Comparison of the myocardial effects of desflurane and isoflurane in healthy patients: assessment by continuous oesophageal aortic blood flow echo-Doppler

P.-Y. GUEUGNIAUD, G. VAUDELIN, M. BERTIN-MAGHIT, C. BOUCHARD, R. STAGNI AND P. PETIT

Summary
Experimentally, desflurane causes a moderate positive inotropic effect and a transient increase in arterial pressure with rapid increases in concentration compared with isoflurane. We used a continuous oesophageal aortic blood flow echo-Doppler device to study the myocardial effects of equi-anaesthetic concentrations of isoflurane and desflurane in 32 healthy patients undergoing superficial surgery. After induction of anaesthesia with midazolam, etomidate and fentanyl, general anaesthesia was maintained in 16 patients with 0.6% end-expired concentration of isoflurane and in 16 patients with 3% end-expired concentration of desflurane. Isoflurane induced a rapid decrease in aortic blood flow (ABF) which remained almost stable whereas desflurane induced an early, moderate and transient increase in ABF (1 min after introduction of the halogenated agent, mean ABF was 107 (sd 3)% in the desflurane group vs 95 (9)% in isoflurane group compared with control values before introduction of the inhalation agent; P = 0.005), followed by a marked secondary decrease in ABF. The maximal decrease in ABF reached 71 (15)% of its initial value in the desflurane group compared with 80 (14)% in the isoflurane group (ns). Neither agent caused significant changes in other variables except for $\frac{P}{P_{CO_2}}$, which decreased in both groups. Continuous ABF echo-Doppler monitoring demonstrated an early transient positive inotropic effect of desflurane. (Br. J. Anaesth. 1998; 81: 844–849).

Keywords: measurement techniques, blood flow; measurement techniques, echo-Doppler; anaesthetics volatile, desflurane; anaesthetics volatile, isoflurane; heart, myocardial function

Isoflurane and desflurane are inhalation anaesthetic agents which classically result in similar decreases in cardiac function. However, desflurane may allow maintenance of higher mean arterial pressure by less decrease in systemic vascular resistance than isoflurane. In contrast with isoflurane, rapid increase in desflurane concentration can increase heart rate and arterial pressure by sympathetic activation. The precise mechanism of this sympathetic activation is not completely understood and may involve airway irritation by this pungent agent, transient disinhibition of centres modulating sympathetic efferent outflow, and/or peripheral action on sympathetic nerve endings. A recent in vitro study suggested that in rat myocardium, desflurane induced a moderate positive inotropic effect compared with isoflurane. Experimental studies comparing the cardiovasuclar effects of isoflurane and desflurane are numerous but clinical investigations in healthy patients are not available. Invasive haemodynamic monitoring is necessary for such assessment, but is generally not indicated in common surgical procedures.

A non-invasive method using an aortic blood flow (ABF) ultrasound machine has previously proved reliable and recently its value for anaesthetic monitoring has been documented. Therefore, we conducted a clinical study to non-invasively compare haemodynamic changes induced by general anaesthesia with equi-anaesthetic concentrations of isoflurane or desflurane, using this new continuous oesophageal ABF echo-Doppler device.

Patients and methods
With the approval of the local Ethics Committee and after obtaining written informed consent, we studied 32 consecutive patients, aged 18–65 yr, ASA I, who suffered burns (burn surface area = 1–30% of the total body surface area) and who required superficial surgical procedures. Patients undergoing surgery during the first 5 days after injury and those with an inhalation injury, sepsis or suspected oesophageal disease were excluded. The 32 patients were allocated randomly to receive either isoflurane or desflurane.

