Brief Clinical Reports

Fatal cardiac ischaemia associated with prolonged desflurane anaesthesia and administration of exogenous catecholamines

J.M. Murray MA FFARCSI,
S.R. Luney FFARCSI

Purpose: Four cardiac ischaemic events are reported during and after prolonged anaesthesia with desflurane.

Clinical features: We have evaluated desflurane in 21 consecutive patients undergoing advanced head and neck reconstructive surgery. Four deaths occurred which were associated with cardiac ischaemic syndromes either during or immediately after operation. All patients in the study received a similar anaesthetic. This comprised induction with propofol and maintenance with alfentanil and desflurane in oxygen-enriched air. Inotropic support (either dopamine or dobutamine in low dose, $5 \mu\text{g}\cdot\text{kg}\cdot\text{min}^{-1}$) was provided as part of the anaesthetic technique in all patients. Critical cardiovascular incidents were observed in each of the four patients during surgery. These were either sudden bradycardia or tachycardia associated with ST-segment electrocardiographic changes. The four patients who died had a documented past history of coronary heart disease and were classified American Society of Anesthesiologists (ASA) II or III. One patient (#2) did not survive anaesthesia and surgery and the three others died on the first, second and twelfth postoperative days. Enzyme increases (CK/CK-MB) were available in three patients and confirmed myocardial ischaemia.

Conclusion: These cases represent an unexpected increase in the immediate postoperative mortality for these types of patients and this anaesthetic sequence.

Objectif : Quatre incidents ischémiques myocardiques ont été rapportés pendant et après une anesthésie prolongée au desflurane.

Aspects cliniques : Nous avons évalué le desflurane chez 21 patients successifs devant subir une chirurgie reconstructive avancée de la tête et du cou. Quatre décès sont survenus, associés à des syndromes ischémiques du myocarde, pendant ou immédiatement après l'opération. Tous les patients de l'étude ont reçu un anesthésique similaire. Ce qui comprenait l'induction avec du propofol et le maintien avec de l'alfentanil et du desflurane dans de l'air enrichi d'oxygène. Un soutien inotrope (dopamine ou dobutamine en petites doses, $5 \mu\text{g}\cdot\text{kg}\cdot\text{min}^{-1}$) a été fourni comme faisant partie de la technique anesthésique chez tous les patients. Des incidents cardiovasculaires critiques ont été observés chez chacun des quatre patients pendant la chirurgie. C'était de la bradycardie soudaine ou de la tachycardie associée à des changements électrocardiographiques des segments ST. On a pu vérifier chez les quatre patients décédés, classés II ou III selon l'American Society of Anesthesiologists (ASA), une histoire de maladie coronarienne. Un patient (n° 2) n'a pas survécu à l'anesthésie et à la chirurgie et les trois autres sont morts le premier, le deuxième ou le douzième jour postopératoire. Des hausses d'enzymes (CK/CK-MB) se sont présentées chez trois patients et ont permis de confirmer une ischémie myocardique.

Conclusion : Les cas rapportés représentent une hausse inattendue de mortalité postopératoire immédiate chez les sujets souffrant de maladie coronarienne et recevant la séquence anesthésique mentionnée.

From the Departments of Anaesthesia, The Royal Group of Hospitals, Grosvenor Road, Belfast BT10 6BA.

Address correspondence to: Dr J.M. Murray, The Regional Intensive Care Unit, The Royal Victoria Hospital, Grosvenor Road, Belfast BT12 6BA, United Kingdom.

Accepted for publication September 26, 1998

PERIOPERATIVE mortality and morbidity within specific patient populations is often predictable.¹ This is particularly relevant to patients with cardio-respiratory disease.²

We report four cases of perioperative myocardial ischaemia during and after prolonged desflurane anaesthesia that resulted in a fatal outcome.

Case reports

Demographic data, past medical history and anaesthetic methods are shown in Table I. Table II outlines the type and duration of surgery, perioperative critical incidents, outcomes and the measured CK/CK-MB fractions.

