and Other Interventional Techniques

Mechanical ventilation with positive end-expiratory pressure preserves arterial oxygenation during prolonged pneumoperitoneum

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Abstract

Background: Laparoscopic surgery usually requires a pneumoperitoneum by insufflating the abdominal cavity with carbon dioxide (CO_2). Increased intraabdominal pressure causes diaphragmatic displacement resulting in compressed lung areas, which leads to formation of atelectasis, especially during mechanical ventilation. Application of positive end-expiratory pressure (PEEP) can maintain pulmonary gas exchange. The objective of this study was to investigate the effect of abdominal gas insufflation on arterial oxygenation during mechanical ventilation with and without PEEP in rats.

Methods: In experiment 1, two groups of six rats were continuously insufflated with CO_2 at 12 mmHg for 180 min. Group 1 was ventilated with 8 cm H_2O PEEP and group 2 had 0 cm H_2O PEEP. Group 3 served as a control. This group had abdominal wall lifting and was ventilated with 0 cmH_2O PEEP. In experiment 2, two groups of six rats had abdominal CO_2 insufflation and were ventilated with or without PEEP during 180 min (group 4 and 5). In this experiment, abdomens were desufflated in both groups for 5 min at 60 and 120 min. Blood pressure monitoring and measurement of arterial pO_2 was performed by placement of an indwelling carotid artery catheter in both experiments.

Results: In both experiments, p_aO_2 values decreased significantly in insufflation groups that were ventilated with 0 cmH_2O PEEP (groups 2 and 5). Insufflation groups ventilated with 8 cmH_2O PEEP had p_aO_2 values comparable to these of control group. There were no significant differences in mean arterial pressure between insufflation groups ventilated with or without PEEP.

Conclusion: PEEP preserves arterial oxygenation during prolonged pneumoperitoneum in rats with minimal adverse hemodynamic effects.

Laparoscopic surgery requires the use of a pneumoperitoneum to create a working space in the abdominal cavity in order to allow safe introduction of trocars and instruments and exposure of the abdominal contents. Intraperitoneal insufflation with carbon dioxide (CO_2) is the most common method to elevate the abdominal wall and suppress the viscera. During laparoscopy CO_2 absorption through the peritoneal membrane leads to hypercapnia and acidosis, and in order to ameliorate these effects, minute ventilation has to be adjusted [3].

During anesthesia lungs are compressed by a cranial shift of the diaphragm and changes in the thoracoabdominal configuration, resulting in the formation of compression atelectasis [4, 13]. During laparoscopic surgery the cranial shift of the diaphragm is enhanced by the increase in intraabdominal pressure, which could lead to further atelectasis formation [10]. An increase of atelectasis will decrease the number of sufficiently ventilated alveoli, resulting in increased dead space, a ventilation–perfusion mismatch, and a decrease in arterial oxygenation (p_aO_2) [8, 14]. During short laparoscopic procedures, these changes in cardiorespiratory parameters seldom have a clinically significant adverse effect. However, it is well recognized that with expansion of laparoscopy, laparoscopic operations will become longer, more complex, and applied to a broader patient population [2]. Minimally invasive techniques have already been applied in elderly patients or patients with
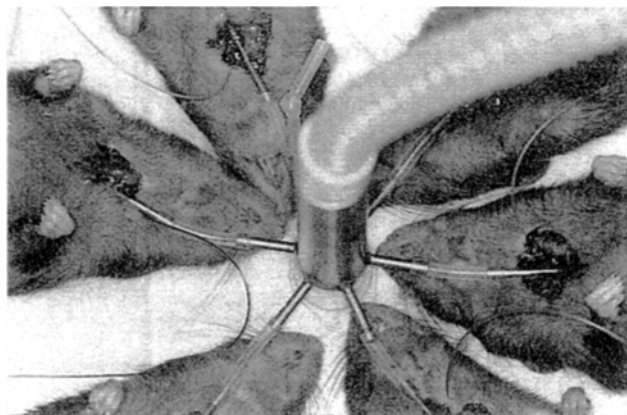
Fig. 1. Positioning of the rats during the experiment. Rats are mechanically ventilated through a tracheotomy. An indwelling carotid artery catheter is placed for blood pressure monitoring and collection of blood samples.

poor cardiopulmonary reserves [11]. Application of positive end-expiratory pressure (PEEP) has been shown to reduce atelectasis formation during anesthesia [4, 13]. However, the use of PEEP in the presence of pneumoperitoneum remains controversial because their simultaneous application may reduce cardiac output [5].