All patients were premedicated with hydroxyzine 100 mg and alprazolam 1 mg orally, 1 h before surgery. General anaesthesia was induced with midazolam 0.05 mg kg$^{-1}$, etomidate 0.4 mg kg$^{-1}$ and fentanyl 3 μg kg$^{-1}$ i.v. and neuromuscular block was achieved with vecuronium 0.1 mg kg$^{-1}$. After orotracheal intubation, the lungs were ventilated mechanically (tidal volume 12 ml kg$^{-1}$, ventilatory frequency 12 bpm) (Cato, Dräger, Lübeck, Germany). Anaesthesia was maintained initially by nitrous oxide (40% oxygen–60% nitrous oxide), and after the first

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haemodynamic measurements, by isoflurane or desflurane at equi-anesthetic concentrations, using a rebreathing (semi-closed) system with soda lime as the carbon dioxide absorbent: the planned end-expired concentration (EEC) of isoflurane was 0.6% and desflurane, 3%.

After induction of anaesthesia, non-invasive continuous haemodynamic monitoring was performed with an oesophageal echo-Doppler aortic blood flowmeter (Dynemo 3000, Sometec Inc, Paris, France). Using continuous data provided by this device, an initial haemodynamic assessment was made after insertion of the probe, 5 min after the end of induction, and just before introduction of the halogenated agent \( \tau_I \). Thereafter, data were recorded at the following times: 1 min after the introduction of the halogenated agent \( \tau_I \); 5 min after the EEC of isoflurane reached a constant of 0.6% or of desflurane, 3% \( \tau_D \); 30 min after a constant EEC of halogenated anaesthetic \( \tau_H \); and just before the end of the isoflurane or desflurane inhalation period \( \tau_T \).

**MEASUREMENT PRINCIPLE**

By definition, the flow rate \( \dot{Q} \) passing through a cross-section of a blood vessel can be expressed as: 
\[
\dot{Q} = A \times \bar{v},
\]
where \( A \) = cross-section of the vessel and \( \bar{v} \) = a spatial average velocity of blood over the entire cross-section. From the circular section of the thoracic aorta, the cross-sectional area can be calculated when the diameter is known (\( A = \pi d^2/4 \)). Velocity is measured using the Doppler formula: 
\[
\bar{v} = \left( \frac{C \times \Delta F}{2F_c \times \cos \Phi} \right),
\]
where \( C = \) ultrasound velocity inside the blood, \( \Delta F = \) frequency variation of emitted ultrasound, \( F_c = \) emission frequency and \( \Phi = \) angle between the beam and the direction of blood motion. Determination of the real ABF requires simultaneous and continuous measurement of the aortic cross-section and of the blood velocity inside the aorta, at the same anatomical level where the aorta and oesophagus are nearly parallel. For the velocity measurement, the angle of incidence remains constant because a water-inflated balloon surrounding the transducers maintains the probe in a fixed position.

**FLOWMETER AND PROBE**

The flowmeter comprises three main parts: M-mode imaging system for continuous aortic diameter measurement, pulsed Doppler for descending aortic blood velocity measurement and a microprocessor system allowing flow calculations and integrating signals from peripheral devices to create a non-invasive haemodynamic profile.

The oesophageal probe has two ultrasound transducers. The first is a 10-MHz M-echo scanner with an emission narrow parallel beam of only 3 mm. It is located at the distal part of the probe perpendicular to the centre line. The second is a 5-MHz Doppler pulsed emission transducer mounted at an angle of 60° in relation to the centre line of the probe: the pulsed Doppler is emitted with a 20° divergent beam and the gate Doppler signal depth is adapted automatically to the diameter of the aorta. Divergence of \( \pm 20° \) of the Doppler beam allows insonation of the whole surface of the cross-section of the aorta. Insonation may be partial, if only part of the Doppler emission reaches the aortic target. To avoid errors from partial insonation of the aorta by the Doppler beam, the Dynemo 3000 uses an echographic orientation of the Doppler beam. Another error may occur if the negative systolic speed waves determined by blood cells moving back column does not occupy the whole section of the aorta. If the negative flow is calculated using the total aortic section, overestimation is systematically obtained. To avoid this problem, a proper balance of the diastolic velocity measurement, based on the detection of the residual energy of the Doppler signal, is used.

