Myocardial metabolism and haemodynamic responses with enflurane anaesthesia for coronary artery surgery

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Ten patients were studied before, during and after enflurane anaesthesia for coronary vein grafting. All had good ventricular function and nine were receiving effective beta blockade. Cardiac output and vascular pressures were measured, plus coronary sinus blood flow (CBF), myocardial oxygen consumption (MVO₂) and lactate extraction (MLE). Enflurane induction (10 minutes, mean 1.72 per cent end tidal) reduced blood pressure (MAP), due to decreased cardiac index (CI), with no change in heart rate or systemic resistance. Intubation returned MAP and CI to control level but the heart rate increased. Subsequently, enflurane kept MAP, CI and stroke work below the awake level. CBF decreased on induction, rose again on intubation and remained normal before bypass. MVO₂ fell on induction from an increase in CS oxygen content, which remained elevated. Normal MLE continued in every patient. There was no evidence of myocardial ischaemia in patients on beta blockade, when haemodynamics were maintained at or below those of the sedated, awake state.

Key words

HEART: oxygen consumption; ANAESTHESIA: cardiovascular; ANAESTHETICS, VOLATILE: enflurane; SURGERY: cardiovascular.

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Maintenance of myocardial oxygen balance during anaesthesia is essential, particularly for patients with coronary artery disease, to avoid major ischaemic episodes or frank infarction. Increased oxygen consumption due to a hyperdynamic circulation must be avoided. Moderate depression of myocardial contractility by potent anaesthetic drugs is desirable but must be controllable. The adequacy of myocardial oxygenation can now be assessed in the operating room, by measuring coronary sinus blood flow, myocardial oxygen consumption and lactate extraction. Myocardial oxygenation can be maintained in coronary patients with halothane-oxygen but not so with 1 mg·kg⁻¹ of morphine, and oxygen.¹ Delaney *et al.*² reported, in patients having coronary vein grafts (CABG), myocardial function and haemodynamic effects of enflurane, but correlation of haemodynamics with CBF, MVO₂ and MLE has not been documented. We present the haemodynamic and myocardial metabolic effects of enflurane-oxygen anaesthesia from pre-induction, through anaesthesia and operation for CABG and for 24 hours afterward.

Methods

Study population

Ten male patients gave their informed consent. Mean age was 53.7 years (range 34–62), mean weight 79.2 Kg (68–91); eight had known previous infarction. Their disability by NYHA Class was: II – one patient, III – seven and IV – two; all patients were normotensive. Nine were kept on effective beta blockade (average: propranolol dose 40 mg q.i.d.) until operation. Although nine had signi-

ficant areas of hypokinesis, normal myocardial function was present at cardiac catheterization: mean ejection fraction = 0.62 (50–78), LVEDP = 12 mmHg (7–20) and CI = $2.77 \text{ l} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$ (1.9–3.5).

They subsequently received mean 2.5 aorto-coronary vein grafts. All patients recovered and were discharged at the usual time.

Study protocol

The protocol had approval from the institutional ethics committee. Premedication was with oral diazepam, 10–15 mg and intramuscular morphine, 15–20 mg. After the patient's arrival in the operating room, an additional mean dose of 5.5 mg of diazepam was given intravenously to enhance sedation. With local anaesthesia, a #20 radial arterial needle was placed, plus two thermodilution catheters via the right internal jugular vein. The pulmonary arterial catheter³ was followed by another special catheter,⁴ manipulated into the mid-coronary sinus (CS) with the aid of fluoroscopy, its position verified by injecting contrast medium. To measure CBF, room temperature fluid is infused by pump at $40 \text{ ml} \cdot \text{min}^{-1}$. Two temperatures are recorded: (1) within the catheter; and (2) CS blood 1 cm downstream from the injection port. From these, flow in $\text{ml} \cdot \text{min}^{-1}$ is calculated. After a quiet period following instrumentation, a study was done with the awake, sedated patient breathing air, followed by seven sequential studies during anaesthesia, and at 1 and 24 hours later (see Figures). Each individual study included recording central and arterial pressures, cardiac output (duplicate), CBF and arterial and CS blood samples for oxygen saturation (by co-oximetry), haemoglobin and lactate determination (Boehringer Mannheim Canada Ltd.). Other variables were calculated from standard formulae. MVO_2 is CBF multiplied by the arterial-CS difference of oxygen content. MLE is that portion of arterial lactate extracted by the ventricular muscle: arterial minus CS divided by arterial concentrations. Statistical analyses were done by analysis of variance and paired t-tests with $p < 0.05$ considered significant.

