Cardiovascular response of a continuous variable rate alfentanil infusion for abdominal aortic surgery

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A prospective study was undertaken to determine the cardiovascular response of a continuous alfentanil infusion during abdominal aortic surgery (AAS). Each subject (n = 20) received a beta-blocking drug preoperatively, and was premedicated with oral lorazepam. Anaesthesia was induced with alfentanil $50 \mu\text{g} \cdot \text{kg}^{-1}$ and thiopentone $3 \text{ mg} \cdot \text{kg}^{-1}$, and was maintained with a variable rate infusion of alfentanil and 66 per cent nitrous oxide in oxygen. During the infusion, boluses of alfentanil, $7.5 \mu\text{g} \cdot \text{kg}^{-1}$, were administered to maintain heart rate and blood pressure within 20 per cent of awake baseline values. Haemodynamic stability during surgery was achieved with infusion rates varying between 0.5 and $2.5 \mu\text{g} \cdot \text{kg}^{-1}$, which resulted in mean alfentanil serum concentrations ranging from 186 ± 53 to $315 \pm 98 \text{ ng} \cdot \text{ml}^{-1}$. The mean cumulative alfentanil dose was $15.4 \pm 6.2 \text{ mg} \cdot \text{patient}^{-1}$ for surgery which lasted an average of $141 \pm 41 \text{ min}$. Throughout surgery, no patient required inhalational anaesthetic agents or vasoactive drugs. Fifteen of the 20 patients had perioperative Holter monitoring. No myocardial ischaemia was detected during the intraoperative period. However, there was a 33 per cent incidence of myocardial

ischaemia on the first postoperative day. There were no myocardial infarcts and no deaths. We conclude that in beta-blocked patients undergoing aortic reconstructive surgery, a variable rate alfentanil infusion administered with 66 per cent nitrous oxide provides anaesthesia characterized by good haemodynamic control without the need for supplemental agents or vasoactive drugs.

Une étude prospective fut entreprise lors de la chirurgie aortique abdominale afin de déterminer les réponses cardiovasculaires d'une perfusion continu d'alfentanil. Les sujets (n = 20) ont reçu des bêta-bloqueurs en période pré-opératoire et furent prémédiqués avec du lorazepam par voie orale. L'anesthésie fut induite avec de l'alfentanil $50 \mu\text{g} \cdot \text{kg}^{-1}$ et du thiopentone $3 \text{ mg} \cdot \text{kg}^{-1}$ et a été maintenu avec une perfusion à taux variable d'alfentanil et 66 pour cent de protoxyde d'azote-oxygène. Lors de la perfusion, des bolus d'alfentanil de $7,5 \mu\text{g} \cdot \text{kg}^{-1}$ ont été administrés afin de maintenir la fréquence cardiaque et la pression artérielle à l'intérieur de 20 pour cent de la valeur de base. La stabilité hémodynamique lors de la chirurgie a été acquise avec un taux de perfusion variable entre $0,5$ et $2,5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ avec des concentrations sériques moyennes d'alfentanil s'étendant de 186 ± 53 à $315 \pm 98 \text{ ng} \cdot \text{ml}^{-1}$. La dose cumulative moyenne d'alfentanil était de $15,4 \pm 6,2 \text{ mg} \cdot \text{patient}^{-1}$ pour la chirurgie qui a duré en moyenne de $141 \pm 41 \text{ min}$. Tout au long de la chirurgie, aucun patient n'a requis des agents anesthésiques ou des drogues vasoactives. Quinze des 20 patients avaient un Holter en période pré-opératoire. Aucune ischémie myocardique n'a été détectée durant la période pré-opératoire. Cependant on a noté une incidence de 33 pour cent d'ischémie myocardique la première journée post-opératoire. Il n'y avait aucun infarctus myocardique et aucun décès. On conclut que chez les patients ayant reçu un bêta-bloqueur et devant subir une chirurgie aortique, une perfusion à taux variable d'alfentanil administrée avec 66 pour cent de protoxyde d'azote et d'oxygène fournit une anesthésie caractérisée par un bon contrôle hémodynamique sans le recours aux agents supplémentaires et aux drogues vasoactives.