Patient #1

During surgery there were two critical cardiovascular incidents. One hour after induction of anaesthesia there was a sudden decrease in heart rate from 70 to 50 bpm unrelated to surgical stimulation which resolved with 0.6 mg atropine *iv*. Four hours later there was widespread ST-segment depression of the ECG, which was temporarily related to the commencement of a dopamine infusion at 5 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$. The ECG changes resolved following a decrease in the end tidal concentration of desflurane to 2.0%, cessation of the dopamine and the introduction of 5 $\text{mg}\cdot\text{hr}^{-1}$ glyceryl trinitrate and 2.5 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ dobutamine *iv*.

The immediate postoperative course was complicated by further episodes of acute myocardial ischaemia as evidenced by elevated serum CK-CKMB fractions (CK; 3212 3412 and 2578, CK-MB; 320, 359, 246). Over the following week the patient's cardiac status deteriorated and he died 12 days after surgery.

Patient #2

This patient had suffered a myocardial infarction nine years before the present surgery from which he had made an uneventful recovery. There were two cardiovascular events during operation. A decrease in heart

rate to 42 bpm occurred one hour after induction of anaesthesia and resolved with 0.6 mg atropine *iv*. After resection of the tumour, 5 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ dopamine was started to provide optimum cardiovascular indices for the planned microvascular graft. Within five minutes the arterial blood pressure decreased from 110/60 mmHg to 75/40 mmHg and this was associated with widespread ST-segment depression and was rapidly followed by cardiovascular collapse from which the patient could not be resuscitated. Post-mortem examination revealed almost complete occlusion of both the right and left coronary arteries with recent bleeding into an atheromatous plaque of the left anterior descending coronary artery. The left ventricle was hypertrophied (14-16 mm thick). There were some foci of thrombosis, up to 5 mm in diameter, scattered throughout its walls. No recent necrosis was seen.

Patient #3

Six hours after operation he developed a sinus tachycardia of 120 bpm associated with a decrease in arterial blood pressure from 110/60 to 70/40 mmHg. Prompt volume loading with 1 litre gelatin and increasing the dobutamine infusion from 5 to 10 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ only marginally improved the situation with an increase in systolic arterial blood pressure to 80 mmHg. Blood was obtained for CK and CK-MB fractions (CK 2022, CK-MB 247). A pulmonary artery catheter was inserted when the patient remained oliguric (< 10 $\text{ml}\cdot\text{hr}^{-1}$) and hypotensive (75/40 mmHg; mean 55 mmHg). Despite further aggressive inotropic and fluid therapy the patient died 14 hr later. No post-mortem examination was performed.

Patient #4

One serious cardiovascular event occurred. This was an isolated and sudden ST-segment depression associated with unifocal ventricular ectopic beats five minutes after the introduction of dobutamine hydrochloride (5

TABLE I Demographic data, past medical history and ASA status.

	Patient #1	Patient #2	Patient #3	Patient #4
Age (yr)	62	68	72	69
Weight (kg)	56	85	64	92
Gender	Male	Male	Male	Male
Past medical history	Myocardial Infarction - 6 yr previously Stable angina COPD	Myocardial infarction - 9 yr previously Stable angina	Angina - 10 yr No myocardial infarction COPD	Myocardial infarction - 12 yr previously Stable angina COPD
Medications	Nifedipine Atenolol	Glyceryl trinitrate Nifedipine	Metoprolol Diltiazem	Glyceryl trinitrate Nifedipine
ASA status	III	II	III	III

TABLE II Surgery, anaesthesia, outcome and CK/CK-MB data.

