Comparison of the effects of sevoflurane and isoflurane on arterial oxygenation during one lung ventilation

J. Y. Y. WANG, G. N. RUSSELL, R. D. PAGE, M. JACKSON AND S. H. PENNEFATHER

Summary

We have compared the effects of sevoflurane and isoflurane on arterial oxygenation, heart rate and mean arterial pressure during one lung anaesthesia in a prospective, crossover study. We studied 28 patients undergoing oesophagogastrectomy, allocated alternately to one of two groups. Patients in group I/S (n=14) received 1 MAC (1.1%) of isoflurane in oxygen from induction until the end of 30 min of open chest one lung ventilation (OLV) in the lateral position. This was followed by 1 MAC (2.1%) of sevoflurane in oxygen for the next 30 min of OLV. Patients in group S/I (n=14) received the two anaesthetic agents in the reverse order. We found no significant difference in arterial oxygenation, heart rate or mean arterial pressure between the two potent inhalation agents. In the subgroup of patients with pulmonary artery catheters (n=12), we found a significant increase (P<0.05) in derived shunt during sevoflurane anaesthesia. There was no significant difference in mixed venous saturation and cardiac output. We conclude that during one lung ventilation, the choice between sevoflurane and isoflurane did not significantly influence arterial oxygenation. (Br. J. Anaesth. 1998; 81: 850–853).

Keywords: anaesthetics volatile, sevoflurane; anaesthetics volatile, isoflurane; oxygen, partial pressure; ventilation, one lung; lung, shunting

One lung ventilation (OLV) is required for several thoracic operations. Adequate arterial oxygen is not achieved in some patients despite an accurately placed endobronchial tube and high inspired oxygen. Minor changes in arterial oxygen tension caused by changes in anaesthetic technique may be important in these patients. The effects of anaesthesia and OLV on arterial oxygenation are complex and not fully understood. Potent inhalation agents are used widely for thoracic anaesthesia; they have several desirable properties, including ease of administration, rapid onset and offset, and ability to cause bronchodilatation. One potential drawback is inhibition of hypoxic pulmonary vasoconstriction (HPV).

Isoflurane has been shown previously to be superior to both halothane and enflurane with respect to arterial oxygenation during one lung anaesthesia. Sevoflurane has some advantages over isoflurane. Its non-pungent odour facilitates smooth and rapid gaseous induction and its lower blood-gas partition coefficient results in faster recovery from anaesthesia. Rapid emergence from anaesthesia is important after some thoracic procedures, for example lung resection surgery. In vitro, sevoflurane inhibits hypoxic pulmonary vasoconstriction in a dose-related manner similar to isoflurane. Acceptable arterial oxygenation was achieved during one lung ventilation in sheep anaesthetized with sevoflurane. The purpose of this study was to compare the effects of sevoflurane and isoflurane on arterial oxygenation, heart rate and mean arterial pressure during one lung anaesthesia. In a subgroup of patients, we also compared mixed venous saturation, derived shunt and cardiac output.

Patients and methods

This prospective crossover study was approved by the Liverpool Research Ethics Committee. Informed written consent was obtained from adult patients undergoing oesophagogastrectomy. Exclusion criteria were previous lung resection and contraindications to epidural analgesia. Patients were allocated alternately to one of two groups.

Baseline heart rate, arterial pressure and spirometry were recorded on the day before operation. Patients were premedicated with diazepam 0.15 mg kg⁻¹. On arrival in the anaesthetic room, 10 ml kg⁻¹ of i.v. fluid were given over 20 min followed by infusion of 10 ml kg⁻¹ h⁻¹. A radial arterial cannula and a mid-thoracic epidural catheter were inserted under local anaesthesia. No epidural test dose was given. An arterial blood-gas sample during air breathing was obtained before induction of anaesthesia. After pre-oxygenation, general anaesthesia was induced with fentanyl 1.5 μg kg⁻¹ and propofol 2–3 mg kg⁻¹. Neuromuscular block was achieved with vecuronium, followed by intubation with a left double-lumen endobronchial tube (Rusch, Kernen, Germany). Correct tube position was confirmed with a fibreoptic bronchoscope.