The objective of this study was to determine the cardiopulmonary effects of pneumoperitoneum during mechanical ventilation with and without PEEP in a rat model. We investigated the effects of continuous CO_2 insufflation on arterial oxygenation and blood pressure. In addition, we studied the effects of abdominal desufflation during these two ventilation strategies.

Material and methods

Animals

Male rats of the inbred Brown Norway strain, weighing 250–300 g and aged 10–12 weeks, were obtained from Charles Riven (Someren, The Netherlands). Rats were bred under specific pathogen-free conditions. The animals were kept under standard laboratory conditions (temperature, 20–24°C; relative humidity, 50–60%; 12 h light/12 h dark), fed with laboratory diet (Hope Farms, Woerden, The Netherlands). Before the experiment, all animals had free access to food and water. The experimental protocols adhered to the rules laid down by the Dutch Animal Experimentation Act and were approved by the Committee on Animal Research of the Erasmus University Rotterdam.

Operative procedures

Rats were anesthetized with 65% nitrous oxide/33% oxygen/2% isoflurane (Pharmachemie BV, Haarlem, The Netherlands), and a polyethylene catheter (0.8-mm outer diameter) was inserted into a carotid artery for blood pressure monitoring and for drawing arterial blood samples. Next rats were tracheotomized and a metal cannula was inserted into the trachea (Fig. 1). Gaseous anesthesia was discontinued and replaced with (20 mg/kg/h) pentobarbital sodium intraperitoneally (Nembutal, Sanofi Sante Animale Benelux BV, Maassluis, The Netherlands), given every 30 min. Replacement of gaseous anesthesia by intraperitoneal anesthetic agents was done because in rodents intraperitoneal anesthesia provides a more stable anesthesia.

Rats were placed at the operating table in supine position and, subsequently, muscle relaxation was attained and maintained by hourly intramuscularly injections of 2.0 mg/kg pancuronium (Pavulon, Organon Technika, Boxtel, The Netherlands). After muscle relaxation, the animals were connected to a ventilator (Servo Ventilator 300, Siemens-Elema, Solna, Sweden) in a pressure-controlled mode at a peak inspiratory pressure (PIP) of 12 cm H_2O, a PEEP of 2 cmH$_2$O, an FiO$_2$ of 1.0, a frequency of 30 beats per minute (bpm), and an I/E ratio of 1: 2. In order to reopen atelectatic lung areas induced by induction of anesthesia and the surgical procedure, PIP was increased to 26 cmH$_2$O for 30 s, after which ventilator settings were returned to starting values. Abdomens were shaved and cleaned with 70% alcohol and dried with gauze. After making a 5-mm skin incision in the midline of the abdomen two-third of the way between the xiphoid process and the pubis, a shortened 5-mm trocar (Ethicon Endo-Surgery, Cincinnati, OH, USA) was introduced and secured with a purse-string suture. Measurements for mean arterial pressure (MAP) and arterial blood gases were recorded using conventional methods (ABL 505, Radiometer, Copenhagen, Denmark). For determination of p_aO_2, a blood sample of 0.3 ml was drawn. After each sample, circulating volume was supplemented with 1 ml of saline. One milliliter was given instead of 0.3 ml to compensate for fluid loss from ventilation and pneumoperitoneum. Other means of volume expansion were not employed. There were no differences in fluid management between groups. Body temperature was kept within normal range by means of a heating lamp.