Key words

ANAESTHESIA: cardiovascular;

ANAESTHETICS, INTRAVENOUS: alfentanil, continuous infusion;

PHARMACOKINETICS: plasma concentrations;

SURGERY: abdominal aortic surgery.

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The anaesthetic management of patients undergoing abdominal aortic surgery (AAS) must take into consideration the frequent occurrence of coexisting medical problems. This includes a 30–70 per cent incidence of coronary artery disease (CAD), which may be clinically silent.^{1,2} Anaesthesia for these patients should maintain the delicate balance between the determinants of myocardial oxygen supply and demand, without inducing depression of myocardial contractility.^{3,4} In addition, the anaesthetic technique must control cardiovascular responses to intraoperative surgical stimulation, and attenuate the haemodynamic impact of aortic cross-clamping and declamping.⁴

Narcotic anaesthesia provides good haemodynamic stability for cardiac surgery, and has been shown to reduce the incidence of complications following major vascular surgery.⁵ However, anaesthesia with unsupplemented high-dose fentanyl or sufentanil does not consistently control the hyperdynamic response to surgical stimulation during AAS; adjunctive agents including potent inhalational agents or vasodilators are often required.^{6,7} A further disadvantage of high-dose narcotic-oxygen anaesthesia for abdominal aortic surgery is that both fentanyl and sufentanil have prolonged elimination half-lives in this patient population, which may result in prolonged recovery.^{8,9}

Recently, the technique of infusing the short-acting opiate analgesic alfentanil has been described.¹⁰ In combination with nitrous oxide, the administration of alfentanil by infusion permits easy titration to achieve effective analgesic concentrations in response to varying levels of stimulation during surgery of intermediate and long duration.¹¹ It was hypothesized that such a technique would also achieve haemodynamic stability during major vascular surgery. The current study was therefore undertaken to determine the cardiovascular response of alfentanil, when administered as a continuous variable rate infusion with nitrous oxide, in patients undergoing abdominal aortic surgery.

Methods

Patient population

Twenty patients undergoing elective abdominal aortic aneurysm resection or aorto-bifemoral bypass grafting for vaso-occlusive disease entered this prospective study. All patients gave written, informed consent to the protocol approved by the Hospital Human Experimental Procedures Committee. Patients over age 75 yr, and those with a history of congestive heart failure, myocardial infarction within the preceding six months, or severe systemic disease, were excluded.

Protocol

Antianginal and antihypertensive medications were administered up to and including the morning of surgery. Patients who did not receive chronic beta-blocker therapy before entry into the study were given metoprolol, 50 mg orally, on the evening before and on the morning of surgery. Premedication consisted of lorazepam 0.04 mg · kg⁻¹ PO given 90 min preoperatively.

In the operating room, intravenous, radial artery, and thermodilution pulmonary artery (PA) catheters were inserted under local anaesthesia prior to induction of anaesthesia. Electrocardiographic leads II and V₅ were applied and monitored continuously. The concentrations of inspired and end-tidal respiratory gases were also displayed continuously, using mass spectrometry. Body temperature was measured from the PA catheter, and was maintained with the aid of fluid warmers, warming blankets, and a moisture exchanger attached to the circle system.

Following administration of approximately 10 ml · kg⁻¹ of Ringer's lactate, each patient received a loading dose of alfentanil 50 µg · kg⁻¹ over one minute, from a Bard Mini-InfuserTM alfentanil infusion pump. Simultaneously, pancuronium 0.08 mg · kg⁻¹ was administered IV over one minute, followed immediately by thiopentone 3.0 mg · kg⁻¹ IV. Ventilation was assisted, and then controlled with 100 per cent O₂, to maintain the end-tidal PaCO₂ between 35–40 mmHg. Tracheal intubation was performed two minutes after induction. Anaesthesia was then maintained with a variable rate infusion of alfentanil, 66 per cent nitrous oxide with oxygen, and pancuronium as required to maintain adequate neuromuscular blockade. Midazolam was given in 1.0 mg increments, if required, to treat signs of light anaesthesia, as indicated by sweating or lacrimation not associated with hypertension or tachycardia.

