BJA

British Journal of Anaesthesia, 119 (4): 655–63 (2017)

doi: 10.1093/bja/aex230
Advance Access Publication Date: 31 August 2017
Critical Care

Postoperative pulmonary complications, pulmonary and systemic inflammatory responses after lung resection surgery with prolonged one-lung ventilation. Randomized controlled trial comparing intravenous and inhalational anaesthesia

F. de la Gala[1,2,*], P. Piñeiro[1,2], A. Reyes[1,2], E. Vara[3], L. Olmedilla[1,2], P. Cruz[1,2], I. Garutti[1,2] and Contributors[†]

[1]Department of Anaesthesiology, Gregorio Marañón University Hospital, C/Doctor Esquerdo 46, 28009 Madrid, Spain, [2]Biomedical Research Institute of Gregorio Marañón University Hospital, Madrid, Spain and [3]Department of Biochemistry and Molecular Biology III, Universidad Complutense, Madrid, Spain

[*]Corresponding author. E-mail: galareyes@telefonica.net
[†]Members of Contributors group are listed in Appendix.

Abstract

Background. Recent studies report the immunomodulatory lung-protective role of halogenated anaesthetics during lung resection surgery (LRS) but have not investigated differences in clinical postoperative pulmonary complications (PPCs). The main goal of the present study was to compare the effect of sevoflurane and propofol on the incidence of PPCs in patients undergoing LRS. The second aim was to compare pulmonary and systemic inflammatory responses to LRS.
Methods. Of 180 patients undergoing LRS recruited, data from 174 patients were analysed. Patients were randomized to two groups (propofol or sevoflurane) and were managed otherwise using the same anaesthetic protocol. Bronchoalveolar lavage (BAL) was performed in both lungs before and after one-lung ventilation for analysis of cytokines. Arterial blood was drawn for measurement of the cytokines analysed in the BAL fluid at five time points. Intraoperative haemodynamic and respiratory parameters, PPCs (defined following the ARISCAT study), and mortality during the first month and yr were recorded.
Results. More PPCs were detected in the propofol group (28.4% *vs* 14%, OR 2.44 [95% CI, 1.14–5.26]). First-yr mortality was significantly higher in the propofol group (12.5% *vs* 2.3%, OR 5.37 [95% CI, 1.23–23.54]). Expression of lung and systemic pro-inflammatory cytokines was greater in the propofol group than in the sevoflurane group. Pulmonary and systemic IL-10 release was less in the propofol group.
Conclusions. Our results suggest that administration of sevoflurane during LRS reduces the frequency of the PPCs recorded in our study and attenuates the pulmonary and systemic inflammatory response.
Clinical trial registration. NCT 02168751; EudraCT 2011-002294-29.

Key words: anesthetics, inhalation; one-lung ventilation; postoperative complications; propofol; thoracic surgery

Editorial decision: May 17, 2017; **Accepted:** June 22, 2017

Editor's key points

- Lung resection surgery causes a marked inflammatory response and this is associated with a high incidence of postoperative pulmonary complications.
- Volatile anaesthetic agents have anti-inflammatory effects but these are of uncertain clinical relevance.
- In this randomized study of patients undergoing lung resection surgery, pro-inflammatory cytokines were lower in patients receiving sevoflurane compared with propofol.
- Sevoflurane anaesthesia was also associated with a lower incidence of postoperative pulmonary complications, 30-day and one yr mortality. One possible explanation is a beneficial effect of sevoflurane on respiratory mechanics and gas exchange but further data are needed to confirm these findings.

Postoperative pulmonary complications (PPCs) are one of the main causes of morbidity and mortality in patients undergoing surgery requiring anaesthesia.[1] Specifically, the impact on health care and incidence (15%–37.5%) of PPCs in lung resection surgery (LRS) is greater than in other major procedures.[2 3]

Various authors have shown that the exaggerated perioperative inflammatory response observed in LRS can predispose to PPCs.[4 5] A major pro-inflammatory response has been associated with the use of high pressure in the airway during one-lung ventilation (OLV), collapse of the contralateral lung, and surgical manipulation of the lung.[6 7] Therefore, lung-protective ventilation has been routinely used during OLV to reduce postoperative lung injury.[8]

Recently published clinical studies have analysed the effect of anaesthetic drugs on pulmonary inflammation during LRS.[9 10]

The beneficial effects of halogenated anaesthetics stem mainly from their anti-inflammatory properties, although some authors have found that could actually facilitate mechanical ventilation through reduced respiratory resistance.[11 12]

However, the studies cited were only designed to explore the effects of anaesthetic drugs on biological markers and not to investigate differences in clinical practice. Only De Conno and colleagues[9] studied postoperative adverse events as a secondary objective and found fewer respiratory complications in the halogenated group. Recently, the same group studied postoperative outcome as a primary objective and found no differences between anaesthetic drugs.[13]

The present study was designed to compare the incidence of PPCs in patients who received propofol or sevoflurane during LRS. Our secondary objectives were to determine the effect of sevoflurane and propofol on pulmonary and systemic inflammatory markers in these patients.