Experiment 1: Mechanical ventilation (PEEP versus no PEEP) during continuous pneumoperitoneum

The animals were allocated randomly to one of three groups (n = 6 per group). Group 1 had abdominal insufflation of CO_2 at 12 mmHg and underwent ventilation with PIP of 18 cmH$_2$O and a PEEP of 8 cmH$_2$O. Group 2 had CO_2 insufflation at 12 mmHg and was ventilated with a PIP of 12 cmH$_2$O and a PEEP of 0 cmH$_2$O. Group 3 served as gasless control by lifting of the abdominal wall with a suture attached to the trocar; this group underwent ventilation with a PIP of 12 cmH$_2$O with 0 cmH$_2$O PEEP.

In preliminary experiments, tidal volumes of approximately 10 ml/kg proved sufficient in all groups. This volume is commonly used in humans undergoing mechanical ventilation. Although the ventilator settings (pressure levels) cannot be directly translated to patients, they can serve as an indication for ventilator settings in humans. Respiratory rate was adjusted to maintain PaCO$_2$ within normal range. In the groups having pneumoperitoneum, respiratory rate was 100 bpm in the no-PEEP and 70 bpm in the PEEP group. In the gasless control group, the respiratory rate was 25 bpm. All animals were exposed to a procedure lasting 180 min. Because the ventilation rate was adjusted in all groups to maintain normocarbia, PaCO$_2$ and pH values are not described in this study.

p_aO_2 was determined at baseline and at 5, 30, 60, 90, 120, 150, and 180 min after the start of the procedure. Blood pressure was recorded at 5, 15, and then every 15 min for 3 h after the start of the procedure. After 180 min, abdomens were desufflated in all animals, followed by a final measurement of p_aO_2 and blood pressure 15 min later. At the end of the experiment, all animals were euthanized with an overdose of pentobarbital sodium injected into the carotid artery.

Experiment 2: Mechanical ventilation (PEEP versus no PEEP) during pneumoperitoneum, discontinued by abdominal desufflation

In two groups of six animals pneumoperitoneum was established by insufflation of CO_2 at 12 mmHg. One group underwent ventilation with a PIP of 18 cmH$_2$O and a PEEP of 8 cmH$_2$O (group 4) and another group was ventilated with a PIP of 12 cmH$_2$O and a PEEP of 0 cmH$_2$O (group 5). In both groups, intraperitoneal insufflation was performed during 180 min, but at 60 and 120 min abdomens were desufflated for 5 min (D1 and D2, respectively). During these episodes of desufflation, respiratory rate was adjusted to maintain normocarbia. p_aO_2 was determined at baseline and at 5, 60, 120, and 180 min after the start of the procedure. In addition, a blood sample was collected directly after desufflation (D1 and D2) and again after resumption of gas insufflation. Blood pressure was recorded at baseline and at 5, 15,
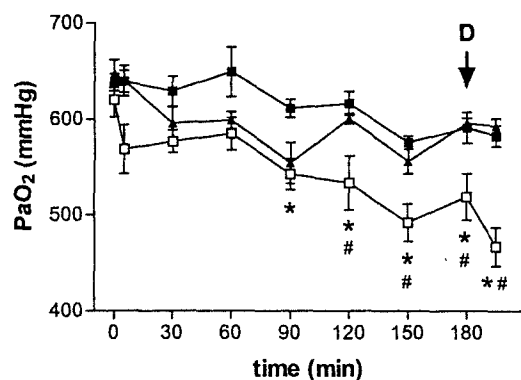
Fig. 2. p_aO_2 values in animals that had intraperitoneal CO_2 insufflation and 8 cmH_2O PEEP (group 1, ■), CO_2 insufflation and 0 cmH_2O PEEP (group 2. □) and abdominal wall lifting and 0 cmH_2O PEEP (group 3, ▲). Data points represent mean ± SEM for each group. D, abdominal desufflation. *p < 0.05 for group 2 compared to preinsufflation levels. #p < 0.05 for group 2 compared to groups 1 and 3.

