Effects of adding small amounts of oxygen to a carbon dioxide–pneumoperitoneum of increasing pressure in rabbit ventilation models

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Objective: To evaluate the metabolic consequences of the addition of oxygen to the CO_2-pneumoperitoneum.
Design: Prospective randomized study in rabbits. After 30 minutes of ventilation pneumoperitoneum was maintained for 90 minutes with pure CO_2 or CO_2 with 2% or 6% of oxygen. The intraperitoneal pressure was increased from 10 to 15 and 20 mm Hg every 30 minutes. Ventilation rate was either fixed or a progressive hyperventilation. End points were changes in arterial blood gases (P_{CO_2}, P_{O_2}), pH, acid-base balance (actual base excess [ABE], standard bicarbonate [SBC], standard base excess [SBE], hydrogen carbonate [HCO_3^-], concentration of total carbon dioxide [T_{CO_2}]); oxygen and oximetry (oxyhemoglobin [O_2Hb], oxygen saturation [S_{O_2}], reduced hemoglobin [RHb], total oxygen concentration [T_{O_2}], and oxygen tension at half saturation assessing hemoglobin oxygen affinity [p50]); and lactate concentrations assayed every 15 minutes.
Setting: University research center.
Animals: Twenty-four adult female New Zealand white rabbits.
Intervention(s): Anesthesia, mechanical ventilation, and pneumoperitoneum.
Result(s): The effects of CO_2-pneumoperitoneum on all end points increased with the elevated intraperitoneal pressure and were more pronounced when ventilation was fixed. Changes were less when 2% or 6% of oxygen had been added to the CO_2-pneumoperitoneum. With use of logistic regression, the addition of oxygen, intraperitoneal pressure, and ventilation were found to be independent variables affecting P_{CO_2}, pH, ABE, SBE, HCO_3^-, O_2Hb, S_{O_2}, p50, and end-tidal CO_2.
Conclusion(s): The metabolic consequences of the combined effect of increased intraperitoneal pressure and CO_2-pneumoperitoneum were less when 2% to 6% of oxygen was added or when animals were hyperventilated. We suggest that metabolic and mesothelial hypoxemia caused by CO_2 absorption can be reduced by adding small amounts of oxygen and by hyperventilation. (Fertil Steril® 2009;92:778–84. ©2009 by American Society for Reproductive Medicine.)

Key Words: CO_2-pneumoperitoneum, carboxemia, acidosis, metabolic and mesothelial hypoxemia

During laparoscopic surgery, for safety reasons, CO_2 is the gold standard for the pneumoperitoneum because of its high solubility in water, thus decreasing the risk of gas embolism, and because of its high exchange capacity in the lungs. Eventually, hyperventilation permits control of increased CO_2 concentrations, which, moreover, can be monitored easily by capnography (1, 2). Carbon dioxide absorption increases with the duration of surgery and with insufflation pressure (intraperitoneal pressure) (3).

Carbon dioxide–pneumoperitoneum through CO_2 absorption is known to affect blood gases and acid-base balance with carboxemia, acidemia, acidosis, and base deficit. In addition, respiratory and cardiovascular disturbances occur, such as changes in minute ventilation, peak inspiratory pressure, pulmonary vascular resistance, alveolar CO_2 concentration, the calculated physiologic shunt, central venous pressure, systolic and diastolic arterial pressure, systemic vascular resistance, and cardiac output (4–7). If not compensated, in a rabbit model this carboxemia and acidemia lead to respiratory and later to metabolic acidosis. Finally, metabolic hypoxemia occurs through the Bohr effect (8). The addition of 6% of oxygen to the CO_2-pneumoperitoneum strongly attenuated these effects (9).

