Airway pressures during xenon anaesthesia

M. Schmidt, T. Marx, C. Papp-Jambor, H. Reinelt, U. Schirmer

Dept. Cardiac Anaesthesia, University of Ulm, Germany

Abstract

Background: Because of the higher density and viscosity of xenon/oxygen mixtures in comparison to nitrogen/oxygen, increases of the pulmonary resistance have been reported. We have investigated the relevance of these findings to practical anaesthesia.

Methods: 14 pigs were randomly assigned to receive either xenon/oxygen or nitrogen/oxygen mixtures (75/25) under condition of normo-, hypo- and hyperventilation. Airway pressures were measured in the ventilator system and endobronchially by an inserted measuring catheter.

Results: Ventilator pressures were significantly higher in xenon ventilated animals as compared with nitrogen/oxygen ventilation. Endobronchial pressures were equal or significantly lower in xenon ventilated animals.

Discussion: Ventilation with xenon/oxygen mixtures leads to a markable pressure decrease along endotracheal tubes. High ventilator system pressures do not correspond with high endobronchial pressures. In clinical xenon anaesthesia high ventilator pressures can be accepted.

The only inert gas, having anaesthetic properties under atmospheric pressures is xenon. Xenon is regarded to be close to the ideal inhalation anaesthetic [1]. Currently xenon is undergoing the approval process as an inhalation anaesthetic in Germany and Europe. One of the advantages of xenon anaesthesia seems to be the absence of adverse effects on the central nervous system. In an investigation by Fink and co-workers intact cerebral autoregulation was found during xenon ventilation. In own investigations this result was confirmed and in addition, xenon seems not to have influences on intracranial pressure [2;3].

Whether patients with impaired cerebral autoregulation or increased ICP can benefit from xenon anaesthesia must be a subject of further investigation. Nevertheless it can be anticipated that hyperventilation has to be applied through these anaesthetic procedures. During animal experiments with normoventilation and hyperventilation we noticed an increase of ventilator pressures when the inspiratory gas mixture was changed from air to xenon/oxygen. The effect is caused by the higher density of xenon/oxygen mixtures (70% Xenon+30% oxygen: 4.523 kg x m^{-3}) as compared with oxygen/nitrogen mixtures (1.304 kg x m^{-3}) and the higher viscosity (Xe/O$_2$: 24.3 x 10^{-6} Pa x sec^{-1}, N$_2$/O$_2$: 19.5 x 10^{-6} Pa x sec^{-1}). Different studies have revealed increases of pulmonary resistance during xenon ventilation in anaesthetic concentrations [4;5;10]. The value was found to be 4.0 ± 1.7 cm H$_2$O x s^{-1} x l^{-1} in xenon anaesthesia as compared to 2.6 ± 1.1 cm H$_2$O x s^{-1} x l^{-1} during ventilation with air [4]. In an investigation by Rueckoldt et al. higher pressures in the ventilator system during ventilation with xenon in inspiratory concentrations of 67% were measured. As a result it was speculated that higher endotracheal pressures could be a potential negative side effect of xenon ventilation [6]. On the other hand Volta et al. found an increased resistance of the respiratory system and higher airway pressures during xenon anaesthesia as compared with oxygen ventilation, whereas the esophageal pressures did not reveal significant differences. The effect is caused by higher pressure decreas-

es along endotracheal tubes in xenon anaesthesia as compared with nitrous oxide anaesthesia [7]. This effect could lead to a reduced endobronchial pressure during inspiration. To assess the effect under routine anaesthetic conditions, we measured airway pressures at the ventilator side of the endotracheal tube (ETT) and have compared them with values, measured with a pressure measuring catheter being introduced into the trachea.

Methods

Anaesthesia

After approval of the Animal Care Commission, 14 pigs (German Landrace, 45.5, SD ± 4 kg body weight) were studied. The investigation was carried out in the central animal research facility of the University of Ulm. Each animal was fastened over night with free access to water. The animals were premedicated with intramuscular azaperone 4 mg (Stresnil®, Janssen-Cilag, Neuss, Germany) and atropine 1.5 mg (Atropinsulfat®, Braun AG, Melsungen, Germany). Anaesthesia was induced with 8 mg/kg pentobarbital sodium (Narkodorm-n®, Alvetra GmbH, Neumunster, Germany) and 0.3 mg buprenorphine (Temgesic®, Essex Pharma, Munchen, Germany) administered *via* an ear vein. The animal was rested in the dorsal recumbent position and the trachea was intubated during spontaneous respiration. A Ruesch PVC tube I.D. 9.0 mm was used in each animal. For adaptation to the ventilator a single intravenous dose of 0.1 mg/kg pancuronium bromide (Pancuronium®, Curamed Pharma, Karlsruhe, Germany) was administered. Neuromuscular relaxation was not repeated during anaesthesia. Volume controlled ventilation was performed with a closed circuit anaesthesia device (Cicero, Dragerwerk Lubeck, Germany) with minute volume set to achieve normocapnia. Breathing frequency was 12 min^{-1} with an in/expiratory relation of 1:2. A PEEP of + 3cm H_2O was administerd.

