Diffusion of Xenon and Nitrous Oxide into the Bowel

Helmut Reinelt, M.D., Uwe Schirmer, M.D.,† Thomas Marx, M.D.,‡ Pantelis Topalidis,§
Michael Schmidt, M.D.**

Background: Nitrous oxide diffuses easily from blood into air filled spaces. Xenon is also a relatively insoluble gas, like nitrous oxide. Therefore, the authors measured xenon diffusion into obstructed bowel segments during xenon anesthesia and compared this with nitrous oxide and nitrogen diffusion.

Methods: Twenty-one pentobarbital-anesthetized pigs were randomly assigned to three groups to receive either xenon–oxygen, nitrous oxide–oxygen, or nitrogen–oxygen (75%–25%), respectively. In each animal, four bowel segments of 15-cm length were isolated. A pressure-measuring catheter was inserted into the lumen, and 30 ml of room air was injected into the segments. Anesthesia with the selected gas mixture was performed for 4 h. Pressure in the segments was measured continuously. The volume of gaseous bowel content was measured on completion of the study.

Results: The median volume of bowel gas in animals breathing nitrous oxide was 88.0 ml as compared with 39.0 ml with xenon anesthesia and 21.5 ml in the nitrogen–oxygen group. After 4 h of anesthesia, the intraluminal pressures in the nitrous oxide group were found to be significantly greater than in the control group and in the xenon group.

Conclusions: The amount of diffused gas was significantly lower during xenon anesthesia than with nitrous oxide anesthesia but greater than with controls. Blood solubility can therefore be regarded as an important factor influencing gas diffusion into air filled cavities.

XENON is an inert gas with a blood–gas partition coefficient of 0.12–0.14.[1,2] Its low blood solubility leads to a rapid increase and decrease of plasma concentrations and rapid onset and emergence from anesthesia.[2] With a minimum alveolar concentration of 71%, it is administered in similar inspiratory concentrations to nitrous oxide.[3]

One well-known side effect of nitrous oxide is diffusion into air-filled spaces, including the bowel. In dogs, Eger and Saidman[4] found an increase of gas volumes in obstructed bowel of 100–200% after 4 h of nitrous oxide anesthesia. Investigations concerning diffusion of xenon

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* Staff Anesthesiologist, † Head, ‡ Staff Anesthesiologist and Leader of the Xenon Research Group, § Student.

Address reprint requests to Dr. Marx: Department of Cardiac Anesthesia, University of Ulm, 89070 Ulm, Germany. Address electronic mail to: Thomas.Marx@ Medizin.uni-ulm.de. Individual article reprints may be purchased through the Journal Web site, www.anesthesiology.org.

into air-filled spaces are not available. The amount of gas diffusing into air-filled spaces depends on the transport capacity of the blood as given by the blood–gas partition coefficient (nitrous oxide: 0.47) and membrane characteristics of the tissues where the diffusion process takes place (*e.g.*, porous–nonporous).[5] Because some of these parameters are not known for xenon, modeling is not possible. We therefore measured the diffusion of xenon into obstructed bowel segments.

Materials and Methods

Anesthesia

After obtaining approval from the Animal Care Commission of the University of Ulm, 21 pigs (German Landrace; body weight 45.5 ± 4 kg) were studied. The investigation was conducted 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). Anesthesia was induced with 8 mg/kg pentobarbital sodium (Narkodorm-n; Alvetra GmbH, Neumuenster, Germany) and 0.3 mg buprenorphine (Temgesic; Essex Pharma, Muenchen, Germany) administered *via* an ear vein. The animal was rested in the dorsal recumbent position, and the trachea was intubated during sponaneous respiration. A single intravenous dose of 0.1 mg/kg pancuronium bromide (Pancuronium; Curamed Pharma, Karlsruhe, Germany) was administered, which was not repeated during anesthesia. Mechanical ventilation was performed with a closed-circuit anesthesia device (Cicero; Draegerwerk, Luebeck, Germany) with minute volume set to achieve normocapnia. During induction and surgical preparation, the animals were ventilated with an inspiratory mixture of oxygen–nitrogen 25%–75%. Anesthesia was maintained with a continuous infusion of pentobarbital sodium (0.13 mg · kg^{-1} · min^{-1}) and buprenorphine (0.07 μg · kg^{-1} · min^{-1}). After surgical preparation, the animals were left for 1 h without stimulation to ensure hemodynamic parameters to be uninfluenced from surgical stimuli and to monitor the intraluminal pressures for possible gas leaks. The animals were randomly assigned to one of three groups to receive 75% xenon, 75% nitrous oxide, or 75% nitrogen. An inspiratory concentration of 75% was chosen to administer the tested substance in the highest concentration, possibly suitable for anesthesia. Anesthesia time for the studied substance was 240 min. Xenon or nitrous oxide in oxygen initially was applied with a high fresh gas flow of