Carbon dioxide–pneumoperitoneum has a series of local intraperitoneal effects such as a decrease in peritoneal pH (3, 10–13), a change in tissue O_2/CO_2 exchange (3, 13, 14), a morphologic disruption of mesothelial integrity (15–17), and changes in parietal and visceral microcirculation (5). Moreover, it changes blood microcirculation in splanchnic organs (18), as well as the circulation of larger vessels of the abdominal cavity (3). Carbon dioxide–pneumoperitoneum parameters are

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correlated negatively with free radical scavengers and total glutathione levels (19) and in a graded fashion with an increased level of free radical marker 8-isoprostaglandin $F_{2\alpha}$, as well as with lipid peroxidation in the peritoneal tissue (20, 21).

It is shown in animal models and in vitro studies that CO_2-pneumoperitoneum has an impact on tumor implantation and port-site metastasis (22–25). In mice and rabbits, adhesion formation increases with the duration of CO_2-pneumoperitoneum and with intraperitoneal pressure (20, 26, 27). Because this increase in adhesion formation is prevented by the addition of >2% and <10% of oxygen to the CO_2-pneumoperitoneum, and because the effect is absent in HIF knockout mice (28), the underlying mechanism was suggested to be mesothelial hypoxia. We therefore wanted to confirm and extend the metabolic effects of CO_2-pneumoperitoneum (3, 8, 9) by evaluating the effect of different insufflation pressures and their prevention by adding as little as 2% instead of 6% of oxygen to the CO_2-pneumoperitoneum in fixed and hyperventilated rabbit models.

MATERIALS AND METHODS

Animals

Adult female New Zealand white rabbits (N = 24) weighing between 2.7 and 3.0 kg were used. The animals were kept under standard laboratory conditions at a temperature between 20°C and 25°C and a relative humidity of 40% to 70%. They had a day cycle of 14 hours light and 10 hours dark, a standard laboratory diet (Hope Farms, Woerden, the Netherlands), and free access to food and water. The animals were housed at the Centre for Laboratory Animal Care of the Catholic University of Leuven (Animalium, St. Rafael Hospital, Katholieke Universiteit Leuven, Leuven, Belgium). The experiment was approved by the Institutional Review Board and Animal Care Committee.

Experimental Design

After a baseline (control) period of 30 minutes with ventilation, pneumoperitoneum started at the intraperitoneal pressure of 10 mm Hg, then every 30 minutes the intraperitoneal pressure was subsequently increased to 15 and 20 mm Hg. As insufflation gas, pure CO_2 (group 1; n = 8), CO_2 with 2% of oxygen (group 2, n = 8), or CO_2 with 6% of oxygen (group 3, n = 8) was used, and in each group half of the rabbits were ventilated with a continuously fixed ventilation (series a) and the other half with progressive hyperventilation (series b). Animals were block randomized by day. Two animals died, one in group 1a and one in group 1b, at the beginning of the experiment. In the absence of data, they were excluded from the analysis. The three rabbits with pure CO_2-pneumoperitoneum and fixed ventilation died some 15 minutes after the intraperitoneal pressure had been elevated to 20 mm Hg. As a result, last end points at 120 minutes are absent in this group. At the end of the experiments, all animals were killed with an IV injection of 0.3 mL/kg T61 (Hoechst Roussel Vet GmbH, Frankfurt, Germany).