Fig. 3. Mean arterial pressure (MAP) in animals that had intraperitoneal CO_2 insufflation and 8 cmH_2O PEEP (group 1, ■), CO_2 insufflation and 0 cmH_2O PEEP (group 2, □), and abdominal wall lifting and 0 cmH_2O PEEP (group 3, ▲). Data points represent mean ± SEM for each group. D, abdominal desufflation. *p < 0.05 for groups 1 and 2 compared to preinsufflation levels.

and then every 15 min for 180 min after the start of the procedure. After 180 min, abdomens were desufflated in all animals (D3), followed by a final measurement of p_aO_2 and blood pressure 15 min later. At the end of the experiment, all animals were euthanized as previously described.

Statistical analysis

Statistical analysis was performed utilizing the SPSS 10.0 statistical software package (SPSS, Inc., Chicago). Intergroup comparisons were analyzed by analysis of variance (ANOVA). Intragroup comparisons were analyzed with repeated measures of ANOVA. If ANOVA resulted in p < 0.05. Tukey post hoc test was performed. Statistical significance was accepted at p < 0.05.

Fig. 4. p_aO_2 values in animals that had intraperitoneal CO_2 insufflation and 8 cmH_2O PEEP (group 4, ●) and CO_2 insufflation and 0 cmH_2O PEEP (group 5, ○). Data points represent mean ± SEM for each group. D1, D2, and D3, abdominal desufflation after 60, 120, and 180 min, respectively. *p < 0.05 for group 5 compared to preinsufflation levels. #p < 0.05 for group 5 compared to group 4.

Results

There were no significant differences between the groups in body weight, time between induction of anesthesia, and start of procedure. Baseline measurements did not differ among groups.

Experiment 1

The effects of ventilation with and without PEEP during pneumoperitoneum on arterial oxygenation are shown in Fig. 2. In the group that had pneumoperitoneum with PEEP (group 1), p_aO_2 levels showed no significant differences during the 3 h study period. When no PEEP was applied during CO_2 insufflation (group 2), p_aO_2 values decreased. In the gasless control group (group 3) there were no significant differences in p_aO_2 levels during the experiment. Although there were no significant differences in arterial oxygenation between the three experimental groups at 5, 30, and 60 min, p_aO_2 levels in group 2 were significantly lower compared to preinsufflation levels after 90 min. From 120 min until the end of the experiment, p_aO_2 levels in group 2 were significantly lower compared to p_aO_2 levels in groups 1 and 3. After desufflation, p_aO_2 levels decreased further in group 2, which had gas insufflation and 0 cmH_2O PEEP, whereas
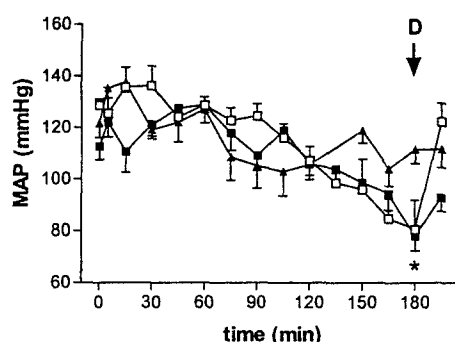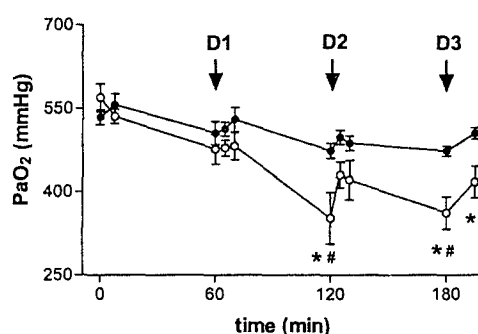
p_aO_2 remained stable in group 1, in which pneumoperitoneum was combined with PEEP.

Figure 3 shows the data on MAP of groups 1–3. For 180 min, there was no significant change in blood pressure in group 3. In groups 1 and 2, MAP was significantly lower compared to preinsufflation levels after 180 min. However, there were no significant differences in MAP between group 1 and group 2 during 180 min of pneumoperitoneum. Abdominal desufflation caused an increase in MAP in groups 1 and 2, which was more pronounced in group 2.

