Comparison of the effects of propofol and isoflurane anaesthesia on right ventricular function and shunt fraction during thoracic surgery†

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Summary
I.v. anaesthetic agents, including propofol, have not been shown to inhibit hypoxic pulmonary vasoconstriction (HPV). This may encourage the use of propofol in thoracic surgery where one lung ventilation (OLV) is required. We have compared the effects of maintaining anaesthesia with either isoflurane or propofol infusion on right ventricular function and shunt fraction. We studied 10 patients who received isoflurane and 12 who received propofol. When OLV commenced there was a greater reduction in both mean cardiac index (3.2 (SEM 0.2) to 2.4 (0.1) litre min\(^{-1}\) m\(^{-2}\) for propofol, and 3.4 (0.2) to 3.3 (0.4) litre min\(^{-1}\) m\(^{-2}\) for isoflurane) and right ventricular ejection fraction (0.45 (0.03) to 0.37 (0.02) for propofol, and 0.48 (0.02) to 0.42 (0.02) for isoflurane) in patients who received propofol. Furthermore, these reductions were sustained for longer in the propofol group. However, propofol was not associated with a significant increase in shunt fraction during OLV, which increased threefold in patients who received isoflurane. (Br. J. Anaesth. 1995; 75: 578–582)

Key words

While it is generally accepted that volatile anaesthetic agents inhibit hypoxic pulmonary vasoconstriction (HPV) and may promote hypoxaemia during one lung ventilation (OLV), there are limited data on the effect of propofol on HPV, or of the effect of either volatile agents or propofol on right ventricular function. We have investigated the effects of a maintenance anaesthetic regimen, comprising either propofol or a volatile anaesthetic agent (isoflurane), on right ventricular function and shunt fraction in patients undergoing elective thoracotomy requiring a period of OLV.

Patients and methods
The study was approved by the local hospital Ethics Committee and all patients gave informed written consent. We studied 23 patients undergoing elective thoracotomy requiring OLV. Patients were excluded if they were less than 18 or greater than 75 yr of age, and if their cardiac rhythm was not predominantly sinus, because of technical difficulties with the pulmonary artery catheter associated with measurement of right ventricular volumes in these patients. After obtaining consent, patients were allocated randomly to receive either isoflurane or propofol for maintenance of anaesthesia after standard premedication and induction.

All patients were premedicated with atropine 0.6 mg i.m., pethidine 1.5 mg kg\(^{-1}\) i.m. and promethazine 25 mg i.m. On arrival in the anaesthetic room, monitoring was established under local anaesthesia, including insertion of an REF-1 right ventricular ejection fraction pulmonary artery catheter (American Edwards Laboratories, CA, USA). Baseline haemodynamic measurements were performed with patients conscious and breathing air.

After preoxygenation anaesthesia was induced with fentanyl 5 μg kg\(^{-1}\) i.v. and etomidate 0.3 mg kg\(^{-1}\) i.v. In addition, all patients were given cefuroxime 1.5 g as prophylaxis. As soon as the patients lost consciousness, the allocated maintenance regimen was started. The lungs of patients in both groups were ventilated with 50 % nitrous oxide in oxygen throughout the operation. Patients in the isoflurane group (n = 11) also received isoflurane at an inspired concentration of 1–1.5 %. Patients in the propofol group (n = 12) were given an infusion of 10 mg kg\(^{-1}\) h\(^{-1}\) reducing at 10-min intervals to 8 and then 6 mg kg\(^{-1}\) h\(^{-1}\). After neuromuscular block with atracurium 0.5 mg kg\(^{-1}\), the appropriate endobronchial tube was inserted, and its position checked by intermittent clamping and careful auscultation in all lung zones.

Patients were turned to the lateral position in preparation for surgery, and the tube position checked again. Throughout the study the lungs were ventilated to normocapnia (arterial carbon dioxide tension 4.5–5.5 kPa). After induction all measurements were made by the same observer who was not blinded to the anaesthetic regimen used, at the following times: TLV, after 20 min of the allocated...
Results

No patient required blood or crystalloid administration. Additional intraoperative analgesics were not given. The inspired oxygen concentration of three patients in each group was temporarily increased to 100% because of significant arterial desaturation (SpO₂ < 90%) occurring during the early phase of OLV. This was reduced to 50% after 20 min of stable ventilation of all remaining lung tissue.