Patients assigned to group I/S received 1 MAC (1.1%) of end-tidal isoflurane in oxygen from induction until the end of the first 30 min of open chest OLV in the lateral position. They then received 1 MAC (2.1%) of end-tidal sevoflurane in oxygen for the next 30 min of OLV. During the changeover, fresh gas flow 6 litre min⁻¹ was used to facilitate washout of the previous anaesthetic agent and washin of the new anaesthetic agent. Patients...
assigned to group S/I received the two inhalation agents in reverse order.

A pulmonary artery catheter (Baxter, Edwards Critical-Care Division, Irvine, CA, USA) was inserted in those patients undergoing left thoracotomy and who had consented to this additional monitoring. In all patients other monitoring included: ECG, pulse oximetry, nasopharyngeal temperature, neuromuscular block, ventilation pressures and volumes (Cato, Drager, Lubeck, Germany), end-tidal carbon dioxide concentration and anaesthetic gases by infrared spectroscopy (Cato, Drager, Lubeck, Germany). After the patient was placed in the semilateral position (45° tilt from the horizontal), a forced-air warming blanket (Bair Hugger, Augustine Medical, Inc; Eden Prairie, MN, USA) was placed on the lower extremities. Pressure transducers (Omeda, Herts, UK) were zeroed at the mid-vertebral line. All patients received an epidural bolus dose of fentanyl 1 μg kg⁻¹ followed by an infusion of 1 μg kg⁻¹ h⁻¹ during the study. Motor block of more than 80% was maintained with incremental doses of vecuronium. During OLV, tidal volume was set initially at 10 ml kg⁻¹ and reduced if required to maintain peak inspiratory pressure of less than 30 cm H₂O. The E/E ratio was set at 1:2 and ventilatory frequency was adjusted to maintain arterial carbon dioxide tension at 4.7–5.9 kPa. Before the onset of OLV, the position of the double-lumen endobronchial tube was rechecked with the aid of a fibreoptic bronchoscope. Collapse of the non-dependent lung was confirmed by direct observation. Intraoperative arterial pressure was maintained within 20% of baseline measurement with i.v. fluid or i.v. fentanyl as required.

Intraoperative haemodynamic (Tram 600, Marquette Electronics, Inc; Milwaukee, WI, USA) and blood-gas measurements (IL1640 BGElectrolytes Analyser and CO-Oximeter, Barcelona, Spain) were obtained at the end of 30 min OLV by the same observer who was not blinded to the anaesthetic used. Cardiac output was measured using the thermodilution technique. Derived shunt and oxygen consumption were calculated using standard formulae. Shunt equation: \[ Q_S/Q = \frac{(C_{O₂} - C_{O₂})}{(C_{O₂} - C_{O₂})} \]

where \( C_{O₂} \) = pulmonary capillary blood oxygen content assuming 100% saturation of capillary blood; \( C_{O₂} \) = arterial blood oxygen content; and \( C_{O₂} \) = mixed venous blood oxygen content.

Power analysis was performed using a mean difference in \( P_{A\text{O}_2} \) of greater than 3 kPa as clinically significant and an estimated SD of the differences of 5.4 kPa. To detect this mean difference with 80% power at the 5% level of significance, we needed to recruit 27 patients.

Results are given as mean (SD). Statistical analysis was performed in accordance with the simple crossover design methodology.

Treatment effect (isoflurane vs sevoflurane) was sought under the expectation that there were no treatment effects. Thus we compared treatment effect using the null hypothesis: \( \text{Iso}_{\text{group S/I}} - \text{Sev}_{\text{group S/I}} = \left( \text{Iso}_{\text{group S/I}} - \text{Isogroup I/S} \right) \) and \( \text{Sev}_{\text{group S/I}} = \left( \text{Sev}_{\text{group S/I}} - \text{Sev}_{\text{group I/S}} \right) \). Period (transfer) effect was sought under the expectation that there was no period effect. Thus period effect was analysed using the null hypothesis: \( \left( \text{Iso}_{\text{group S/I}} - \text{Sev}_{\text{group S/I}} \right) = \left( \text{Iso}_{\text{group I/S}} - \text{Sev}_{\text{group I/S}} \right) \). In the comparison between sevoflurane and isoflurane treatment effect, there was no significant difference in arterial oxygenation, heart rate or mean arterial pressure. In the subgroup of patients with pulmonary artery catheters, there was a significant increase in derived shunt during sevoflurane anaesthesia compared with isoflurane. There was no significant difference in mixed venous saturation or cardiac output. In patient with pulmonary artery catheters, a significant period effect was found only in mixed venous saturation (table 3).