We hypothesised that the immunomodulatory effect of sevoflurane would decrease the incidence of PPCs.

Methods

We performed a randomized clinical trial (NCT 02168751; EudraCT 2011-002294-29), which was approved by the local Clinical Investigation Ethics Committee (N° 181/11), Madrid, Spain (Chairperson Dr Fernando Diaz) in August 2011.

Patients

The study population comprised 180 patients undergoing LRS between September 2012 and June 2014. All of the patients fulfilled the inclusion criteria and none of the exclusion criteria (See Supplementary data online).

Patients were recruited consecutively and randomized to two groups depending on the anaesthetic used (propofol or sevoflurane). The dose was titrated to maintain a bispectral index between 40 and 60. On arrival in the operating room, patients were assigned in a 1:1 ratio to one of the two groups, according to computer-generated randomization codes (EPIDAT 3.1). The codes were kept in sealed envelopes. These envelopes were provided to the anaesthetist responsible for intraoperative care by a researcher not involved in patient care. All participating researchers were blinded to treatment assignment.

Intervention

All patients were managed according to the same anaesthetic protocol. Analgesia was administered via a paravertebral catheter inserted into the hemithorax of the surgery with an initial dose of 0.5% bupivacaine (0.3 mL kg^{-1}) followed by continuous infusion (6–10 mL h^{-1}). Induction was with propofol (2–3 mg kg^{-1}), fentanyl (3 μg kg^{-1}), and rocuronium (0.6–1 mg kg^{-1}). Orotracheal intubation was effected with a double-lumen tube. Correct placement was verified with a fibreoptic bronchoscope. The parameters applied during two-lung ventilation (TLV) were volume-controlled ventilation, tidal volume (Vt) 8 ml kg^{-1} (ideal weight), PEEP 5 cm H_2O, Fi_{O_2} 0.4–0.5, and respiratory rate adjusted to maintain end-tidal carbon dioxide ($P_{E'CO_2}$) 4–4.7 kPa . The values applied during OLV were Vt 6 ml kg^{-1}, PEEP 5 cm H_2O, permissive hypercapnia, and Fi_{O_2} 0.6-1 in order to maintain Sa_{O_2}>90%. Recruitment manoeuvres were performed[14] and continuous positive airway pressure was used in the nondependent lung when it was needed to resolve hypoxaemia (Sp_{O_2}<90%). Restrictive fluid therapy with crystalloids was administered at 2 mL kg^{-1} h^{-1} to maintain diuresis >0.5 mL kg^{-1} h^{-1}. A fluid bolus of 250 mL of crystalloids was administered when diuresis was <0.5 mL kg^{-1} h^{-1}.

The radial artery was catheterised in all cases using the FloTrac sensor (*Edwards Life Science Corp., Irvine, California, USA*) for monitoring of cardiac index, stroke volume variation, stroke volume index, and invasive arterial pressure. These values were recorded at baseline during TLV, at 30 min after initiation of OLV, and at the end of OLV. Depending on the data recorded, vasoactive drugs were administered in order to ensure optimal haemodynamic parameters for the intrapulmonary shunt. The respiratory parameters recorded during surgery were as follows: (TLV at baseline, 30 min after initiation of OLV, and the end of OLV) (*Primus, Drägerwerk, AG&Co. KGaA, Lübeck, Germany*) Fi_{O_2}, Sp_{O_2}, $P_{E'CO_2}$, Vt, minute volume, respiratory rate, peak pressure, plateau pressure, mean pressure, end expiratory pressure, lung dynamic compliance (Cdyn), and driving pressure.[15]

Sample and measurement methods

Bronchoalveolar lavage (BAL) samples were obtained from both lungs five min before initiating OLV and at the end of OLV, once TLV was established. Sampling was performed using a 4.5-mm fibreoptic bronchoscope wedged into the selected segment of the bronchus of the left lower lobe and middle or right lower lobe, with 100 mL of 0.9% saline solution in 25-mL aliquots for analysis of inflammatory markers (IL-1, IL-2, IL-4, IL-6, IL-7, IL-8, IL-10, IL12, TNF-α, monocyte chemoattractant protein [MCP 1], and vascular endothelial growth factor [VEGF]).

Arterial blood was drawn for measurement of Pa_{O_2}, Sa_{O_2}, Pa_{CO_2} and of the inflammatory markers analysed in BAL at five time