6 l/min. Inspiratory and expiratory xenon concentrations were measured by mass spectrometry (Xenotec 2000; Leybold Heraeus, Koeln, Germany). The response time of the device is 8 ms, and 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 (Luebeck, Germany). Measuring time of this device is 280 ms, and accuracy is 0.2 vol%. After inspiratory and expiratory concentrations were approximately equal, the system was closed by reducing the fresh gas flows to hold the preselected concentrations of the gases without overfilling or underfilling of the system's breathing bag, which in the device serves as the fresh-gas reservoir.

Surgical Preparation

Each experiment was supervised and assisted by an approved veterinary surgeon. A median laparotomy was performed. Four segments of small intestine 15 cm in length were isolated. A 4-mm polyvinyl chloride pressure-measuring catheter was inserted into the lumen of each segment by Seldinger technique. Each segment was occluded on both ends and rendered gas-tight by elastic rubber bands (vessel loops). Special care was taken not to injure the vascular arcades leading to the segments. After preparation of all segments, the abdomen was closed by suture. Thirty milliliters of room air was injected into each of the segments *via* the inserted catheter, and intraluminal pressure was measured. Thirty milliliters was chosen because of the clinical impression that this restored the volume of the segment to "normal," equivalent to what was the content before emptying and catheterization. Pressure in the segments was monitored during 1 h before the start of the experiments to further exclude possible gas losses.

Measurements

Arterial blood pressure was measured continuously *via* a femoral artery catheter. Cardiac output was measured with a Swan Ganz catheter that was introduced *via* an internal jugular vein. Hemodynamic measurements were recorded with a Datex CS3 Monitor (Datex-Engstrom, Helsinki, Finland). Pressure in the bowel segments was measured with a transducer of the PM 8020 monitor (Draeger), which was calibrated to atmospheric pressure and to a test pressure of 50 mmHg. All pressures were monitored continuously and recorded every 30 min. During measurement, no gas was extracted from the bowel segments. After the anesthesia time of 4 h, the suture of the laparotomy was reopened, and the bowel segments were inspected to ensure the correct position of the catheters and to exclude kinking. Repeated rinsing of the surface of the bowel segments with saline solution and inspection for bubbling was used for leakage testing. The segments were then totally emptied of gas under visual control. Bowel segments with detect-
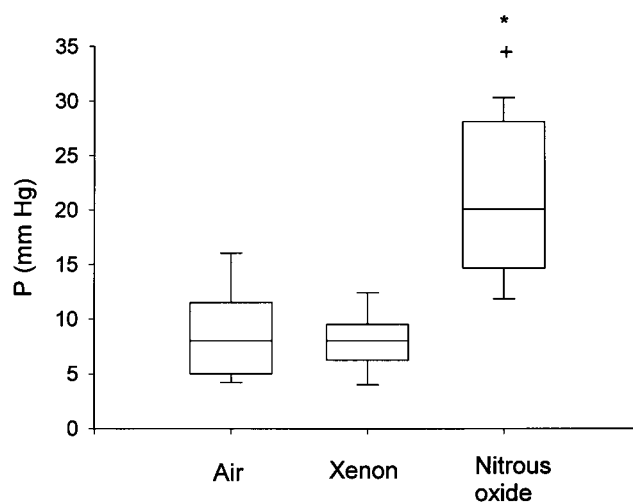

Fig. 1. Pressures in obstructed bowel segments after 4 h of anesthesia (median; box, 25–75th percentile; whiskers, 10–90th percentile). After 4 h of anesthesia, intraluminal pressures were found to be significantly greater in the nitrous oxide group as compared with xenon anesthesia (*) and control (+).

able leakages or occluded catheters were not included in the calculations.