The animals were premedicated with an IM injection of 30 mg/kg ketamine 1000 (Sanofi, Sante Animale Benelux, Belgium) and 6 mg/kg of 2% xylazine hydrochloride solution (VMD NV, Berendonk, Belgium). After intubation (a 3.5 mm endotracheal tube; Sheridan Catheter Corp., New York, NY), anesthesia was performed with 2.5% halothane (Fluothane; Zeneca, Destelbergen, Belgium) mixed with oxygen and room air, with use of the vaporizer connected to a small animal ventilator (model 683; Harvard Apparatus Inc., Holliston, MA). The oxygen concentration in the inspired gas (F_{IO_2}) was 70%. In the fixed ventilation series, the tidal volume was 7 mL/kg and was kept constant during the experiment. In the hyperventilated series, the baseline tidal volume of 7 mL/kg was increased to 8.33, 9.66, and 11 mL/kg at the 30th, 60th, and 90th minute, that is, when the intraperitoneal pressure was increased to 10, 15, or 20 mm Hg, respectively. These respiratory rates had been established during pilot experiments to obtain an arterial P_{CO_2} <45 mm Hg as described by Liem et al. (29) and Steinman et al. (30). The pulse rate and oxygen saturation (Spo_2, in percentage) in peripheral blood (ear vessels and capillaries), end-tidal CO_2 (P_{ETCO_2}), and respiratory pressure were monitored continuously with use of a pulse oximeter (Nellcor, Boulder, CO), a capnograph (Capnomac; Datex, Finland), and a manometer, respectively. To monitor arterial blood pressure, a 20-gauge (1.1 × 48 mm) catheter (Insyte-W; Becton Dickinson, Madrid, Spain) was inserted into the ear artery and connected to the blood pressure monitor (HP78304A; Hewlett-Packard, Palo Alto, CA). Electrocardiographic monitoring was performed with use of standard animal probes and the electrocardiograph (Soxil MRC 3277; Loxley Medical Supplies Ltd., London, UK). Parietal peritoneum surface temperature was monitored with use of the flexible temperature-sensing probe inserted and fixed in the abdominal cavity near the trocar, and it was connected to the extra blood pressure monitor line (HP78304A; Hewlett-Packard). Arterial blood pressure, pulse rate, electrocardiogram, and parietal peritoneum surface temperature parameters were continuously registered and stored in a personal computer with use of a special device and program (Dataq Instruments Inc., Akron, OH).

Surgical Protocol

The animals were placed in supine position, and the abdomen was shaved and disinfected with povidone-iodine (Iso-Betadine; Asta Medica, Brussels, Belgium). A 10-mm trocar (Apple Medical Corporation, Marlborough, MA) was placed caudally to the sternum, and the pneumoperitoneum was created with a Thermoflator Plus (Karl Storz, Tüttlingen, Germany), a humidifier (Aquapor; Dräger, Lübeck, Germany) and a heating device (Opti Therm; Karl Storz) keeping insufflation temperature between 35°C and 37°C. In addition, a water valve was used to dampen insufflation pressure changes. The intraperitoneal pressure was controlled with a manometer, connected to an 18-gauge (1.3 × 45 mm) catheter (Insyte-W) inserted in the abdominal cavity near the trocar. A 22-gauge (0.9 × 25 mm) catheter (Insyte-W, Vialon; Becton Dickinson) inserted through the abdominal wall allowed us to obtain a continuous (120 mL/min) flow (26) through the abdominal wall.

Assays

The ear artery was catheterized with a 20-gauge (1.1 × 48 mm) catheter (Insyte-W) for blood sampling. Before each blood sample, the syringe and catheters were rinsed with a mixture of saline solution and heparin (Heparine Rorer; Rhône-Poulenc Rorer, Brussels, Belgium) to prevent clotting. Blood samples were taken every 15 minutes, from the beginning of the experiment up to 120 minutes later (n = 9 samples). They were immediately put on ice pending analysis in duplicate in the blood gas analyzer (ABL system 525/620; Radiometer, Copenhagen, Denmark). Results covered arterial blood gas parameters such as partial pressures of oxygen (Po_2) and carbon dioxide (Pco_2); pH; acid-base parameters such as concentrations of hydrogen carbonate (HCO_3^-), standard bicarbonate (SBC), actual base excess (ABE), standard base excess (SBE), and the concentration of total carbon dioxide (Tco_2); lactate concentrations; blood oximetry parameters such as oxygen saturation (So_2), oxyhemoglobin (O_2Hb), and reduced hemoglobin (RHb); oxygen status parameters such as total oxygen concentration (To_2) and oxygen tension at half saturation assessing hemoglobin oxygen affinity (p50).