The animals were randomly assigned to one of two groups to receive either 75% xenon in oxygen or 75% nitrogen in oxygen, respectively. An inspiratory concentration of 75% was chosen to administer the tested substance in the highest concentration, possibly suitable for anaesthesia. After the trachea was intubated, anaesthesia was maintained with a constant infusion of 0,2 mg x kg^{-1} x min^{-1} of pentobarbital and 0,2µg x kg^{-1} x min^{-1} buprenorphine. The rate of infusion was

adapted to the level of anaesthesia. The level of anaesthesia was assessed using a bispectral EEG monitor. Special care was taken to hold anaesthetic depth close to a target BIS level of 50, which is regarded to be sufficient in humans and animals [8;9]. Ringer's lactate solution was infused at a rate of 8ml x kg^{-1} x h^{-1} with an infusion pump (Infusomat, Braun, Melsungen, Germany). Body temperature (blood temperature) was recorded from the thermistor of the pulmonary artery catheter and was maintained constant using a heating blanket. During instrumentation of the animals controlled ventilation was performed using room air. Inspiratory and expiratory xenon concentrations were measured by mass spectrometry (Xenotec 2000, Leybold Heraeus, Köln, Germany). The response time of the device is 8 ms, the accuracy is 0.01 Vol %. Inspiratory and expiratory concentrations of nitrous oxide, oxygen and carbon dioxide were measured with a Draeger PM 8020 infrared monitor. Measuring time of this device is 280 ms, accuracy is 0.2 Vol %.

Measurement of airway pressures pre-ETT was carried out using the measuring system of the ventilator. The accuracy is given by 1%. Post-ETT pressures were measured with an electronic pressure measuring device Digitron P 200 (Farnell Electronic, Grünwald, Germany). Accuracy of the device is certified to be 0.2% of the measured value. Pressure values were obtained using a 4mm (outer diameter) PVC-catheter, which was introduced into the bronchoscope inlet of the ETT-connector and rendered gas-tight using silicon-rubber-glue. Gas-tightness was tested by blocking the system in a glass tube and applying pressures of 80 cm H_2O without increases of the system's leakage. The catheter was placed to be at 2 cm beyond the end of the ETT. The device is giving digital values at intervals of 1/1000 sec. Possible obstruction of the catheter by mucous substances is visible by the absence of changes in the measured values. In addition, all catheters were inspected after the experiments for possible obstructions, which did not occur.

During the experiment we recorded Bispectral Index (Aspects A 2000, Aspect Medical Systems Inc., Natick, MA, USA), body temperature, ECG, inspiratory oxygen concentration, endtidal CO_2-concentration and minute volume.

Blood gases were controlled by online measuring of expiratory CO_2-concentrations and were verified by blood gas analysis, using a blood gas analyser in combination with a hemoximeter (ABL 700 / OSM 3, Radiometer, Copenhagen, Denmark), which was calibrated for porcine blood. Hyperventilation was applied for

10 minutes until a $paCO_2$ of 30 mmHg was reached. After a stabilization phase of 30 minutes, hypoventilation was proceeded until a $paCO_2$ of 50 mmHg was measured.

Statistical analysis

The Mann-Whitney Rank Sum Test was used for statistical comparisons. A p-value of 0.05 was regarded to be statistically significant.

Results

All haemodynamic parameters remained stable during the experiments. The mean preparation time was 3.5 hours ± 20 min. Therefore neuromuscular relaxation was not present during the investigation.

The values, measured in the ventilator system and at the end of the ETT are presented in Table 1.