A cylindrical latex balloon is mounted on the sheath to be inflated with 8 ml of water. This inflated balloon maintains a constant angle of incidence of the ultrasound beams and allows the transducers to rotate freely without contact against the oesophageal mucosal wall. It ensures transmission of ultrasound waves without air interposition and dissipates any heat produced. The 10-MHz M-mode scan and the 5-MHz pulsed Doppler system allow very clear image resolution. The angle of incidence of the Doppler beam at 60° (complementary: 30°) was chosen to permit the Doppler ultrasound cut to be performed at the same level as the echocutic cut over the descending aorta, allowing measurement of the diameter and blood velocity simultaneously at the same anatomical level.

**HAEMODYNAMIC MONITORING**

Just after induction of anaesthesia, the oesophageal ultrasonic probe was inserted and positioned. The depth of the probe in the oesophagus varied according to the height of the patient. The probe was first placed on the skin surface along the naso-oesophageal route and depth was measured on the probe between the echo transducer externally placed on the third intercostal juxtasternal space and a slide rubber ring placed at the level of the nose. The corresponding mark on the probe is a guide to depth limit. This distance corresponded to the approximate level where the aorta and oesophagus are parallel. The probe is then introduced into the oesophagus. Other monitoring devices are connected to the flowmeter: an oscillometric non-invasive sphygmomanometer which provided systolic and diastolic arterial pressure values; and an ECG (Propaq 104 EL, Protocol, Beaverton, USA).

The device calculates ABF, mean arterial pressure (MAP), heart rate (HR), stroke volume (obtained from the formula \( SV = ABF/HR \)) and systemic vascular resistance (SVR = MAP/ABF × 79.9 whenever a new arterial pressure is provided). These two variables are indexed to ABF. Systolic time intervals (STI) were measured from the Q wave of the ECG signal and the acceleration signal was derived from the Doppler velocity signal. Opening and closing of the aortic valve were detected from the acceleration signal. The computer determined the duration of the pre-ejection period (PEP) between the Q wave and the beginning of the systolic acceleration front, corresponding to aortic valve opening. Starting at the end of PEP, left ventricular ejection time (LVET) was obtained by detecting the acceleration signal, the second maximum of systolic deceleration corresponding to aortic valve closure.16 PEP and LVET were mea-
Table 1 Patient and operation characteristics (mean (SD) [range]). BSA = Burned surface area; Anaesthesia = duration of anaesthesia

<table>
<thead>
<tr>
<th>Variable</th>
<th>Isoflurane group</th>
<th>Desflurane group</th>
</tr>
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<tbody>
<tr>
<td>Age (yr)</td>
<td>36.4 (18–53)</td>
<td>34.6 (18–52)</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>68 (11) [52–85]</td>
<td>72 (9) [47–85]</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>169 (9.5) [152–185]</td>
<td>172 (6.3) [157–180]</td>
</tr>
<tr>
<td>BSA (%)</td>
<td>13.3 (12.1) [1–30]</td>
<td>7.06 (5.8) [2–20]</td>
</tr>
<tr>
<td>Anaesthesia (min)</td>
<td>112.8 (72.8) [30–270]</td>
<td>83.6 (41.5) [45–230]</td>
</tr>
<tr>
<td>PEP/LVET</td>
<td>0.40 (0.04)</td>
<td>0.42 (0.05)</td>
</tr>
<tr>
<td>(Iso)</td>
<td>0.42 (0.05)</td>
<td>0.43 (0.08)</td>
</tr>
<tr>
<td>(Des)</td>
<td>0.43 (0.08)</td>
<td>0.45 (0.07)</td>
</tr>
<tr>
<td>Pre-jection period indexed to HR; LVETi</td>
<td>172 (6.3) [157–180]</td>
<td>172 (6.3) [157–180]</td>
</tr>
<tr>
<td>PEP/LVET ratio</td>
<td>0.41 (0.06)</td>
<td>0.43 (0.05)</td>
</tr>
<tr>
<td>(Iso)</td>
<td>0.43 (0.05)</td>
<td>0.46 (0.07)</td>
</tr>
<tr>
<td>(Des)</td>
<td>0.46 (0.07)</td>
<td>0.50 (0.07)*</td>
</tr>
<tr>
<td>EEC(%)</td>
<td>99 (1)</td>
<td>99 (1)</td>
</tr>
<tr>
<td>(Iso)</td>
<td>99 (1)</td>
<td>99 (1)</td>
</tr>
<tr>
<td>(Des)</td>
<td>99 (1)</td>
<td>99 (1)</td>
</tr>
<tr>
<td>Aortic diameter (mm)</td>
<td>19.5 (2.9)</td>
<td>19.3 (2.7)</td>
</tr>
<tr>
<td>(Iso)</td>
<td>19.3 (2.7)</td>
<td>19.2 (2.9)</td>
</tr>
<tr>
<td>(Des)</td>
<td>19.2 (2.9)</td>
<td>19.6 (2.9)</td>
</tr>
</tbody>
</table>