Methods

Induction began with thiopentone (mean 125 mg) followed by oxygen with enflurane, mean maximum end tidal concentration 1.72 per cent (0.93–3

per cent). The systolic pressure was intentionally reduced by 25–30 per cent and held there with enflurane for ten minutes. Pancuronium ($0.1 \text{ ml} \cdot \text{kg}^{-1}$) was given before the preintubation study and mean PaCO_2 was maintained at the awake level (44 mmHg); it averaged 46 before intubation and 42 mmHg postintubation. After intubation, enflurane-oxygen was given at concentrations aimed to maintain a slightly reduced blood pressure, without response to stimuli. This concentration ranged from 0.5 to 3 per cent. Enflurane was given via the pump-oxygenator and also during chest closure. No intravenous fluid was given during induction and intubation, other than as a drug vehicle. The mean total of IV fluids given in the operating room was 2.85 litres, separate from that used in the pump-oxygenator. No inotropic agents were given at any time except for 1 Gm of CaCl_2 prior to the end of cardiopulmonary bypass.

Results

(All data are presented as mean $\pm$ standard deviation.)

The mean arterial pressure (MAP) (Figure 1) fell on induction from a mean of 97 to 63 mmHg ($p < 0.001$) and returned to the awake level following intubation. Subsequently, MAP was kept below the

FIGURE 1 Central venous, pulmonary capillary wedge and mean arterial pressures. Ten sequential studies are shown from the awake state through anaesthesia, operation and at one and 24 hours postoperatively. $\mu = 10$.

FIGURE 2 Heart rate and pulmonary (PUL VR) and systemic (SVR) vascular resistances. $\mu = 10$.

awake level, but it rose to 108 mmHg by one hour after the operation. Wedge pressure (PCW) decreased on induction ($p < 0.005$) and was below the awake level 24 hours postoperatively. Right atrial pressure decreased ($p < 0.05$) only after induction.

Mean heart rate (Figure 2) did not change on induction but rose from 64 to 73 beats·min⁻¹ ($p < 0.001$) after intubation. It remained above the control level throughout and was highest (mean 91) at 24 hours. With MAP consistently decreased and rate continuously above the awake level, rate-pressure product changed only on induction, from 8700 to 5800. At 1 and 24 hours RPP was higher than before induction, at 11,900 and 10,800.

Mean total pulmonary vascular resistance remained unchanged except for a rise ($p < 0.02$) after chest closure. Systemic vascular resistance (SVR) was unchanged during anaesthesia but rose ($p < 0.01$) to 2250 dynes·sec·cm⁻⁵ at one hour following operation.

Cardiac index (Figure 3) decreased ($p < 0.001$) on induction and remained below control at most of the sequential studies during and after operation. Consequently, stroke work and volume indices fell

($p < 0.001$) on induction and remained so throughout.

Mean CBF (Figure 4), which was 116 ml·min⁻¹ in the ten awake, sedated subjects, fell to 79 on induction ($p < 0.05$) and rose again to 118 on intubation. Thereafter it was unchanged until higher flow occurred in the two studies early postpump. Oxygen saturation and content of CS blood increased on induction and was elevated postintubation and presterotomy. Immediately postpump, CS O₂ content fell below awake level from hemodilution, rising to the preanaesthetic quantity after chest closure. Mean MVO₂ of 10.2 ml·min⁻¹, present in the awake sedated state, fell ($p < 0.001$) on induction, rose on intubation and was below the awake level again only prior to the surgical incision.

Arterial lactate content (Figure 5) rose above the control level after sternotomy; both arterial and CS content were elevated from the postpump study through one hour postoperatively. Before anaesthesia, mean MLE was normal at 24 per cent and no significant changes occurred subsequently. In one awake patient CS lactate was 45 per cent greater than arterial; this changed to 55 per cent extraction after induction. No lactate production was found subsequently in any patient at any time.

FIGURE 3 Cardiac index, stroke work index and stroke volume index. $\mu = 10$.

Discussion

An aim of general anaesthetic techniques should be to maintain a steady, mild depression of the circulation without response to autonomic stimulation. Greater cardiac work from increased heart rate and blood pressure creates, in the patient with coronary disease, a greater risk of myocardial oxygen need exceeding supply, distal to stenotic lesions. The problem is to know, from readily available haemodynamic monitoring, when oxygen supply is being exceeded. Rate-pressure product is not the simple helpful aid that we had hoped.⁵ Since the advent of regular use of the pulmonary arterial catheter³ and direct arterial pressure monitoring, the haemodynamic responses to the major anaesthetic agents have been thoroughly documented. But information on myocardial oxygenation had to await practical methods of determining coronary flow and MVO_2 in the operating room. This can now be done with the argon washin technique⁶ or the thermodilution measurement of coronary blood flow.⁴ With the latter, we have studied the major

FIGURE 4 Coronary blood flow (CBF), coronary sinus oxygen content (CSO₂) and myocardial oxygen consumption (MVO₂). $\mu = 10$.

