de Castro J, Van de Water A, Wouters L, et al: Comparative study of cardiovascular, neurological and metabolic side effects of eight narcotics in dogs. *Acta Anaesthesiol Belg* 30:5-99, 1979
7. de Castro J: Practical applications and limitation of analgesic anesthesia. *Acta Anaesthesiol Belg* 27:107-128, 1976
8. Stanley TH, Webster LR: Anesthetic requirements and cardiovascular effects of fentanyl-oxygen and fentanyl-diazepam-oxygen anesthesia in man. *Anesth Analg (Cleve)* 57:411-416, 1978
9. Stanley TH, Berman L, Green O, et al: Plasma catecholamine and cortisol responses to fentanyl-oxygen anesthesia for coronary artery operations. *ANESTHESIOLOGY* 53:250-253, 1980
10. Hill AB, Nahrwold ML, de Rosayro AM, et al: Prevention of rigidity during fentanyl-oxygen induction of anesthesia. *ANESTHESIOLOGY* 53:S68, 1980
11. Comstock MK, Franklin LS, Carter JG, et al: Rigidity and hypercarbia on fentanyl-oxygen induction. *ANESTHESIOLOGY* 51:S28, 1979
12. Reddy, P, Liu WS, Port JD, et al: Comparison of haemodynamic effects of anaesthetic doses of alphaprodine and sufentanil in the dog. *Can. Anaesth Soc J* 27:345-350, 1980
13. Hempelman G, Seitz V, Piepenbrock S, et al: Vergleichende Untersuchungen zu kardialen und vaskularen effekten des neuens analgetikums sufentanil (R 30730) und fentanyl. *Prakt Anaesth* 13:429-437, 1978
14. Van de Wall J, Lauwers P, Andriaensen H: Double blind comparison of fentanyl and sufentanil in anesthesia. *Acta Anaesthesiol Belg* 27:129-135, 1976
15. Kay B, Rolly G: Duration of analgesic supplements to anesthesia: a double blind comparison between morphine, fentanyl and sufentanil. *Acta Anaesthesiol Belg* 28:25-32, 1977
16. Stanley TH, de Lange S, Boscoe MB: The influence of chronic preoperative beta-adrenergic blocker therapy on intraoperative cardiovascular dynamics and narcotic requirements in patients with coronary artery disease. *ANESTHESIOLOGY (In Press)* abstract, 1981
17. Bovill JG, Sebel PS: Pharmacokinetics of high-dose fentanyl. A study in patients undergoing cardiac surgery. *Br J Anaesth* 52:795-802, 1980

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