Discussion

Due to experimental limitations of the study, it was not possible to register pressure/flow curves. The main finding of our study is that during xenon anaesthesia with normoventilation or hyperventilation significant higher pressures are measured in the ventilator system as compared with the pressures in the bronchial system and as compared with nitrogen/oxygen ventilation. These findings were reported in a study by Rueckoldt et al. In this study it was speculated, that the increase in ventilator pressures would lead to an elevated and potentially dangerous increase in pleural pressures [6]. In our investigation, the ventilator pressures did not

correspond to pressures measured in the bronchial system. The result can be explained by the higher density and viscosity of xenon, leading to reduction of pressure along the endotracheal tube. Lachmann et al. reported a higher expiratory resistance of the lung at the end of xenon anaesthesia. On the other hand, no differences were found as compared with nitrous oxide anaesthesia [10]. In an investigation by Volta et al. increased resistances of the respiratory system were found in patients during ventilation with xenon/oxygen as compared with pure oxygen. Pressure drops in endotracheal tubes were calculated using different tube sizes and flows. Higher pressure drops at comparable flows and tube sizes were calculated for xenon anaesthesia as compared with anaesthesia using nitrous oxide/oxygen [7]. In our experiments we intended to investigate pressures under a strictly clinical situation using volume controlled ventilation to achieve different levels of paCO2. Different tube sizes were not used during our experiments because changing of tubes in not relaxated animals would have led to undesirable impairments of the experimental protocols. These influences already have been described in the investigation by Volta et al. and can be confirmed by our results comparing xenon/oxygen with nitrogen/oxygen mixtures. Comparing pressure differences during xenon anaesthesia with those found during ventilation with nitrogen/oxygen, the losses of pressure in the xenon group were approximately 2.5-fold higher as compared with the control group. Zhang and coworkers like Calzia and co-workers, using the formula of Poiseuille, calculated an 1.5-fold higher decrease of airway pressures during xenon anaesthesia as compared to air ventilation [4;5]. In our investigation, the pressure differences along the endotracheal tube in xenon anaesthesia were found to be higher. A possible explanation for that finding is that in curved tubes the

Table 1. Maximum (P_{max}) and mean (P_{mean}) airway pressures (cmH_2O) in the ventilator system (pre ETT) and the bronchial side of the endotracheal tube (post ETT) during xenon (Xe) anaesthesia and anaesthesia in nitrogen/oxygen (N2).

	P_{max} pre ETT	P_{max} post ETT	P_{mean} pre ETT	P_{mean} post ETT
Normoventilation	XE: 32.0 (30.5-33.5) * N$_2$: 25.5 (25.0-27.0)	XE: 14.5 (14.0-16.0) N$_2$: 17.5 (17.0-22.0)*	XE: 26.0 (24.0-26.0)* N$_2$: 20.5 (10.0 – 22.0)	XE: 4.0 (4.0-4.0) N$_2$: 4.5 (4.0-5.0)
Hyperventilation	Xe: 48.0 (47.25-56.75)* N$_2$: 37.0 (28.5-38.0)	XE: 17.0 (15.25-20.0) N$_2$: 20.0 (19.5-27.0)*	XE: 42.0 (32.0-43.5)* N$_2$: 24.0 (12.0-26.5)	XE: 4.0 (4.0-5.0) N$_2$: 5.0 (5.0-5.25)*
Hypoventilation	XE: 26.5 (24.0-28.0) * N$_2$: 21.0 (20.25-23.25)	XE: 14.0 (12.0-14.0) N$_2$: 14.0 ((13.5-15.0)	XE: 23.0 (18.0-24.0)* N$_2$: 12.0 (8.0-15.5)	XE: 4.0 (3.0-4.0) N$_2$: 4.0 (2.0-4.0)*

* Significant, p< 0.05.

formula of Ito better approximates pressure differences than the formula of Poiseuille. Calculating the expected pressure differences with the very complex formula of Ito, 2.3-fold higher decreases of pressure in the xenon ventilated animals would have been expected, which is closer to our experimental findings [11]. Under conditions of practical anaesthesia it is important to know that higher ventilator system pressures have to be expected during xenon anaesthesia, especially during hyperventilation. These pressures are partly lost along the ETT and do not correspond with high pressures, measured in the bronchial system, as speculated in the investigation of Rueckoldt [6]. One important clinical consequence has to be taken into account: If pressure controlled ventilators are used, a decreased compliance can lead to hypoventilation of patients by compression of the gaseous volume. This effect is most relevant in ventilation of infants, using small volumes and tube sizes. During pressure controlled ventilation in infants, a significant lower breathing volume could possibly be administered [12]. In modern volume controlled ventilators the breathing volume is compensated by the amount of compressed volume, which is an important safety feature especially for xenon anaesthesia [13]. In experimental setups, these compensations were found to be adequate in DRAEGER Cato and Cicero ventilators and in the Physioflex ventilator, other ventilators did not reveal sufficient pressure compensation [14]. This effect must also be regarded, if conventional ventilators are modified to be used for xenon anaesthesia [15]. From our results we conclude that a potential risk of elevated pressures in the ventilator during xenon ventilation is not the impairment of the bronchial system but possible hypoventilation using small volumes in pressure controlled ventilation or during volume controlled ventilation with no volume compensation available.