Statistical Analysis

The pressure and volume values of the four bowel segments were averaged for every single animal at corresponding measuring points. These median values were then used for statistical comparisons. Values are expressed as median and 25–75 percentiles. The Mann-Whitney rank sum test with Bonferroni-Holm correction for multiple comparisons was used. *P* values are given with the results.

Results

No gas leaks were detected before and after the test period. No significant differences were measured for cardiac output and mean arterial blood pressures at corresponding measuring points between all groups. Nitrous oxide and xenon both led to an increase of the intraluminal gas volumes relative to nitrogen–oxygen control: control, 21.5 ml (range, 21.5-24.87 ml); xenon, 39.0 ml (range, 34.5- 43.87 ml), nitrous oxide, 88.0 ml (range, 74.37-103.12 ml). The content of gas volume in the nitrous oxide group was significantly greater after 4 h of anesthesia as compared with the control (*P* = 0.0018) and the xenon group (*P* = 0.0034). Significant differences were also found between xenon and control (*P* = 0.0023). Comparing intraluminal pressures, the pressure in the nitrous oxide group was significantly greater as compared with the control group (*P* = 0.0018) and the xenon group (*P* = 0.0012). No difference between xenon and the control group was found (fig. 1).

Discussion

Volume Differences

The median increase of volume in the obstructed bowels was found to be 30% in xenon anesthesia as compared with 193% during nitrous oxide anesthesia. Our findings in the nitrous oxide group are in agreement with those of Eger and Saidman,[4] who observed a 100–200% increase of gaseous bowel volume in dogs after 4 h of nitrous oxide anesthesia. Xenon has a fourfold lower blood–gas partition coefficient as compared with nitrous oxide. From this finding, a lower transport capacity of the blood to the tissues and a lower rate of diffusion into air filled spaces might be predicted. Diffusibility of xenon, on the other hand, is influenced by the different diameter of the xenon atom as compared with nitrous oxide (characteristic diameter of xenon, 4.055 Å; nitrous oxide, 3.879 Å) and the diffusion coefficient through intestinal membranes, which is not known for xenon. Therefore, the amount of diffusion into bowel cannot be calculated exactly. Higher amounts of diffused nitrous oxide lead to the conclusion that blood solubility is the most important factor influencing the amount of diffused gas.

Pressure Differences

After 4 h of anesthesia, no differences of the median pressure values were found in the xenon and control groups. In the nitrous oxide group, the measured median pressure values were significantly greater. This result was caused by the 6.4-fold lower amount of xenon diffusing into the bowel as compared with nitrous oxide, which did not lead to an increase of pressure.

Variabilities of the intraluminal pressures in bowel segments of equal length and equal priming volume found in our experiments after anesthesia with nitrous oxide or xenon, respectively, might be explained by known influences of nitrous oxide and other inhalation anesthetics on gastrointestinal motility, which was found to be increased by nitrous oxide and decreased by other inhalation anaesthetics.[6]

Clinical Implications

As a consequence of the work by Eger and Saidman,[4] ileus and bowel obstruction is commonly regarded as a relative contraindication to nitrous oxide anesthesia. The increase of bowel volume and the consecutive hypermotility leading to longitudinal traction across anastomoses are regarded as an adverse effect of nitrous oxide application.[7] On the other hand, several studies have revealed no impairment of postoperative bowel function after application of nitrous oxide.[6-12] In patients with preexisting cardiovascular diseases undergoing bowel surgery, the advantages of xenon anesthesia with regard to hemodynamic stability[13] could be a benefit. Based on our results, we conclude that xenon can be used in bowel surgery when nitrous oxide is also used.

The relatively slow increase of the intraluminal bowel pressure in nitrous oxide anesthesia is commonly explained by the high distensibility of the bowel. Other functional disorders such as pneumothorax, pneumoperitoneum, or pneumopericardium may present different volume–pressure relations caused by lower compliance of the cavity walls.[14] Therefore, our findings must be applied with care to these clinical situations until controlled studies of xenon anesthesia in pneumothorax, pneumoperitoneum, or preumopericardium are available.

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