Results

There were no significant differences between groups but there was a trend towards a greater burned surface area and longer anaesthesia in the isoflurane group. The EEC of isoflurane and desflurane were relatively constant after induction (EEC = 1.2% and 4.5%, respectively, during induction, 0.7% and 3.1% at t2, 0.7% and 2.9% at t5, and 0.6% and 2.9% at t10 respectively). Aortic diameter and ABF measurements were easily obtained in all patients. The quality of the aortic wall picture was excellent and diameter remained stable with less than 3% variation during the recordings (maximal recorded variation of the aortic diameter value for the same patient during the entire monitoring). No incident was noted with the device.

Table 2 Comparison of the haemodynamic variations induced by isoflurane and desflurane (mean (SD)). t1 = Before halogenated agent (control values); t2 = 1 min after introduction of the agent; t3 = 5 min after the EEC of isoflurane reached 0.6% or desflurane, 3%; t4 = 5 min after the EEC of isoflurane reached 0.6% or desflurane, 3%; t5 = 5 min after the EEC of isoflurane reached 0.6% or desflurane, 3%; P<0.001 vs baseline values (t0) (ANOVA and Newman–Keuls test).

<table>
<thead>
<tr>
<th>Variable</th>
<th>t0</th>
<th>t1</th>
<th>t2</th>
<th>t3</th>
<th>t4</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>ABF (litre min⁻¹)</td>
<td>3.9 (1.2)</td>
<td>3.7 (1.2)</td>
<td>3.1 (1.0)**</td>
<td>3.0 (1.0)**</td>
<td>3.1 (0.9)**</td>
<td>0.05</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>4.4 (1.3)</td>
<td>4.7 (1.4)</td>
<td>4.2 (1.4)</td>
<td>3.5 (1.2)**</td>
<td>3.1 (0.7)**</td>
<td>0.05</td>
</tr>
<tr>
<td>HR (beat min⁻¹)</td>
<td>80 (19)</td>
<td>79 (16)</td>
<td>79 (17)</td>
<td>75 (16)</td>
<td>76 (14)</td>
<td>ns</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>50 (19)</td>
<td>48 (15)</td>
<td>40 (11)*</td>
<td>41 (12)*</td>
<td>42 (15)*</td>
<td>0.05</td>
</tr>
<tr>
<td>SVR (dyn s cm⁻⁶)</td>
<td>1831 (570)</td>
<td>1912 (654)</td>
<td>2228 (615)*</td>
<td>2240 (666)*</td>
<td>2146 (607)*</td>
<td>0.05</td>
</tr>
<tr>
<td>PEPi (ms)</td>
<td>161 (16)</td>
<td>168 (14)</td>
<td>171 (18)</td>
<td>174 (24)</td>
<td>173 (23)</td>
<td>ns</td>
</tr>
<tr>
<td>PEP/LVET</td>
<td>0.40 (0.04)</td>
<td>0.42 (0.05)</td>
<td>0.43 (0.08)</td>
<td>0.45 (0.10)</td>
<td>0.45 (0.08)</td>
<td>0.05</td>
</tr>
<tr>
<td>PECO₂ (kPa)</td>
<td>4.5 (0.7)</td>
<td>4.4 (0.7)</td>
<td>4.4 (0.5)</td>
<td>4.3 (0.5)</td>
<td>4.3 (0.7)</td>
<td>0.05</td>
</tr>
<tr>
<td>SpO₂ (%)</td>
<td>99 (1)</td>
<td>99 (1)</td>
<td>99 (1)</td>
<td>99 (1)</td>
<td>99 (1)</td>
<td>ns</td>
</tr>
<tr>
<td>Aortic diameter (mm)</td>
<td>19.5 (2.9)</td>
<td>19.3 (2.7)</td>
<td>19.1 (2.9)</td>
<td>19.3 (2.9)</td>
<td>19.6 (2.9)</td>
<td>ns</td>
</tr>
</tbody>
</table>
isoflurane group (96 (17)% vs 122 (35)%, respectively; \(P=0.01\)) (fig. 2). PEPi gradually increased in both groups. LVETi decreased between \(t_1\) and \(t_4\) but more obviously in the desflurane group at \(t_4\) (88 (7)% vs 97 (10)%, respectively; \(P=0.02\)). PEP/LVETi ratio was significantly greater in the desflurane group compared with the isoflurane group at the end of the inhalation period (at \(t_4\): 132 (22)% vs 112 (16)% respectively; \(P=0.003\)).