Discussion

Patients undergoing oesophagogastrectomy were studied because this operation allowed at least 1 h of OLV with minimal trauma to the non-dependent lung. We chose 30 min as the duration before the changeover of anaesthetic agent. This was based on previous human studies which showed that \( P_{A\text{O}_2} \)
stabilized as early as 20 min after initiation of OLV.12–14 The initial washout of inhalation agent was rapid, but low concentrations persisted for several hours which can potentially exert a biological effect. This raises the question of period effect in this study, which can potentially exert a biological effect. This study would consent to insertion of a pulmonary artery catheter. We did not know in advance how many of the 27 patients required for this study would consent to insertion of a pulmonary artery catheter. We alternately allocated our patients in order to ensure an equal distribution of patients with a pulmonary catheter between the two groups. This method is unlikely to bias the outcome in this study as the same surgeon (R. D. P.) performed all surgery and the same anaesthetist (J. Y. Y. W.) gave all anaesthetics. Further, only one oesophagogastrectomy was performed at each operating session and there was no regular pattern to the scheduling of cases. Finally, we found no significant difference in preoperative data between the two groups.

During OLV, adequate oxygenation can be a concern, especially in the supine position and in patients with poor pre-existing lung function. Therefore, it is important for anaesthetists to be aware of all the variables which can influence oxygenation. Arterial oxygenation ($P_{\text{aO}_2}$), and therefore cardiac output ($Q_0$), depends on $P_{\text{aO}_2}$ and $P_{\text{aO}_2}$–V. The initial washout of inhalation agent was rapid, but low concentrations persisted for several hours which can potentially exert a biological effect. This raises the question of period effect in this study, which can potentially exert a biological effect. This study would consent to insertion of a pulmonary artery catheter. We did not know in advance how many of the 27 patients required for this study would consent to insertion of a pulmonary artery catheter. We alternately allocated our patients in order to ensure an equal distribution of patients with a pulmonary catheter between the two groups. This method is unlikely to bias the outcome in this study as the same surgeon (R. D. P.) performed all surgery and the same anaesthetist (J. Y. Y. W.) gave all anaesthetics. Further, only one oesophagogastrectomy was performed at each operating session and there was no regular pattern to the scheduling of cases. Finally, we found no significant difference in preoperative data between the two groups.

### Table 2

<table>
<thead>
<tr>
<th>Group</th>
<th>Isoflurane</th>
<th>Sevoflurane</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beat min$^{-1}$)</td>
<td>84 (8.4)</td>
<td>81 (9.4)</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>75 (7.3)*</td>
<td>75 (6.1)*</td>
</tr>
<tr>
<td>$P_{\text{aO}_2}$ (kPa)</td>
<td>21.2 (11.8)</td>
<td>23.4 (17)</td>
</tr>
<tr>
<td>SVR (dyn s cm$^{-5}$)</td>
<td>19.7 (3.1)</td>
<td>20.3 (3.2)</td>
</tr>
<tr>
<td>CO (litre min$^{-1}$)</td>
<td>6.8 (2)</td>
<td>6.4 (1.4)</td>
</tr>
<tr>
<td>$Q_0$ (ml min$^{-1}$)</td>
<td>80 (4.2)</td>
<td>77 (4.9)</td>
</tr>
<tr>
<td>$Q_0$/$Q_t$ (%)</td>
<td>43 (4)</td>
<td>44 (4)</td>
</tr>
<tr>
<td>$O_2$ consumption (ml min$^{-1}$)</td>
<td>190 (34)</td>
<td>187 (49)</td>
</tr>
</tbody>
</table>