The initial alfentanil infusion rate was set at 1.0 µg · kg⁻¹ · min⁻¹ and then adjusted between 0.5 and 2.5 µg · kg⁻¹ · min⁻¹, in order to maintain heart rate and blood pressure within 20 per cent of each patient's respective baseline preinduction values. At any time during surgery, if systolic blood pressure and/or heart rate increased by more than 20 per cent, 7.5 µg · kg⁻¹ bolus doses of alfentanil were given at three-minute intervals, in addition to increasing the infusion rate in increments of 0.5 µg · kg⁻¹ · min⁻¹. If four successive boluses, and the maximum rate of infusion did not achieve appropriate haemodynamic control, isoflurane was administered. During maintenance of anaesthesia, the infusion rate of alfentanil was titrated downward in decrements of 0.25–0.50 µg · kg⁻¹ · min⁻¹ every 15 to 20 min, in order to achieve the minimal effective rate required to maintain

haemodynamic stability. As the lungs were routinely ventilated in the initial postoperative period, the infusion was not terminated until the end of surgery, following which fentanyl $3\text{--}5\text{ }\mu\text{g}\cdot\text{kg}^{-1}$ was administered to facilitate a smooth transition to the recovery room.

Intraoperative fluid administration was guided by serial haemodynamic assessments and frequent estimates of blood losses and urinary output. Mean pulmonary capillary wedge pressure (PCWP) was maintained in the range of 10–12 mmHg during surgery, and 12–14 mmHg prior to declamping. Intraoperative blood losses were replaced with packed red cells, and each patient received two units of albumin 25 per cent.

While the lungs were ventilated postoperatively, patients were sedated with intravenous diazepam and morphine. According to standard practice at this institution, mechanical ventilation was continued for a minimum of four hours to provide a period of stabilization and to ensure normothermia (body temperature = 37°C measured from the PA catheter) prior to extubation. Each patient was assessed by the attending anaesthetist, and the trachea was extubated when the patient was awake, haemodynamically stable, and meeting the respiratory criteria for extubation. Monitoring was then continued in the ICU for a minimum of 48 hr. Before discharge from hospital, each patient was visited and specifically asked about intraoperative awareness.

Measurements

Heart rate (HR), mean arterial (MAP), and pulmonary capillary wedge pressures (PCWP) were measured directly. Cardiac output (CO) was determined from the average of three values within 20 per cent of each other at end-expiration, using 10 ml indicator boluses of D5W at room temperature. Cardiac index (CI) and systemic vascular resistance index (SVRI) were calculated using standard formulae.¹² Serial measurements of left ventricular ejection fraction (EF) were recorded from a non-invasive thoracic electrical bioimpedance monitor (Bo-Med NCCOM3TM Cardiac Monitor). The use of this monitor and its accuracy in measuring EF have been previously described.^{14,15}

Haemodynamic measurements were recorded one minute before and one minute after induction of anaesthesia (IND), one minute after tracheal intubation (INT), and one minute before and after skin incision (INC), aortic cross-clamping (XCL) and aortic declamping (DCL). As bifurcation grafts were used, the declamping measurements were standardized by recording haemodynamic variables following abrupt declamping after reperfusion of the first limb.

Arterial blood was sampled for determination of alfentanil serum concentrations corresponding to the

TABLE I Demographic data (mean $\pm$ SD)

Age (yr)	63.4 $\pm$ 6.3
Sex (m/f)	12/8
Weight (kg)	68.6 $\pm$ 18.3
SBP (mmHg)	139 $\pm$ 15
DBP (mmHg)	82 $\pm$ 10
Pathology	
– Aneurysm	15/20
– Occlusion	5/20
Beta blockers	5/20
Calcium antagonists	5/20

Preoperative characteristics: SBP = systolic blood pressure, DBP = diastolic blood pressure.

periods of peak haemodynamic stress intraoperatively, and every hour for the first three hours postoperatively. Plasma was separated from blood specimens and stored at -20°C until assayed. Alfentanil plasma concentrations were determined in duplicate by radioimmunoassay using a commercially available kit.¹⁵ The sensitivity of this assay was $0.1\text{ ng}\cdot\text{ml}^{-1}$ with a coefficient of variation of approximately 10 per cent.