Discussion

Desflurane is a relatively new inhalation anaesthetic agent which differs from isoflurane only in the substitution of a fluorine for a chlorine atom,20 with a lower blood solubility and a lower tissue–blood partition coefficient.21 These characteristics indicate more rapid equilibration between tissues and blood and more precise control of alveolar anaesthetic concentration for desflurane.21 Consequently, desflurane could be a useful agent, but its effects on the circulation have yet to be well established.

Comparisons between the cardiovascular effects of isoflurane and desflurane have been made for several years. Weiskopf and colleagues22 and Merin and colleagues2 studied the cardiovascular effects of desflurane in chronically instrumented swine or dogs, and showed that desflurane induced myocardial depressant effects which were similar to those produced by equi-anaesthetic concentrations of isoflurane. Pagel and co-workers23 reported that desflurane induced less depression of myocardial contractility and less decrease in arterial pressure than isoflurane in chronically instrumented dogs. These differences were suppressed by autonomic nervous system block, suggesting that desflurane has a less depressant effect on autonomic activity.

Ebert and Muzi4 reported that, in contrast with isoflurane, an increase in the vaporizer setting for desflurane from 1 to 1.5 MAC increased mean arterial pressure and muscle sympathetic nerve activity in human volunteers. Weiskopf and colleagues,5 in a randomized clinical study, demonstrated that rapid increases in desflurane concentration to greater than 1 MAC caused transient sympathetic activation with increases in heart rate and arterial pressure. Sites mediating this sympathetic activation appeared to be located in the upper and lower airways, but the possibility of sites outside the airway must be considered.7,8

A recent in vitro study in isolated rat myocardium showed that desflurane induced a moderate positive inotropic effect compared with isoflurane.9 This effect was related to intra-myocardial catecholamine release. Intra-myocardial catecholamine release could be one of the mechanisms participating in the sympathetic activation observed in vivo with desflurane.

In our study, whereas we did not observe any variation in HR or MAP, ABF and SV increased transiently in the desflurane group at the beginning of inhalation. This transient increase in ABF and SV with desflurane confirms the possible positive inotropic

Figure 1 Changes in mean arterial pressure (MAP) and heart rate (HR) with desflurane and isoflurane, expressed as percentage of control values (\(t_0\)). Data are mean (SD). No significant differences.