### Table 3

<table>
<thead>
<tr>
<th>Group</th>
<th>Iso–Sevo</th>
<th>Sevo–Iso</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beat min$^{-1}$)</td>
<td>3.07 (5.99)</td>
<td>1.36 (5.44)</td>
</tr>
<tr>
<td>MAP (mm Hg)</td>
<td>−0.14 (6.42)</td>
<td>−2.79 (8.47)</td>
</tr>
<tr>
<td>$P_{\text{aO}_2}$ (kPa)</td>
<td>−2.17 (9.97)</td>
<td>−4.01 (11.24)</td>
</tr>
<tr>
<td>MPAP (mm Hg)</td>
<td>−0.67 (2.94)</td>
<td>0.83 (1.83)</td>
</tr>
<tr>
<td>$Q_0$ (ml min$^{-1}$)</td>
<td>4.03 (1.3)</td>
<td>0.15 (0.39)</td>
</tr>
<tr>
<td>SVR (dyn s cm$^{-5}$)</td>
<td>−59 (142)</td>
<td>−145 (175)</td>
</tr>
<tr>
<td>$S_{\text{vO}_2}$ (%)</td>
<td>2.37 (2.6)</td>
<td>3.15 (4.5)</td>
</tr>
<tr>
<td>$Q_0$/$Q_t$ (%)</td>
<td>−1 (1.8)</td>
<td>4.1 (4.7)*</td>
</tr>
<tr>
<td>$O_2$ consumption (ml min$^{-1}$)</td>
<td>3.23 (33.4)</td>
<td>−27.6 (14.6)</td>
</tr>
</tbody>
</table>
potent inhalation agents, such as halothane, enflurane, isoflurane and sevoflurane, directly inhibit HPV in a dose-related manner to a similar degree. In vivo, this direct inhibitory effect on shunt and PAO₂ is more difficult to demonstrate as haemodynamic effects of the general anaesthetic agents can also influence these variables. In human studies, comparing i.v. anaesthetic agents with inhalation anaesthetic agents during OLV, 1 MAC of halothane caused a slight but significant increase in shunt and a decrease in PAO₂, up to 2 MAC of enflurane caused no significant change in shunt or PAO₂, and 1 MAC of isoflurane caused no significant change in shunt or PAO₂. In a study comparing isoflurane with enflurane during OLV, PAO₂ and PCO₂ were found to be significantly higher during isoflurane anaesthesia; there was no significant difference in shunt or oxygen consumption, and the authors postulated that the difference in oxygenation may be explained by better preservation of Qt that occurred during isoflurane anaesthesia. Total i.v. anaesthesia with propofol infusion is a widely accepted technique. Propofol infusions in the range of 6–12 mg kg⁻¹ h⁻¹ do not inhibit HPV. When isoflurane was compared with propofol–alfentanil, there was no significant difference in PAO₂. A separate study comparing isoflurane and propofol anaesthesia showed a significant increase in shunt and cardiac output during isoflurane anaesthesia. The increase in Qr during isoflurane anaesthesia could explain why there was no difference in PAO₂ despite the increase in shunt.

Inhalation anaesthesia is generally favoured over i.v. anaesthesia for surgery requiring OLV because it has several advantages. These include ease of drug delivery, offset independent of hepatic or renal function, end-tidal concentration monitoring, bronchodilation and the option of gaseous induction. Sevoflurane is a relatively new anaesthetic agent with some advantages over isoflurane. A non-pungent odour allows rapid and smooth inhalation induction without the arrhythmogenic potential of halothane. A lower blood-gas partition coefficient allows more rapid onset, easier titration and most importantly faster recovery from anaesthesia. Earlier recovery of spontaneous respiration and cough reflexes can potentially benefit the thoracic patient. In our study, there was no difference in PAO₂, heart rate or mean arterial pressure between sevoflurane and isoflurane. In patients with pulmonary artery catheters, there was a significant increase in derived shunt during sevoflurane anaesthesia. There was no significant difference in PAO₂, or cardiac output. These results are not unexpected as the two anaesthetic agents have a similar dose–response manner in vitro and have a similar cardiovascular profile with the possible exception of a lower heart rate with sevoflurane. The combined dose of i.v. and epidural fentanyl given in this study could have masked any difference in heart rate between isoflurane and sevoflurane.

Combining data from the two groups gave an average shunt of 39% for isoflurane. This is consistent with three previous studies in which the inspired oxygen was 100%. Shunt during OLV in these studies were 38%, 39% and 41%. In summary, there was no significant difference in arterial oxygenation in patients anaesthetized with sevoflurane or isoflurane in the semi-lateral position during OLV. As sevoflurane offers some advantages over currently used potent inhalation agents, its suitability for thoracic anaesthesia warrants further evaluation.

References
22. Kellow NH, Scott AD, White SA, Feneck RO. Comparison of the effects of propofol and isoflurane anaesthesia on right ven-