FIGURE 5 Arterial and coronary sinus lactate levels and per cent lactate extraction. $\mu = 10$.

agents: halothane and morphine,¹ nitrous oxide,^{7,8} fentanyl⁹ and isoflurane.¹⁰ This report examines, in similar fashion, enflurane anaesthesia given to patients having CABG.

The patients selected were as those for all our coronary flow studies to date: with coronary lesions requiring bypass grafts but with ventricular function preserved. None had other complicating factors, as valvular or pulmonary disease, hypertension, heart failure or recent myocardial infarction. They did have significant regional hypokinesia or akinesia and were kept on adequate beta blockade. Those whose wedge pressure on catheter insertion was less than 12 mmHg were given fluid to raise it to 12 before the awake study, to begin from a more uniform base of ventricular function. The preinduction study was done with patients in a quiet state, more normodynamic than the unpremedicated patients studied by Reiz *et al.*¹¹ with the same instrumentation. We believe that the minimal amount of thiopentone given to begin the induction had no major effect on the next measurement after ten minutes of enflurane.

Measurement of coronary sinus blood flow

The Ganz catheter for measuring CBF has been

available since 1971⁴ but has been little used in anaesthesia research. The infusate (by pump) emerges near the tip and the external thermistor measures temperature of coronary venous blood downstream, which temperature is influenced by the cooler infusate and the rate of blood flow past the probe. Through a second introducer placed close to that for the PA catheter, into the right internal jugular vein, the CS catheter is advanced to the right atrium. With this catheter attached to a pressure transducer and using fluoroscopy, it is not difficult to insert it into the coronary sinus. We position the catheter several centimeters into the sinus and not far up the great cardiac vein, by injecting contrast medium. Displacement by the surgeon has been rare and there have been no complications from its presence in the sinus for 30 hours. In this position, the measurement is of total CS blood flow, shown to be almost all the left coronary inflow.¹² Elevated right atrial pressure affects CS outflow; in our patients RAP was normal. Each measurement takes about 40 seconds and can be repeated in two minutes, a great advantage over the argon washin technique.⁶

The measurement is highly reproducible. We have found in 12 awake patients that duplicate flows three minutes apart averaged 113.8 ± 0.1 and 112.9 ± 0.1 ml·min⁻¹. As did Ganz initially,⁴ we regularly find a broad range of CBF in patients with coronary disease, which gives a wide standard deviation when analysed. While other factors, such as heart size, MVO₂ and cardiac output may be involved, one correlation we find is of coronary flow to arterial pressure. In seven patients of our previous study,¹ with the highest MAP when awake (mean 112 mmHg), mean CBF was 151 ml·min⁻¹. In the seven patients in that study with the lowest arterial pressure when awake (mean 86 mmHg), mean CBF at that time was 69 ml·min⁻¹. This fits with the fact that blood pressure is a major determinant of CBF, along with coronary resistance. The flow measured is global for the left ventricle and wide differences in regional flow may be present in coronary disease.

Circulatory responses

A ten-minute induction with enflurane-oxygen at a mean end-expiratory concentration of 1.72 per cent, decreased blood pressure 35 per cent, due to a fall in cardiac index without change in heart rate or

systemic resistance. This appeared to be a response to reduced stroke work and not to depressed myocardial contractility, since both wedge and RA filling pressures diminished. In contrast, Delaney *et al.*² found in CABG patients given 0.75 MAC enflurane, no decrease in cardiac index but a fall in systemic resistance, reducing the blood pressure. In the dog, Merin *et al.*¹³ reported that 2.3 and 3.6 per cent enflurane caused dose-dependent decreases in blood pressure, stroke work and volume, a rise in heart rate and left atrial pressure, but no change in systemic resistance. They concluded that enflurane was at least as depressing as halothane for the dog heart. Our halothane study¹ used the same protocol as for enflurane: we saw the same fall in MAP but the decreases in cardiac index and systemic resistance were not significant, with halothane concentrations during induction of less than one MAC.

In contrast to morphine¹ and high dose fentanyl,⁹ a controlled state of circulatory depression was maintained with enflurane in CABG patients. With effective beta blockade continued until operation, heart rate remained slow on induction and intubation. Blood pressure on intubation returned only to normal after its decrease on induction. Control of blood pressure during operation was by reduction of cardiac index since systemic resistance remained unchanged. While control of blood pressure with enflurane was present during anaesthesia, hypertension and elevated rate appeared early afterward, on awakening. This hyperdynamic state has the risks of postsurgical bleeding and major ischaemic events, so it must be avoided by intravenous opiates, sedatives and vasodilators.

