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Respiration and Airway

Influence of xenon on pulmonary mechanics and lung aeration in patients with healthy lungs

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A preliminary account of the results of this study has been presented at the European Society of Anaesthesiology annual meeting, Geneva, Switzerland, June 3–5, 2017.

Abstract

Background: The anaesthetic xenon shows potent organ-protective properties. Due to high density and dynamic viscosity, peak inspiratory pressure (P_{max}) increases during xenon application. Thus, barotrauma may counteract organ protection. Accordingly, we investigated the influence of xenon on lung mechanics and lung aeration in patients with normal and reduced thoracic wall compliance.

Methods: After registration and ethical approval, 20 patients free of pulmonary disease undergoing routine xenon-based anaesthesia were mechanically ventilated. The primary outcome variable transpulmonary pressure (P_{tp}) was determined from plateau pressure and intraoesophageal pressure before and after xenon wash-in. We recorded P_{max}, and calculated airway resistance (R_{AW}), and static (C_{stat}) and dynamic (C_{dyn}) respiratory compliances. Finally, lung aeration was quantified by electrical impedance tomography-derived centre of ventilation index (CVI) and global inhomogeneity index (GI) in the awake state, before and during xenon.

Results: Xenon increased P_{max} [20.8 (SD 3) *vs* 22.6 (3) cm H_2O, $P<0.001$] and R_{AW} [0.9 (0.2) *vs* 1.4 (0.3) cm H_2O litre^{-1} s, $P<0.001$], without affecting P_{tp} [1.5 (4) *vs* 2.0 (4) cm H_2O, $P=0.15$]. While C_{stat} remained unchanged, C_{dyn} was reduced [33.9 (7) *vs* 31.2 (6) ml (cm H_2O)$^{-1}$, $P<0.001$]. A ventral tidal volume shift after anaesthesia induction [CVI 0.53 (0.03) *vs* 0.59 (0.04), $P<0.001$] was unaltered during xenon [CVI 0.59 (0.04), $P=0.29$]. Homogeneity of lung aeration was also unchanged during xenon [GI 0.37 (0.03) *vs* 0.37 (0.03), $P=0.99$]. There were no clinically meaningful differential BMI-related effects.

Conclusions: Xenon increases calculated airway resistance and peak inspiratory pressure without affecting transpulmonary pressure, independent of BMI.

Clinical trial registration: NCT02682758.

Keywords: anaesthetics, inhalation; mechanical ventilation; respiratory mechanics; tidal volume; xenon

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Editor's key points

- Xenon is much denser than air, but the effects on pulmonary mechanics during mechanical ventilation are unknown.
- Inhaled xenon 60% increased peak airway pressure and airway resistance, but transpulmonary pressure was unchanged.
- Altered distribution of ventilation after induction of anaesthesia was unaffected by xenon.
- These effects were similar in obese patients.
- These data do not support the concept of xenon-related barotrauma in healthy patients.

Mechanical ventilation at high volume and high inspiratory pressure is deleterious to the lungs in various animal models.[1,2] In patients with injured lungs, mortality is decreased when peak inspiratory pressure (P_{max}) and tidal volume are restricted to 30 cm H_2O and 6 ml kg^{-1}, respectively.[3] Also, in patients with healthy lungs, low tidal volumes in combination with PEEP have been beneficial.[4,5] The success of these strategies is attributed to the reduction of transpulmonary pressure (P_{tp}), decreasing pulmonary mechanical stress, and barotrauma.[6] Secondly, the addition of PEEP and the use of recruitment manoeuvres counterbalance anaesthesia-related formation of atelectasis[7,8] and reduces atelectasis-induced postoperative pulmonary complications.

The noble gas xenon is an inhalation anaesthetic with cardioprotective,[9,10] neuroprotective,[11–13] and nephroprotective[14,15] properties. Moreover, xenon attenuates inflammatory stress in lung epithelial cells by activation of the hypoxia-inducible factor-1-alpha pathway and inhibition of apoptosis.[16] However, compared with air, xenon is characterised by peculiar physicodynamic properties: it has a 380% higher density and a 25% higher dynamic viscosity. In this context, an increase in P_{max} is regularly observed when xenon is applied in mechanically ventilated patients.[17] However, it is unclear whether this is exclusively caused by viscosity-dependent prolongation of gas flow with a consecutive increase of airway resistance (R_{AW}) during inspiration,[18] or whether xenon actually increases P_{tp}. In addition, inhalation of high-density gases may cause homogenisation of tidal volume distribution[19] and therefore counterbalance anaesthesia-induced atelectasis.