Data Analysis and Statistical Methods

The factorial design of the experiments enabled us to simultaneously evaluate these variables: ventilation effects (fixed or hyperventilated), the pneumoperitoneum gas used (100% CO_2, 98% CO_2 + 2% O_2, or 94% CO_2 + 6% O_2), and the intraperitoneal pressure (0, 10, 15, or 20 mm Hg). Considered as a 2*2*2 factorial design with 4 rabbits in each cell, the statistical power is only slightly less for each factor than if two groups of 16 rabbits were used. Considered as a 2*3*4 factorial design, the power becomes even much higher, that is, close to a 96-rabbit experiment. Because the intraperitoneal pressure was, however, sequentially increased, the design was not a pure factorial for pressure, and when interpreting the results it should be taken into account that the observed metabolic effects might be influenced by the metabolic effects induced by the previous pressure. This might affect the magnitude of the observed effect but will not affect the overall conclusions. Considering the effects and variability observed in the previous experiments, the power of two groups of 16 rabbits was >90% at the .05 level.

Data were analyzed by using logistic regression (Proc LOGISTIC; SAS, Inc., Chicago, IL) to simultaneously evaluate the effects of ventilation, of the pneumoperitoneum gas used, and of the intraperitoneal pressure on each end point. Samples were analyzed as if each pressure increase were investigated in a different rabbit, thus disregarding the sequential pressure increase. Strictly speaking, the results are therefore valid only for the gas mixture and for the type of ventilation used because insufflation pressures were increased sequentially, and some carryover effect cannot be ruled out because the statistical significances for each intraperitoneal pressure might be influenced by the previous pressures. The results estimating the overall pressure effect, however, remain valid. We thought it preferable to list intraperitoneal pressure significances in the Results but acknowledge their potential limitations. Mean ± SD is indicated unless stated otherwise.

RESULTS

The three rabbits with pure CO_2-pneumoperitoneum and fixed ventilation died approximately 15 minutes after the intraperitoneal pressure had been raised from 15 to 20 mm Hg, that is, after approximately 105 minutes. All other animals survived. The parietal peritoneum surface temperature was decreased in both the fixed and hyperventilated series, and there were no differences between the pure CO_2 groups and the oxygen-added groups (results are not shown).