Figure 2 Changes in aortic blood flow (ABF) and systemic vascular resistance (SVR) with desflurane and isoflurane, expressed as percentage of control values (\(t_0\)). Data are mean (SD). *\(P<0.05\), **\(P<0.001\) vs control values.
effects observed in isolated rat myocardium, and also the sympathetic activation described during a rapid increase in desflurane inhalation.\(^5\)\(^7\) We found a more marked decrease in ABF during maintenance of anaesthesia in the desflurane group. The lack of variation in MAP and HR could explain the increased SVR with isoflurane and desflurane during anaesthesia, but as SVR is calculated from ABF, the accuracy of this variable could be suspect. After the transient increase in ABF and SV in the desflurane group, we observed a consistent decrease in ABF, associated with an increase in PEP/LVET ratio in both groups. PEP/LVET ratio provides a simplified expression of alterations in STI, and thus the variations in PEP/LVET ratio reflect inotropic variables. In normal adults, this ratio averages 0.35 (0.05), and a PEP/LVET ratio increasing to 0.44 denotes decreased left ventricular performance.\(^2\)\(^4\) Hence the longer term changes with both halogenated anaesthetic agents probably indicates a late decrease in myocardial contractility. The concomitant decrease in \(P_{\text{CO}_2}\) can reflect impairment in tissue perfusion,\(^1\)\(^2\)\(^5\)\(^25\) which could also be related to late alterations in cardiac performance, particularly in the desflurane group. Nevertheless, we cannot exclude the fact that the primary effects of these agents were on SVR and were unrelated to myocardial contractility. Unfortunately, because of rapid recovery with desflurane, we could not assess a reliable and comparable final measurement in both groups after the end of inhalation.

The main value of this study was the clinical conditions: usual premedication and induction of anaesthesia, maintenance of anaesthesia with halogenated agent associated with nitrous oxide in oxygen. All patients were ASA I and surgery was superficial and limited, and was unlikely to cause any haemodynamic changes. Thus our findings were attributed to the cardiovascular effects of the anaesthetic agents.

Nevertheless, several limitations have to be emphasized. First, the echo-Doppler ABF device gives an accurate assessment of aortic output but does not allow precise measurement of cardiac output. The main value of this system is measurement of trends in each variable during surgical and/or anaesthetic procedures. Even if the difficulties initially reported in the measurement of blood flow by ultrasound were solved,\(^26\) thermodilution is a valuable and reliable technique (except for low cardiac output),\(^27\) but remains discontinuous and invasive. In contrast, the ABF echo-Doppler device gives a continuous signal which provides haemodynamic assessment and trends in cardiovascular variables. This method correlates well with electromagnetic flow in animals\(^12\)\(^28\) and with thermodilution in humans,\(^10\)\(^11\) and the haemodynamic trends are useful in the assessment of various surgical procedures,\(^29\)\(^30\) particularly variations induced by inhalation anaesthesia in adults\(^14\)\(^15\) and in infants.\(^14\)\(^15\) Second, MAP was not measured continuously. Transient variations in MAP may not have been recorded so that the accuracy of MAP and of the calculated SVR, is questionable. Third, a clinical study cannot distinguish primary myocardial or vascular effects of anaesthetic agents. Finally, the difference in the duration of anaesthesia could have interfered with \(t_1\) values. Unfortunately, the clinical conditions of this study did not allow conclusions to be made from this late measurement.

In summary, our study has highlighted the value of continuous ABF echo-Doppler monitoring in the detection of moderate haemodynamic variations induced by halogenated anaesthetic agents in healthy patients. During desflurane inhalation, ABF increased transiently and then decreased, whereas during isoflurane inhalation, ABF first decreased and then remained almost stable. In both groups, the final decreases in ABF were 20–30% of their initial values. The concomitant and late increases in PEP/LVET ratio and decreases in \(P_{\text{CO}_2}\) may also indicate slight impairment in tissue perfusion after prolonged halogenated inhalation, especially with desflurane. Such haemodynamic changes suggest caution when using desflurane in patients with hypertension or coronary artery disease.

Acknowledgement

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References