Holter monitors were installed to provide continuous recordings of leads II and V₅ both intraoperatively, and for the first 24 hr postoperatively. The Holter tapes were subsequently interpreted by one cardiologist, using a Marquette 8000T Holter analyzer. Myocardial ischaemia was diagnosed in the presence of new horizontal or downsloping ST segment depression greater than 1 mV at J + 80 msec in either ECG lead. Twelve lead electrocardiograms were also obtained daily for three days, and myocardial infarction was diagnosed in the presence of a new Q wave or elevation of the MB isoenzyme of creatinine kinase.

Statistical analysis

Repeated measures analysis of variance (ANOVA) was performed to test for changes over time for each haemodynamic variable. When the ANOVA was significant, Newman-Keul's test was applied to specify changes at each major anaesthetic and surgical intervention (IND, INT, INC, XCL, and DCL). The results are reported as mean and standard deviation in the figures, text, and tables. Statistical significance was assumed when $P < 0.05$.

Results

Twenty patients completed the study, for which the demographic data are presented in Table I. There was a slightly higher proportion of males than females. All patients were normotensive (SBP $< 160\text{ mmHg}$) preoperatively. Fifteen of the 20 patients (75 per cent) had an abdominal aortic aneurysm, and the remainder (25 per cent) underwent surgery for vaso-occlusive disease.

FIGURE 1 Heart rate (HR) and mean arterial pressure (MAP). Newman-Keul's test was applied to specify differences at each major anaesthetic and surgical intervention ($P < 0.05$). IND = induction, INT = intubation, INC = skin incision, XCL = aortic cross-clamping, DCL = aortic declamping, END = end of surgery.

Haemodynamics

The haemodynamic response to the induction sequence and the surgical interventions are presented in Figures 1, 2 and 3. Heart rate remained stable throughout induction and surgery, with mean values between 62 ± 8 bpm and 67 ± 10 bpm (range 47–95 bpm, Figure 1). During induction, average mean arterial pressure (MAP) decreased from 110 ± 15 to 84 ± 12 mmHg ($P < 0.05$), ranging between 59 and 104 mmHg one min after induction. However, MAP did not increase significantly in response to laryngoscopy and intubation. Six patients (30 per cent) received 5 mg boluses of ephedrine within the three-minute period from the time of induction, for an MAP less than 20 per cent of control. Skin incision was associated with a 23 ± 13 mmHg increase ($P < 0.05$) in MAP (peak MAP = 131 mmHg), but the post-incision MAP (106 ± 15 mmHg) remained slightly below the awake, baseline value. Overall, blood pressure varied minimally during the surgical events following skin incision. Notably, mean arterial pressure was unchanged by aortic cross-clamping, and did not decrease significantly in response to declamping.

No single anaesthetic or surgical intervention significantly altered cardiac index, the mean values of which remained between 2.4 ± 0.6 and 3.1 ± 0.4 L $\cdot$ min $^{-1}$ $\cdot$ m $^{-2}$

FIGURE 2 Pulmonary capillary wedge pressure (PCWP) and cardiac index (CI). For abbreviations refer to legend of Figure 1.

(range 1.6–5.1 L $\cdot$ min $^{-1}$ $\cdot$ m $^{-2}$) intraoperatively (Figure 2). Pulmonary capillary wedge pressure increased by 3.5 ± 2.1 mmHg ($P < 0.05$) in response to skin incision, coincidental with a rise in MAP. Otherwise, mean PCWP values were stable throughout surgery. Systemic vascular resistance index decreased after induction of anaesthesia ($P < 0.05$), and increased during skin incision ($P < 0.05$), associated with a rise in MAP (Figure 3). Despite such changes, SVRI remained within the normal range. Ejection fraction varied minimally throughout the study, and did not change significantly, even in response to the interventions of cross-clamping and declamping of the aorta (Figure 3).

Alfentanil infusion regimen

The serum concentrations resulting from the variable rate infusion of alfentanil are displayed in Figure 4. The loading dose of alfentanil resulted in a mean concentration of 241 ± 89 ng $\cdot$ ml $^{-1}$ at intubation. With the initial infusion rate of 1.0 μ g $\cdot$ kg $^{-1}$ $\cdot$ min $^{-1}$ mean alfentanil plasma concentrations decreased to 186 ± 53 ng $\cdot$ ml $^{-1}$ by the time of skin incision. At this level, 15 of the 20 patients (75 per cent) required supplemental boluses of alfentanil, and adjustment of infusion in order to control increases in MAP. Intraoperatively, haemodynamic stability was achieved with alfentanil infusion rates ranging from 0.5 – 2.5 μ g $\cdot$ kg $^{-1}$ $\cdot$ min $^{-1}$, which resulted in serum con-