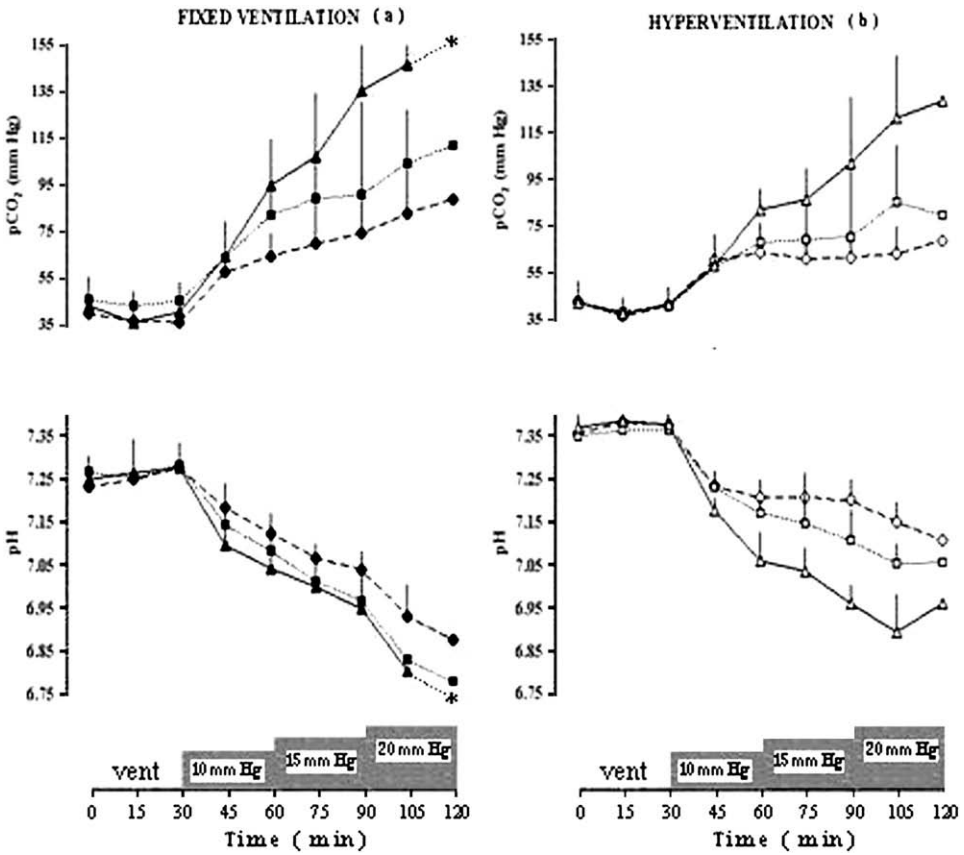
The metabolic effects of CO_2 adsorption increased with intraperitoneal pressure, were lower when the rabbits were hyperventilated, and were much lower when 2% or 6% of oxygen had been added to the CO_2-pneumoperitoneum (Figs. 1 and 2). By logistic regression, the three variables: ventilation, intraperitoneal pressure, and the addition of oxygen to the CO_2-pneumoperitoneum, were found to be independent variables predicting the metabolic changes. Interaction between the three factors was not observed. Ventilation, intraperitoneal pressure, and the addition of small amounts of oxygen to the CO_2-pneumoperitoneum simultaneously influenced blood gas values such as Pco_2 (P value for ventilation not significant [NS]; for intraperitoneal pressure $<.0001$; for oxygen 2% or 6% $<.01$), pH ($P<.0001$; $<.0001$; $<.0001$), acid-base parameters such as ABE ($P<.0001$; $<.0001$; $<.0001$), SBE ($P<.0001$; $<.0001$; $<.0001$), HCO_3^- (P=NS; $<.0001$; $<.0001$;), and oxygen and oximetry indicators such as O_2Hb ($P<.0001$; $<.001$; $<.0003$), So_2 ($P<.001$; $<.01$; $<.003$), p50 ($P<.0001$; $<.0001$; $<.0001$), and concentrations of $Petco_2$ ($P<.0001$; $<.05$; $<.0002$).

To evaluate whether the effects of intraperitoneal pressure occurred between 10 and 15 mm Hg or between 15 and 20 mm Hg, we analyzed both increases in intraperitoneal pressure separately. They both were found to affect Pco_2 (P for 10 vs. 15 mm Hg $<.03$ and 15 vs. 20 mm Hg $<.003$), p50 ($P<.0001$ and $<.0001$), and $Petco_2$ ($P<.04$ and $<.001$) and to decrease pH ($P<.0001$ and $<.0001$), ABE and SBE ($P<.0001$ and $<.0001$), O_2Hb (P=NS and $<.04$), and So_2 ($P<.05$ and $<.01$).

Subsequently, we evaluated whether the effect of adding oxygen occurred between 0% and 2% or between 2% and 6%. Increasing oxygen from 0% to 2% and from 2% to 6% both decreased the metabolic effects, but the effects of raising oxygen from 0 to 2% were slightly less pronounced than the raising of oxygen from 2% to 6%, for ABE (P for 0 vs. 2% $<.003$ and 2% vs. 6% $<.0006$), SBE ($P<.003$ and $<.0006$), O_2Hb ($P<.05$ and $<.006$), So_2 ($P<.05$ and $<.006$), and $Petco_2$ ($P<.01$ and $<.03$), For the other parameters, differences between 0 to 2% and 2% to 6% of oxygen were comparable for Pco_2 (P for 0 vs. 2% $<.001$ and 2% vs.