Cardiac output was measured using the thermodynamic technique, by forcibly injecting 10 ml of 5% glucose at room temperature through the proximal port of the pulmonary artery catheter. This was repeated until three readings within 10% of each other were obtained. Measurements included the following: cardiac index (CI), heart rate (HR), mean arterial pressure (MAP), pulmonary vascular resistance index (PVRI), right ventricular ejection fraction (RVEF), end-diastolic and end-systolic volume indices (EDVI, ESVI), and shunt fraction (Qs/Qt). Cardiac output, end-systolic and end-diastolic volumes were calculated by personal computer using standard equations.

Changes in haemodynamic data were analysed using analysis of variance with Bonferroni correction for multiple comparisons, and paired and unpaired t-tests as appropriate. All data are expressed as mean (SEM). Changes were considered significant at the 5% level (P < 0.05).

Table 2  Haemodynamic values (mean (SEM)) at baseline, during two lung ventilation (TLV), one lung ventilation (OLV) and during closure (End). HR = heart rate, MAP = mean arterial pressure, CI = cardiac index, PVRI = pulmonary vascular resistance index, RVEF = right ventricular ejection fraction, EDVI = end-diastolic volume index, ESVI = end-systolic volume index, Qs/Qt = shunt fraction (%). Within-group comparisons: *P < 0.05, **P < 0.01; between-group comparisons: †P < 0.05.
within 5 min in all patients and 20 min of stability was allowed before the OLV readings were taken.

One other patient in the isoflurane group was eliminated from the study after arterial desaturation which did not respond to increasing the inspired oxygen concentration. It improved with insufflation of oxygen into the non-dependent lung and intermittent reinflation with oxygen. The data from this patient were not included in the analysis as he had undergone periods of re-expansion and ventilation of the non-dependent lung during OLV.

Results therefore refer to 10 patients in the isoflurane group and 12 patients in the propofol group (table 1).

No patient required more than a total of 50 ml of injectate at any time to obtain reproducible cardiac output measurements.

Patients were comparable for all measured and derived variables at baseline (table 2). Both groups exhibited a significant reduction in CI from baseline to TLV (table 2, fig. 1). This returned to near baseline levels in the isoflurane patients during OLV, while it remained depressed in the propofol patients. CI remained depressed significantly from baseline levels at wound closure in both groups. CI was significantly smaller during OLV in the propofol than in the isoflurane group.

The reduction in CI was associated with significant reductions in RVEF which were greater at all times in the propofol group (fig. 2). Between baseline and OLV there was a small but non-significant increase in HR in the isoflurane group while there was a reduction in HR in patients given propofol. There was little change during the study in EDVI, but while ESVI remained relatively stable in the isoflurane group, it increased significantly from baseline at all times in the propofol group. ESVI in patients who received propofol was significantly greater at all times after baseline than in patients who received isoflurane (fig. 3).

Both groups had slightly elevated shunt fractions at baseline, possibly because of the effect of sedative premedication. This was reversed promptly in both groups after intubation and ventilation. During OLV there was a substantial increase from TLV values in mean shunt fraction in the isoflurane patients, which returned to baseline levels at wound closure. Between these two times, shunt increased more than three-fold in the isoflurane group but by less than half in the propofol group (fig. 4).

**Discussion**

The maintenance regimens used in this study were chosen to represent widely used and generally accepted techniques of volatile anaesthesia using isoflurane and total i.v. anaesthesia using propofol. Nitrous oxide is used widely in anaesthesia for
thoracic surgery and has been shown to inhibit HPV in a small and consistent manner [1]. As it was used in the same concentration in both groups, it may seem reasonable to expect any effect on HPV to have been similar in both groups. However, this assumption does not take into account any possible interaction between nitrous oxide and either propofol or isoflurane. On the other hand, any attempt to correct for this would have resulted in an unusual anaesthetic technique, which was not the intention of the study.

It may be argued that endobronchial tube placement should have been verified by the use of a fiberoptic bronchoscope [2]. However, the technique of verifying correct tube placement with a fiberoptic bronchoscope may be technically difficult, particularly with right-sided tubes [3]. Furthermore, endobronchial tubes may commonly move during patient positioning after initial tube placement [4], and it is important not to assume that a tube which was apparently positioned correctly in the anaesthetic room, is still positioned correctly after the patient has been turned to the lateral position. For these reasons left-sided endobronchial tubes are used more frequently than right. We repeatedly checked the position of the endobronchial tubes in our patients, both after initial insertion and after positioning the patient for surgery.

Patients who received propofol experienced a greater and sustained reduction in CI compared with those who received isoflurane. There was a relative increase in ESVI in the propofol group, while there were no significant changes in right ventricular filling, as measured by EDVI, in either group. In the absence of any significant changes in right ventricular afterload in the form of PVRI in either group, these changes may represent a relatively greater impairment of ventricular systolic function in patients receiving propofol.