FIGURE 3 Systemic vascular resistance index (SVRI) and ejection fraction (EF). For abbreviations refer to legend of Figure 1.

centrations between 245 ± 105 and 315 ± 98 ng $\cdot$ ml⁻¹. The number of patients who needed additional boluses of alfentanil for transient elevations in blood pressure decreased progressively during the course of surgery. In every patient, supplemental boluses of alfentanil and adjustment of the infusion rate as required, achieved the desired level of haemodynamic stability. The mean cumulative dose of alfentanil was 15.4 ± 6.2 mg $\cdot$ patient⁻¹ for surgery which lasted an average of 141 ± 41 min. Following termination of the infusion, alfentanil serum concentrations rapidly declined from 245 ± 121 ng $\cdot$ ml⁻¹ to 85 ± 58 ng $\cdot$ ml⁻¹ (range 10–119 ng $\cdot$ ml⁻¹) by the third postoperative hour. The cumulative dose, number of boluses, and infusion rates of alfentanil are summarized in Table II.

TABLE II Intraoperative characteristics (mean $\pm$ SD)

Alfentanil	
- Cumulative dose (mg)	15.4 ± 6.2
- Boluses (n)	3.5 ± 1.8
- Infusion rate (μ g $\cdot$ kg ⁻¹ $\cdot$ min ⁻¹)	0.5 ± 2.5
Adjunctive agents/patient (n)	0/20
Duration of surgery (min)	141 ± 41
Duration of cross-clamp (min)	53 ± 10
Blood loss (ml)	1775 ± 450
Fluids administered:	
- Crystalloid (ml)	4230 ± 1220
- Packed cells (ml)	1260 ± 690
- Colloid (ml)	240 ± 78

ALFENTANIL SERUM CONCENTRATIONS

Mean $\pm$ SD

FIGURE 4 Alfentanil serum concentrations during abdominal aortic surgery, and for the first three hours following discontinuation of the infusion. The mean rates of infusion, and number of patients requiring additional boluses of alfentanil at each measurement period, are also displayed. P + 1, P + 2, P + 3 = 1, 2 and 3 hours postoperatively. For other abbreviations, refer to legend of Figure 1.

Adjunctive agents

Three patients received midazolam ($2\text{--}3$ mg $\cdot$ patient⁻¹) for signs of sympathetic stimulation such as sweating. However, no patient required isoflurane to treat hypertension or tachycardia, nor did any patient require nitroglycerin to control haemodynamic responses during the period of aortic cross-clamping.

Holter analysis

Holter analysis was completed in 15 of the 20 patients. Normal sinus rhythm was maintained throughout surgery in every individual, except for occasional bigeminy in two, and a three-second episode of non-sustained ventricular tachycardia in one patient related to the insertion of a Swan Ganz catheter. There were no episodes of myocardial ischaemia during surgery.

Postoperative course

The important data of the postoperative course are summarized in Table III. No patient had awareness of

TABLE III Postoperative course (mean $\pm$ SD)

Time to awakening (min)	92 ± 51
Time to extubation (hr)	21 ± 11
Length of ICU stay (day)	2.4 ± 1.2
Cardiovascular events:	
- Hypertension (n)	13/20
- Congestive heart failure (n)	0/20
- Myocardial ischaemia (n)	5/15
- Myocardial infarction (n)	0
Death (n)	0

intraoperative events, from the time of anaesthetic induction to completion of surgery. The average time to awakening (defined as first spontaneous eye opening) was 92 ± 51 min. The average duration of postoperative pulmonary ventilation, as determined by the attending anaesthetist and not study protocol, was 21 ± 11 hr; the tracheas of five of the 20 patients were extubated within six hours of the termination of surgery. Thirteen patients (65 per cent) developed postoperative hypertension, defined as SBP > 160 mmHg in the absence of pain, agitation, or blood gas abnormalities. Hypertension was treated with either sublingual or intranasal nifedipine in all cases.