FIGURE 1

Effect of the ventilation (*vent*), pneumoperitoneum pressures (*10, 15,* and *20 mm Hg*), and insufflation gas used on the arterial P_{CO_2} and pH values: 100% CO_2, group 1a (*closed triangles*) and group 1b (*open triangles*); 98% CO_2 + 2% O_2, group 2a (*closed squares*) and group 2b (*open squares*); 94% CO_2 + 6% O_2, group 3a (*closed diamonds*) and group 3b (*open diamonds*). Means ± SD are given. *At this point all animals in pure CO_2 group with fixed ventilation died.



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6% <.001), pH (*P*<.0001 and <.0001), and p50 (*P*<.0001 and <.0001).

To ascertain that these effects were observed in both series, that is, with fixed ventilation and with hyperventilation, we analyzed both ventilation series separately. The previous results were confirmed for both ventilation types. Moreover, this can be observed visually in Figures 1 and 2.

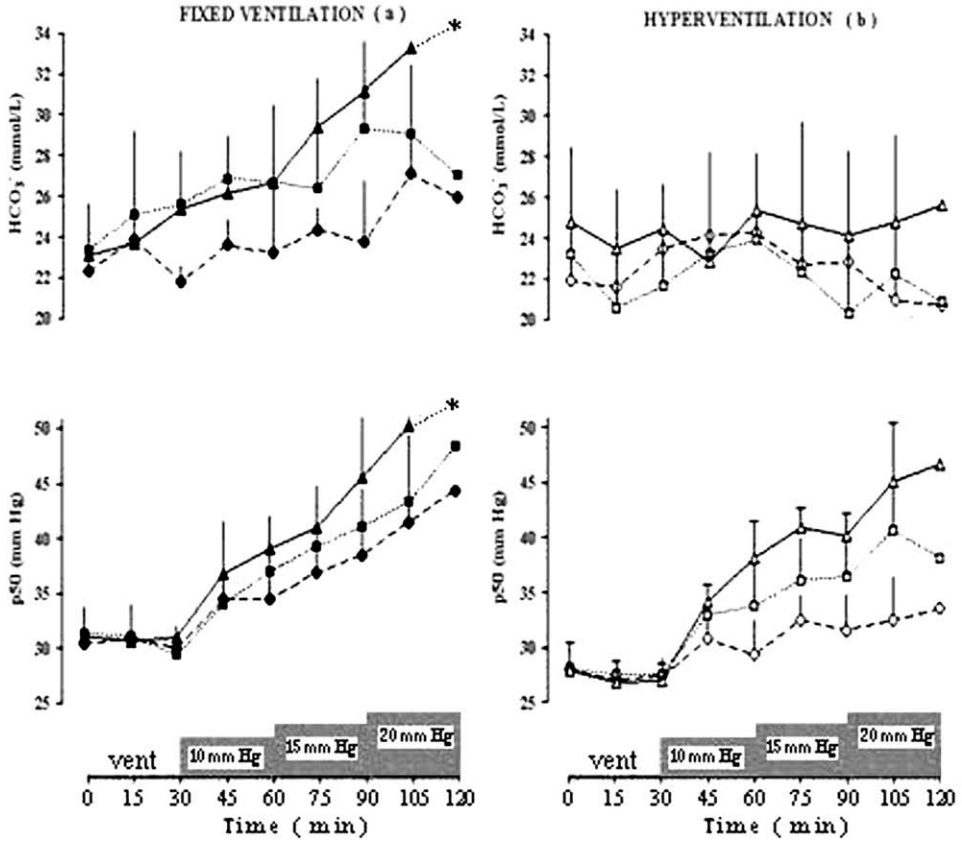
DISCUSSION

These results confirm and extend (1, 2, 31, 32) the observations that CO_2-pneumoperitoneum induces systemic metabolic effects such as hypercarbia, acidemia, and acidosis through CO_2 absorption. The data confirm our previous results, describing in detail the pathophysiology of CO_2 adsorption and its metabolic and local circulatory consequences (3, 8). This model can be summarized as follows: during CO_2-pneumoperitoneum, the mesothelial surface CO_2 tension of the parietal peritoneum is considerably higher than in both venous and arterial blood. This tension gap between the mesothelial surface of the parietal peritoneum and the blood makes CO_2 pass into the blood through the parietal peritoneum tissue and the capillaries. Subsequently, partial pressure of arterial CO_2 increases to establish blood gas and acid-base equilibrium (3). Carboxemia and acidosis are the key events, as reflected in increases in P_{CO_2}, P_{ETCO_2}, and HCO_3^- and in a decrease in pH. These changes subsequently lead to metabolic acidosis reflected in an increase of P_{ETCO_2}, P_{CO_2}, T_{CO_2}, HCO_3^-, and lactate concentrations and in a decrease of pH, ABE, SBE, and SBC. Finally, because of the Bohr effect, the changes lead to metabolic hypoxemia, reflected in increases in RHb and p50 and in decreases in P_{O_2}, T_{O_2}, and O_2Hb. The latter changes are indeed associated with a desaturation and a decreased oxygen availability in tissue, caused by increased RHb and decreased hemoglobin oxygen affinity and, hence, decreased O_2Hb (8).