Thus, we investigated the influence of xenon in mechanically ventilated patients during general anaesthesia on pulmonary mechanics and lung aeration. Since obesity-induced reduction of thoracic wall compliance both influences pulmonary mechanics[20,21] and formation of atelectasis,[22] we differentiated these effects in obese and normal weight patients.

Methods

After registration at clinicaltrials.gov (NCT02682758) and ethical approval (Ethikkommission der Heinrich-Heine-Universität Düsseldorf, Germany, #5161R), 20 consecutive adult patients free of pulmonary disease undergoing routine xenon-based anaesthesia for elective surgery were included into this prospective study after written informed consent had been obtained. To study patients with normal and reduced thoracic wall compliance, patient inclusion was stratified by BMI, facilitating the inclusion of 10 patients with a BMI of $\leq$25 and 10 patients with a BMI of $\geq$30 kg m^{-2}. Patients were excluded when at least one of the following criteria was fulfilled: pregnancy, ASA status >III, cardiac pacemaker or internal cardioverter/defibrillator, obstructive or restrictive pulmonary disease, cardiothoracic or abdominal surgery, history of oesophageal, gastric or nasopharyngeal surgery, liver cirrhosis Child-Pugh B or C with or without the presence of oesophageal varices, or ongoing effective anticoagulation.

Anaesthesia and ventilator management

Xenon-based anaesthesia was performed as to institutional standards: Anaesthesia was induced with propofol (1–2 mg kg^{-1}) and remifentanil (0.3–0.5 μg kg^{-1} min^{-1}) and tracheal intubation was facilitated with rocuronium (0.6 mg kg^{-1}). Effective neuromuscular relaxation was monitored by peripheral stimulation of the ulnar nerve with 50 mA train-of-four stimulation, and double burst stimulation with a 50 Hz tetanus (TOF-watch®; Organon Ltd., Dublin, Ireland). All patients were ventilated with a closed-circuit anaesthesia machine (Felix Dual®; Air Liquide Medical Systems, Antony, France) in volume-controlled mode (tidal volume 8 ml kg^{-1} predicted body weight) with a PEEP of 5 cm H_2O, a ventilatory frequency of 10 and an inspiratory:expiratory ratio of 1:2. Anaesthesia was initially maintained with propofol (8 mg kg^{-1} h^{-1}) and remifentanil (0.15–0.25 μg kg^{-1} min^{-1}), while the lungs were ventilated with 100% oxygen to wash-out residual nitrogen. When denitrogenation was complete (expiratory oxygen fraction >0.9), xenon (Xenon Pro Anaesthesia®; Air Liquide Deutschland GmbH, Düsseldorf, Germany) wash-in was initiated. Because the minimum alveolar concentration (MAC) of xenon has finally been estimated as 51–69% inspiratory concentration[23] and the synergistic effect of remifentanil with xenon on the MAC has to date been poorly investigated, a targeted inspiratory xenon concentration of 60% was chosen as the standard anaesthesia regimen for all patients, reflecting the practice in previous trials.[24] After xenon wash-in, when all measurements were completed, propofol infusion was discontinued and anaesthesia was maintained with xenon and remifentanil (0.15–0.3 μg kg^{-1} min^{-1}, titrated to clinical needs) until the end of surgery.

Measurement of pulmonary mechanics

The primary outcome variable P_{tp}, was derived from plateau pressure (P_{plat}) and intrapleural pressure, which was estimated from intraoesophageal pressure (P_{es}): after induction of anaesthesia, an intraoesophageal balloon catheter (adult oesophageal balloon catheter kit 5 French; CooperSurgical, Trumbull, CT, USA) was connected to a standard pressure transducer (MX960; Smiths Medical, Hythe, UK). The catheter was placed in the stomach and the balloon was inflated. This position was confirmed by gentle compression of the patient's abdomen with the observation of a corresponding pressure response. Next, the catheter was retracted to the lower third of the patient's oesophagus. Correct placement was confirmed by visualisation of cardiac artefacts in the catheter pressure curve and by artefacts caused by compression of the patient's thorax. P_{plat} at end-inspiratory hold with corresponding P_{es} was recorded (1) during initial propofol anaesthesia and (2) after completion of xenon wash-in. P_{tp} was calculated as the difference of P_{plat}–P_{es}. P_{max} was recorded continuously. Subsequently, static (C_{stat}) and dynamic (C_{dyn}) compliance of the respiratory system, and R_{AW} were calculated. To differentiate