In the first 24 hr postoperatively, 12 of the 15 Holter recordings (80 per cent) showed periods of tachycardia defined as HR > 110 bpm. Bigeminy was frequent in 20 per cent of individuals. Five patients (33 per cent) developed myocardial ischaemia postoperatively. One of these had severe prolonged ischaemia (50 min duration), with maximum ST segment depression of 8.5 mm in lead V₅ during a period of hypotension and tachycardia. The ischaemia resolved with stabilization of the haemodynamic status, and the patient did not suffer myocardial infarction. No patient developed congestive heart failure, and there were no deaths.

Discussion

High-dose narcotic-oxygen anaesthesia is widely used for patients undergoing cardiac surgery. However, techniques which employed a single, large dose of fentanyl did not provide consistent haemodynamic control during the stress of abdominal aortic surgery. Friesen *et al.*, using $100 \mu\text{g} \cdot \text{kg}^{-1}$ of fentanyl, reported that hyperdynamic circulatory responses requiring vasodilator therapy occurred in 81 per cent of patients during AAS.⁷ Our group compared intermittent bolus administration of high-dose fentanyl (total dose $125 \mu\text{g} \cdot \text{kg}^{-1}$) and sufentanil-O₂ anaesthesia (total dose $25 \mu\text{g} \cdot \text{kg}^{-1}$) for aortic reconstructive surgery, and also found that supplementation with inhalation agents was required to achieve haemodynamic stability.⁶ As narcotics are not "complete anaesthetics," a technique which incorporates nitrous oxide with an opiate analgesic administered by continuous variable rate infusion may be more appropriate.

Amongst currently available opiates, alfentanil is a relatively new mu agonist, which has a more rapid onset of action and a shorter elimination half-life than both fentanyl and sufentanil.^{16,17} In combination with nitrous oxide, administration of alfentanil by a variable rate infusion permits easy titration of effect in response to changing levels of stimulation for general surgical procedures of both intermediate and long duration.¹⁰ The use of an infusion avoids the large variation in serum concentra-

tions which result from multiple boluses during longer surgical procedures. Furthermore, it has been shown that by maintaining serum concentrations in the lower therapeutic range with an infusion technique, rather than intermittent bolus administration, the cumulative alfentanil dose is reduced, and recovery is more rapid.¹⁸

This study demonstrated that anaesthesia with nitrous oxide and alfentanil administered by continuous infusion provided favourable haemodynamic control in beta-blocked patients undergoing aortic reconstructive surgery. The intraoperative course was characterized by stability of HR, CI and EF and minor variations of MAP, PCWP, and SVR.

At induction of anaesthesia, the decrease in mean arterial pressure was due in part to the peripheral vasodilating effect of alfentanil.¹⁹ Slower administration of the loading dose, at rates not exceeding $30 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$, may minimize this effect. Despite the change in blood pressure, the induction sequence did not significantly alter heart rate, cardiac index or ejection fraction, and prevented any significant haemodynamic change in response to tracheal intubation.

Skin incision caused an increase in mean arterial pressure. This was not surprising, in view of the fact that the mean serum concentration of alfentanil was only $196 \pm 53 \text{ ng} \cdot \text{ml}^{-1}$ at this time. Ausems *et al.* showed that an alfentanil serum concentration of $279 \text{ ng} \cdot \text{ml}^{-1}$ was required to prevent response to skin incision in 50 per cent of individuals.²⁰ Values around this therapeutic range were achieved in the current study by administration of supplemental boluses of alfentanil, and increasing the rate of infusion in 15 of the 20 patients. It is possible that the observed increase in blood pressure secondary to skin incision might have been prevented by administration of a second bolus of alfentanil prior to the event. Nevertheless, in every instance when MAP increased above 20 per cent of baseline, the administration of supplemental alfentanil boluses rapidly achieved the desired haemodynamic response. Therefore, according to protocol, there was no need for supplementation with inhalational anaesthetic agents. This technique also prevented haemodynamic changes in response to aortic cross-clamping, and obviated the need for additional vasodilating agents in order to facilitate volume loading prior to declamping of the aorta.