Hyperventilation eliminates CO_2 and decreases the metabolic consequences of CO_2 absorption. Because of

FIGURE 2

Effect of the ventilation (*vent*), pneumoperitoneum pressures (*10, 15,* and *20 mm Hg*) and insufflation gas used on the concentrations of hydrogen carbonate (bicarbonate, HCO_3^-) and oxygen tension at half saturation (p50) assessing the hemoglobin oxygen affinity: 100% CO_2, group 1a (*closed triangles*) and group 1b (*open triangles*); 98% CO_2 + 2% O_2, group 2a (*closed squares*) and group 2b (*open squares*); 94% CO_2 + 6% O_2, group 3a (*closed diamonds*) and group 3b (*open diamonds*). Means ± SD are given. *At this point all animals in pure CO_2 group with fixed ventilation died.



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anesthesiologic monitoring and assistance during laparoscopic surgery (33) this is a well-known fact in humans and was demonstrated previously in our rabbit model where we compared superficial ventilation with more adequate ventilation (8). In this study, the effect of ventilation is confirmed through changes in arterial P_{CO_2}, pH, ABE, SBE, HCO_3^-, O_2Hb, p50, and S_{O_2} parameters during CO_2-pneumoperitoneum with sequentially increased intraperitoneal pressure.

The metabolic consequences of CO_2 absorption increase with intraperitoneal pressure increase. This was shown previously for 6 to 10 mm Hg (8) and is now confirmed for 10 to 15 mm Hg and 15 to 20 mm Hg. It is suggested that excessive CO_2 absorption is severe enough to become fatal when the intraperitoneal pressure is increased to 20 mm Hg in the animals with pure CO_2 for the pneumoperitoneum and with fixed ventilation. Besides increased CO_2 absorption, blood flow in the vena cava inferior was arrested from 10 mm Hg intraperitoneal pressure onward (3), probably because of mechanical pressure. Moreover, the parietal peritoneum and the abdominal wall are mechanically compressed and stretched (3). These changes in blood flow (3, 5, 18) probably also contributed to decreased blood pH (11, 12) and increased lactate production (3, 8), indicating anaerobic metabolism and tissue ischemia in inadequately ventilated animals.

The addition of 6% of oxygen to the CO_2-pneumoperitoneum was shown to decrease the consequences of CO_2 absorption, as well as to reduce metabolic hypoxemia in blood (9). Indeed, P_{CO_2} increase and the corresponding pH decrease were much less pronounced. Moreover, a plateau was reached after some 60 minutes whereas with pure CO_2 the increase continued up to the end of the experiment.