	<i>Patient #1</i>	<i>Patient #2</i>	<i>Patient #3</i>	<i>Patient #4</i>
Surgical procedure & duration	Glossectomy & laryngectomy. Free flap reconstruction 10 hr	Recurrent head & neck cancer. Resection and free flap reconstruction 3 hr (not completed)	Recurrent head & neck cancer Resection, and free flap reconstruction 10 hr	Oral tumour. Neck dissection. Free flap reconstruction 8 hr.
Per-op Critical incident Anaesthesia	Bradycardia ST-change Propofol Vecuronium Desflurane Alfentanil Oxygen/air	Bradycardia ST-change Propofol Vecuronium Desflurane Alfentanil Oxygen/air	Tachycardia Hypotension Propofol Vecuronium Desflurane Alfentanil Oxygen/air	Isolated ST-change Propofol Vecuronium Desflurane Alfentanil Oxygen/air
Max. end tidal Desflurane %	6.7%	6.9%	7.3%	6.6%
Per-op Inotropes 5 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$	Dopamine Dobutamine	Dopamine	Dobutamine	Dobutamine
CK / CK-MB	3212 / 320 3412 / 359 2578 / 246	N/A	2022 / 247 - -	2165 / 252 2498 / 288 -
Outcome	Death 12th Day	Death Per-op	Death 1st Day	Death 2nd Day
Autopsy	No	Yes	No	No

$\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$). These ST-segment changes resolved following the introduction of glyceryl trinitrate (5-10 $\text{mg}\cdot\text{hr}^{-1}$). After operation there was further ST-segment depression and a decrease in arterial blood pressure to 70/40 mmHg. Aggressive inotropic therapy with norepinephrine (5-10 $\mu\text{g}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$) temporarily improved the hemodynamic status and a presumptive diagnosis of cardiogenic shock secondary to acute myocardial infarction was made. This was supported by considerable increases in CK and CK-MB fraction (CK 2165, CK-MB 252; normal ranges 0-200 and 0-20 respectively). The patient remained critically ill and died 48 hr after operation.

Discussion

We report the deaths of four patients occurring either during or shortly after prolonged desflurane anaesthesia. A disproportionately high incidence of perioperative myocardial ischaemia was observed in this series. All patients had a history of chronic but stable heart disease. One had previously undergone major cancer surgery without incident using a different inhaled anaesthetic.

To our knowledge, this is the first time the concomitant use of desflurane and inotropic agents in patients with coronary artery disease is raised as a possible cause of serious cardiac adverse events. There is no evidence to prove a cause and effect relationship between desflurane anaesthesia and the fatal cardiac outcomes described in this article. However, the 19% incidence of cardiac related deaths in this small series of patients is disturbingly

high and prompted this report. A similar rate of cardiac complications has not been reported in larger scale studies assessing the use of desflurane in patients undergoing coronary artery surgery or major vascular surgery.^{3,4} Many of those patients received inotropic agents without an increased incidence of myocardial ischaemia or infarction. Current evidence does not support the avoidance of desflurane in patients with CAD requiring inotropic agents. If other similar reports become available, further investigation may be necessary to determine the true contribution of desflurane to cardiac ischaemic syndromes in those particular patients.

References

- 1 Derrington MC, Smith G. A review of studies of anaesthetic risk, morbidity and mortality. *Br J Anaesth* 1987; 59: 815-33.
- 2 Strunin L, Forrest JB, Lunn JN, Epstein BS, Duncan PG, Davies JM. Towards excellence in anaesthesia. *Can J Anaesth* 1988; 35: 278-86.
- 3 Thomson IR, Bowering JB, Hudson RJ, Frai MA, Rosenbloom M. A comparison of desflurane and isoflurane in patients undergoing coronary artery surgery. *Anesthesiology* 1991; 75: 776-81.
- 4 Helman J, Leung J, Bellows W, Pineda N, Mangano D, and SPI Research Group. Desflurane anaesthesia and myocardial ischemia: comparative risk vs. sufentanil anaesthesia in patients undergoing coronary artery bypass graft surgery. *Anesthesiology* 1991; 75: A1124.