There was considerable variability in the range of plasma concentrations of alfentanil during the peri-induction period, and during surgery. This is consistent with the observation that significant inter-individual variability exists in alfentanil concentration-response. However, for any one patient, the concentration-response curves for specific intraoperative events have been shown to be quite steep.²⁰ This may partly account for the finding

that the number of supplemental boluses, and adjustments in the rate of infusion, decreased over time, once a patient's therapeutic range had been established. This also provides further justification for use of an infusion regimen which, rather than being fixed, is varied according to individual patient requirements and the level of surgical stimulation.

The study protocol included the preoperative administration of beta-blocking drugs in patients who were not previously receiving beta-blocker therapy. Preoperative beta-blockade has previously been shown to influence haemodynamic events during narcotic anaesthesia.²¹ As approximately 20 per cent of the vascular surgery patients at our institution receive beta-blocking drugs for the treatment of angina pectoris or hypertension, this factor could have been an important confounding variable in the interpretation of alfentanil requirements. Therefore, all patients received beta-blocker therapy, with either their usual dose of beta-blocker or metoprolol, given the evening before and the morning of surgery. This achieved a slow resting heart rate of 63 ± 12 bpm prior to induction of anaesthesia. These slow heart rates, which remained slow intraoperatively, are desirable in a patient population with a high incidence of coronary artery disease.

There was a notable absence of intraoperative myocardial ischaemia, as determined by Holter monitoring. This finding compares favourably with a 31 per cent incidence of intraoperative ischaemia documented by Friesen *et al.*, when using high-dose fentanyl-oxygen anaesthesia for abdominal aortic surgery.⁷ Although perioperative myocardial ischaemia frequently occurs in the absence of haemodynamic changes, recent evidence suggests that a correlation does exist between tachycardia, hypertension, and the development of ischaemia during AAS.²² In the Friesen study, frequent episodes of hypertension and tachycardia occurred during unsupplemented high-dose fentanyl anaesthesia. In the present investigation, slow heart rates and relatively minor fluctuations in systemic blood pressure were observed throughout the intraoperative course when alfentanil was infused in conjunction with 66 per cent nitrous oxide.

In addition to the use of nitrous oxide with alfentanil, the anaesthetic technique also included the administration of lorazepam as a premedicant. It is well known that the effects of opioids are enhanced in a dose-dependant fashion by benzodiazepines. Thus, our use of lorazepam as a premedicant may also partly explain the differences between our findings and those of Friesen, where benzodiazepines were not administered.⁷ One final factor which may account for the favourable haemodynamic response and the absence of intraoperative myocardial ischemia in the present study was the routine preoperative administration of beta-blocking drugs.

One-third of patients developed myocardial ischaemia in the first 24 hr postoperatively. This is in keeping with a 24 per cent incidence of perioperative myocardial ischaemia which occurs in patients with known CAD, or those with two or more CAD risk factors.²³ It is also consistent with the observation that PMI occurs more commonly postoperatively than intraoperatively. Despite the occurrence of postoperative ischaemia, no patient suffered myocardial infarction or other major cardiac complication.

Finally, as it is desirable to ventilate the lungs routinely following aortic reconstruction, no attempt was made to have patients awake at the termination of surgery. Therefore, the time to awakening (92 ± 51 min) was influenced by the use of diazepam and morphine which were administered while the lungs remained mechanically ventilated (21 ± 11 hr). This prevented reliable assessment of the speed of recovery following administration of alfentanil. The data suggest, however, that following termination of the infusion, alfentanil serum levels declined rapidly, and fell below the threshold for spontaneous ventilation (around $200 \text{ ng} \cdot \text{ml}^{-1}$)²⁰ between the first and second postoperative hours. This implies that the cumulative dose of alfentanil, which is required to achieve haemodynamic stability during anaesthesia for AAS, will not result in prolonged respiratory depression which might preclude early extubation (within several hours) following termination of surgery.

We conclude that in beta-blocked patients who are premedicated with a benzodiazepine, anaesthesia with nitrous oxide and a continuous variable rate infusion of alfentanil provides anaesthesia characterized by good haemodynamic control, without the requirement for supplemental agents. Infusion rates ranging from 0.5 to $2.5 \mu\text{g} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ are required in order to maintain alfentanil plasma concentrations in the range of 245 ± 105 to $315 \pm 98 \text{ ng} \cdot \text{ml}^{-1}$ during surgery. This anaesthetic technique is associated with a good outcome in the high-risk patient population undergoing abdominal aortic surgery.

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