All subsequent effects such as an increase in HCO_3^- and a decrease in ABE, SBE, SBC, Po_2, So_2, O_2Hb, and hemoglobin oxygen affinity were much less pronounced and the increase in lactate concentrations occurred much later (in superficially ventilated rabbits) or became nonexistent (in optimally ventilated rabbits). We now confirm the effect of adding 6% of oxygen to the CO_2-pneumoperitoneum. In addition, we demonstrate that even as little as 2% of oxygen added to the CO_2 has significant effects on blood gases, acid-base balance, and oxygen and oximetry values, although the effect is less pronounced than after the addition of 6% of oxygen.

To explain the metabolic effect of prolonged CO_2-pneumoperitoneum and of adding small amounts of oxygen to the CO_2-pneumoperitoneum, the following mechanisms are suggested. First, pure CO_2-pneumoperitoneum affects the mesothelial cells, which retract, that is, cell bulging (15–17), directly exposing the extracellular matrix. From adhesion formation experiments in rabbits and mice, we suggested that this effect is mainly a consequence of mesothelial hypoxia (26, 27). Indeed, adhesion formation increased with CO_2-pneumoperitoneum duration and with intraperitoneal pressure. It decreased after the addition of $>2\%$ and $<10\%$ of oxygen to the CO_2-pneumoperitoneum. This effect of CO_2-pneumoperitoneum–enhanced adhesions is absent in HIF and PlGF knockout mice (28), lending further support to hypoxia. Because CO_2 and helium have similar consequences in tissue oxygen partial pressure (34), these results are in line with our hypothesis that the pneumoperitoneum is a cofactor in adhesion formation, probably via peritoneal mesothelial hypoxia (26, 27). Moreover, the effect of adding oxygen to the CO_2-pneumoperitoneum (2% and 6% $O_2 \cong Po_2$ of 15 to 45 mm Hg at atmospheric pressure) is consistent with the well-known oxygen cascade (35) leading to a physiologic Po_2 of 20 to 40 mm Hg in peripheral tissue. Therefore, direct diffusion of small amounts of oxygen added to the CO_2-pneumoperitoneum can have an important tissue-preserving effect in the hypoxic mesothelial layers of the peritoneal cavity. Recent data (36), demonstrating that controlled respiratory support decreases the impact of CO_2-pneumoperitoneum on tissue-oxygen tension in the retroperitoneal space, present underlying mechanisms of oxygen-tissue metabolism deteriorations during laparoscopic surgery. Moreover, controlled respiratory support impact was significantly pronounced only in mice with high insufflation pressure, and these findings bear comparison with our previous results (8) and present data. Second, in rabbits with fixed ventilation, the metabolic consequences of CO_2 absorption increase progressively over time, whereas after the addition of 6% of oxygen this effect is attenuated. Moreover, the metabolic effects reach a plateau after 45 to 60 minutes. Indeed, the huge differences in metabolic effects between 100% and 94% of CO_2 can be explained by the metabolic impact of oxygen added to the CO_2-pneumoperitoneum. Furthermore, this is consistent with the observed hypoxic retraction of the mesothelial cells and the prevention of this by adding small amounts of oxygen. Because CO_2 absorption increases over time and because in this experiment intraperitoneal pressure was sequentially increased, besides intraperitoneal pressure, the metabolic effects also reflect the duration of pneumoperitoneum, thus magnifying the statistical differences found.

The hypothesis of hypoxic damage to the mesothelial cells due to prolonged CO_2-pneumoperitoneum and the prevention of it by adding $>2\%$ and $<10\%$ of oxygen could explain both the metabolic consequences and the effects on adhesion formation. However, we cannot exclude other oxygen effects because enhanced ventilation was recently shown to reduce adhesion formation in the laparotomy mouse model (37).

In conclusion, these experiments confirm previous observations on the pathophysiology of metabolic changes induced by CO_2 absorption during pneumoperitoneum. We also confirm that the metabolic effects were lower when the intraperitoneal pressure was lower and/or animals were hyperventilated. Most important, the effect of adding as little as 2% of oxygen to the CO_2-pneumoperitoneum, although effective, was less pronounced than after adding 6% of oxygen.

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