References

1. Marx T, Schmidt M, Schirmer U, Reinelt H. Xenon anaesthesia. J Roy Soc Med 2000; 93: 513-7
2. Fink H, Blobner M, Bogdanski R, Hanel F, Werner C, Kochs E. Effects of xenon on cerebral blood flow and autoregulation: an experimental study in pigs. Br J Anaesth 2000; 84: 221-5
3. Schmidt M, Armbruster S, Schirmer U, Marx T, Reinelt H. (Abstract) Influences of nitrous oxide and xenon on ICP. Appl Cardiopulm Pathophys 2000; 9: 116
4. Zhang P, Ohara A, Mashimo T, Imanaka H, Uchiyama A. Pulmonary resistance in dogs: a comparison of xenon with nitrous oxide. Can J Anaesth 1991; 547-53
5. Calzia E, Stahl W, Handschuh T, Marx T, Froba G, Bader S, Georgieff M, Radermacher P. Respiratory mechanics during xenon anesthesia in pigs: comparison with nitrous oxide. Anesthesiology 1999; 91: 1378-86
6. Rueckoldt H, Vangerow B, Marx G, Haubitz B, Meyer MC, Piepenbrock S, Leuwer M. Xenon inhalation increases airway pressure in ventilated patients. Acta Anaesthesiol Scand 1999; 43: 1060-4
7. Volta CA, Ferrari A, Alvisi R, Ferrari E, Righini ER, Marangoni E, Gritti G, Giunta F. Respiratory mechanics during xenon anaesthesia: xenon as an external PEEP? Appl Cardiopulm Pathophys 1998; 7: 201-7
8. Drummond JC. Monitoring depth of anesthesia: with emphasis on the application of the bispectral index and the middle latency auditory evoked response to the prevention of recall. Anesthesiology 2000; 93: 876-82
9. Schmidt M, Papp-Jambor C, Marx T, Schirmer U, Reinelt H. Evaluation of bispectral index (BIS) for anesthetic depth monitoring in pigs. Appl Cardiopulm Pathophys 2000; 9: 83-7
10. Lachmann B, Armbruster S, Schairer W, Landstra M, Trouwborst A, Van Daal GJ, Kusuma A, Erdmann W. Safety and efficacy of xenon in routine use as an inhalational anaesthetic. Lancet 1990; 335: 1413-5
11. Jarreau PH, Louis B, Dassiieu G, Desfrere L, Blanchard PW, Moriette G, Isabey D, Harf A. Estimation of inspiratory pressure drop in neonatal and pediatric tubes. J Appl Physiol 1999; 87: 36-46
12. Schirmer U, Schreiber M, Goertz A, Schutz W, Rockemann M, Georgieff M. [The effect of changes in lung compliance on ventilation in newborns. Results of animal experiments with two different respirators] Einfluss von Störungen der Lungencompliance auf die Ventilation von Neugeborenen. Tierexperimentelle Untersuchung mit zwei verschiedenen Respiratoren. Anaesthesist 1994; 43: 521-7
13. Schirmer U, Villwock J, Fosel T, Schreiber M, Goertz A, Georgieff M. [A study of the parameters of the delivered tidal volume. Ventilation on a lung model using the CICERO anesthetic ventilator] Untersuchung von Einflussgrößen auf das abgegebene Hubvolumen. Beatmung am Lungenmodell mit dem Narkosegerät CICERO. Anaesthesist 1992; 41: 785-9
14. Jaber S, Langlais N, Fumagalli B, Cornec S, Beydon L, Harf A, Brochard L. [Performance studies of 6 new anesthesia ventilators: bench tests] Etude des performances de six nouveaux ventilateurs d'anesthesie: banc d'essai. Ann Fr Anesth Reanim 2000; 19: 16-22
15. Dingley J, Ivanova-Stoilova TM, Grundler S, Wall T. Xenon: recent developments. Anaesthesia 1999; 54: 335-46

Address for corresponding: Prof. Uwe Schirmer, M.D., Department of Cardiac Anaesthesia, University Clinic of Ulm, Steinhövelstr. 9, 89075 Ulm, Germany, E-Mail: uwe.schirmer@uniklinik-ulm.de