The increases in shunt fraction which predominantly affected the isoflurane group did not occur in conjunction with increases in PVRI, suggesting that the changes in shunt fraction were not caused by global pressure or resistance constraints acting throughout the pulmonary vasculature. Rather, it is probable that there were regional differences in pulmonary vascular tone, particularly in the isoflurane group, promoting the diversion of deoxygenated blood through non-ventilated lung units.

Many studies have examined the effect of volatile and i.v. anaesthetic agents on HPV. The phenomenon was described first by Von Euler and Liljestrand [5] in cats anaesthetized with pentobarbitone and undergoing ventilation with gas mixtures containing varying amounts of oxygen in nitrogen. They found that pulmonary artery pressures increased when the animals were given 10.5% oxygen and decreased with 100% oxygen. While human studies have shown conflicting results on the ability of volatile anaesthetic agents to inhibit HPV, animal studies have been generally more conclusive. For example, Carlsson, Bindslev and Hedenstierna [6] studied the effect of administration of isoflurane to patients who were anaesthetized with i.v. barbiturate anaesthesia, when one lung was ventilated with an hypoxic gas mixture containing 6–8% oxygen in nitrogen. Cardiac output was measured by thermodilution and differential lung blood flow was measured by the excretion of the insoluble inert gas sulphur hexafluoride. Administration of the hypoxic gas mixture resulted in reduced study lung blood flow, which the addition of 1–1.5% isoflurane did not significantly increase. There was, however, a small non-significant increase when 1.5% isoflurane was given. In another study, Rogers and Benumof administered i.v. anaesthesia comprising either methohexitone or ketamine to 20 patients receiving either halothane or isoflurane while undergoing thoracotomy [7]. They were stabilized during OLV and the i.v. agent was discontinued while the allocated volatile agent was introduced. No change in PaO_2 occurred. In contrast, many animal studies have confirmed that volatile anaesthetic agents inhibit HPV [8] in a dose-dependent manner [9].

The failure to demonstrate inhibition of HPV by volatile anaesthetic agents in humans may result from the large number of confounding variables in the clinical setting [10]. Marshall and Marshall found an inverse relationship between HPV ratio (percentage flow to the hypoxic segment with anaesthetic divided by the percentage flow without anaesthetic) and cardiac output ratio (cardiac output with anaesthetic divided by cardiac output without anaesthetic) [11]. In the presence of volatile anaesthetic agents the efficacy of HPV was inversely proportional to cardiac output. Thus the clinical effects of any inhibition of HPV by the volatile agent could be offset by a significant reduction in cardiac output, and concomitantly exaggerated by an increase or a moderate decrease in cardiac output. This phenomenon may, at least in part, have accounted for the differences in shunt fraction found between the two groups in our study. The relative preservation of cardiac output in the isoflurane group may have contributed to the greater shunt fractions in these patients.

While the effect of volatile agents and the older i.v. agents have been studied extensively, there are comparably few data on the effect of propofol on HPV in humans. In one study [12] the investigators administered increasing doses of propofol ranging from 6 to 12 mg kg\(^{-1}\) h\(^{-1}\) to patients with left-sided endobronchial tubes whose left lungs alone were being ventilated in the left lateral decubitus position. They found that none of the propofol doses was associated with an increased shunt fraction or changes in arterial oxygenation. In another study [13] the authors found that patients who received 1 MAC of enfurane had a significantly higher shunt fraction than those who received propofol 10 mg kg\(^{-1}\) h\(^{-1}\) during OLV. There were no significant changes in cardiac output in these studies, although no comment was made on changes in cardiac index.

During thoracic surgery it is important to maintain the competence of HPV in order to avoid or minimize arterial hypoxaemia associated with OLV; it is also important to preserve cardiac function as near as
possible to preoperative values. Our findings confirm those of other workers who found that propofol does not appear to inhibit HPV. However, our isoflurane patients experienced a substantial increase in shunt fraction associated with OLV. While this may be a genuine phenomenon, consistent with most findings from animal studies, given the conflicting conclusions from clinical studies and the demonstrated relationship between HPV ratio and cardiac output ratio [11], we cannot conclude that this increase in shunt fraction resulted simply from administration of isoflurane. In contrast, the propofol group experienced greater impairment of systolic function. In the absence of an increase in right ventricular afterload this may represent a finding of genuine clinical significance in some patient groups.

We conclude that both agents are not ideal for thoracic surgery, with disadvantages which may have particular clinical relevance in different groups. However, we have confirmed previous studies showing that propofol did not inhibit HPV, and it may be considered as an alternative to the volatile agents, bearing in mind the relatively greater depression of right ventricular function which was observed in this study.

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References