Coronary flow and myocardial oxygenation

On induction with enflurane, CBF fell 32 per cent due to the reduced MAP, since coronary resistance did not change. On intubation CBF returned to the awake flow, as did the MAP. Flow higher than that awake was present early postpump, without hypertension. The myocardium must have been re-establishing a more normal biochemical milieu after the cardioplegic period. The vein grafts also provided higher coronary flow to a vasodilated coronary bed. CBF decreased postoperatively, likely due to re-establishment of normal coronary vascular resistance. We have no information on the long-term effect of coronary vein grafts on coronary sinus flow.

Oxygen content of coronary venous blood increased on induction of anaesthesia, with a FiO_2 change from 0.2 to 1.0, with also an arterial saturation increase from 96 to 100 per cent. The reduction in oxygen uptake on induction paralleled a 54 per cent reduction in stroke work; this reduction continued throughout the remainder of the study period. The reduced oxygen uptake caused the decreased MVO_2 before perfusion, since coronary flow did not change. Our documentation was of global oxygen usage by the left ventricle; regional ischaemia could have been present and not detected. No changes in ST segment configuration were seen in the V5 lead, but multilead recording possibly could have detected ST changes. However, if global ischaemia was present, it would be shown by lactate production.

The behaviour of arterial lactate during open heart surgery has long been documented,¹⁴ but the pattern in coronary venous blood has not. We found that the latter increased in parallel with the arterial level, indicating a whole body buildup, plus exogenous lactate. Normal extraction by the myocardium continued, of at least 20 per cent of arterial lactate, in all ten patients, indicative of overall myocardial aerobic oxygenation. This was not seen with any other major agent,^{1,7-10} with which individual myocardia produced lactate at some of the measurement times. This absence of myocardial lactate production during enflurane anaesthesia shows the absence of global ischaemia throughout. We cannot conclude that any one major agent is better than others for patients having CABG, due to the small numbers of patients studied using each agent. The important point is that global left ventricular oxygenation is preserved when controlled depression of the circulation is maintained with any agent or combination, except for nitrous oxide.^{7,8}

The intentional decrease in cardiac index, systemic resistance and blood pressure, on induction with enflurane and oxygen, was beneficial and safe. Cardiac work decreased; arterial and coronary venous oxygen content increased: less oxygen was consumed. The fall in coronary flow was not detrimental. Lactate extraction continued; in fact, lactate production, present without other ischaemic evidence, changed to extraction on induction in one patient. Intubation returned haemodynamics to those of the awake state but CS oxygen content remained elevated due to the high FiO_2 . Continuing

to give enflurane in concentrations sufficient to keep the blood pressure slightly below that awake, maintained myocardial oxygen balance without evidence of ischaemia (ECG, lactate). Enflurane effectively accomplished the desired beneficial effects.

In summary, we found that a steady controlled depression of the heart and circulation can be produced and maintained with enflurane-oxygen for patients having CABG. Autonomic response to stimulation can be prevented. Cardiac work decreased and MVO_2 hence also did so. We saw no evidence of inadequate oxygenation, i.e., global ischaemia, of the left ventricle.

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Résumé

Dix malades opérés pour pontage aorto-coronarien sous anesthésie à l'enflurane ont été étudiés. Tous avaient une fonction ventriculaire normale et neuf sur dix étaient sous médication bêta-bloquante adéquate. Les mesures suivantes ont été prises avant, durant et pendant l'anesthésie à l'enflurane: le débit cardiaque, les pressions vasculaires, le flux sanguin du sinus coronaire (CBF), la consommation d'oxygène myocardique (MVO_2) et l'extraction de lactate (MLE). L'induction de l'anesthésie à l'enflurane s'étendant sur une période de dix minutes à une concentration moyenne de fin d'expiration de 1.72 pour cent a diminué la tension artérielle (MAP) par diminution de l'index cardiaque (CI) sans provoquer de changement dans la fréquence cardiaque ou les résistances périphériques. L'intubation a ramené la MAP et le CI au niveau contrôle et a aussi accéléré la fréquence cardiaque. Par la suite, l'enflurane a maintenu la MAP, le CI et le travail du ventricule gauche en-dessous des niveaux mesurés à l'état d'éveil. Le flux coronarien a diminué à l'induction, s'est élevé de nouveau à l'intubation pour se maintenir normal jusqu'à la circulation extracorporelle. La MVO_2 a elle aussi chuté à l'induction comme en témoigne l'élévation du contenu en oxygène du sang du sinus coronarien, contenu qui est demeuré élevé. L'extraction de lactate est demeurée normale chez tous les malades. On n'a donc pas observé d'ischémie myocardique chez les patients adéquatement traités aux bêta-bloquants lorsque les facteurs hémodynamiques ont été maintenus au niveau mesuré à l'état d'éveil chez les patients prémédiqués; de même, on n'a pas observé d'ischémie myocardique lorsque ces facteurs hémodynamiques ont été réduits en bas des niveaux pré-opératoires.