Experiments 2

Figure 4 shows the effects of ventilation with and without PEEP on arterial oxygenation during CO_2 pneumoperitoneum with abdominal desufflation after 60, 120, and 80 min. At 60 min of intraperitoneal insufflation, there were no significant differences between groups 4 and 5. p_aO_2 levels remained stable in both groups during the first desufflation procedure (D1) and after the start of insufflation at 65 min. However, 120 min after the start of pneumoperitoneum, p_aO_2 levels in group 5 were significantly lower compared to preinsuf-
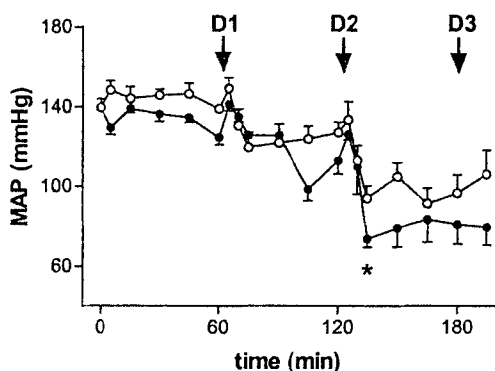
Fig. 5. Mean arterial pressure (MAP) in animals that intraperitoneal CO_2 insufflation and 8 cmH$_2$O PEEP (group 4, ●) and CO_2 insufflation and 0 cmH$_2$O PEEP (group 5, o). Data points represent mean ± SEM for each group. D1, D2, and D3, abdominal desufflation after 60, 120, and 180 min, respectively, $^*p < 0.05$ for group compared to preinsufflation levels.

flation levels and those in group 4. The second procedure of abdominal desufflation (D2) led to an increase in p_aO_2 in both groups. However, after 180 min, p_aO_2 levels were significantly lower in animals that had no PEEP (group 5) compared to animals in group 4. Desufflation of the abdomen (D3) caused a small increase in p_aO_2 in group 5, but these levels remained significantly lower compared to preinsufflation levels.

Figure 5 shows the data on MAP of groups 4 and 5. Over time, blood pressure decreased in both insufflation groups. In animals that had no PEEP (group 5), MAP was not significantly changed compared to preinsufflation levels during 3-h study period. In rats that had PEEP (group 4), MAP was only decreased after 135 min compared to preinsufflation levels. In both groups, the changes in MAP during the periods of desufflation reinsufflation (D1–D3) did not reach statistical significance. During the experiment there were no significant differences between insufflation groups that were ventilated with a PEEP of 8 cmH$_2$O or with a PEEP of 0 cmH$_2$O.

Discussion

This study was designed to investigate changes in arterial oxygenation as a substrate for atelectasis formation in animals undergoing pneumoperitoneum during mechanical ventilation with and without PEEP. The results of this study show that application of PEEP during mechanical ventilation maintains arterial oxygenation during CO_2 pneumoperitoneum. When no PEEP was applied during CO_2 insufflation, p_aO_2 levels decreased significantly.

It has been shown that increased intraabdominal pressure causes a cranial shift of the diaphragm resulting in compressed lung areas, which leads to formation of atelectasis, particularly during mechanical ventilation [10]. Therefore, we first studied the effect of continuous gas insufflation on arterial oxygenation. In rats ventilated without PEEP, p_aO_2 levels decreased after 90 min of abdominal insufflation. After 180 min of gas insufflation, arterial oxygenation was still significantly decreased. These findings demonstrate that increased

intraabdominal pressure results in the formation of atelectatic lung areas. In the abdominal wall lift group, p_aO_2 levels did not significantly change over time. In this group, the small changes in p_aO_2 were most likely caused by end-expiratory alveolar collapse due to the absence of PEEP, which prevents alveolar collapse. Therefore, rats ventilated without PEEP are prone to atelectasis formation, aggravated by supine position and muscular relaxants.

We used arterial oxygenation during mechanical ventilation with 100% oxygen as an accurate indicator for atelectasis formation. In a "normal" lung this will result in p_aO_2 levels up to 600 mmHg [15], as observed in baseline values of p_aO_2 in all animals. When the lung remains inflated, no atelectasis formation occurs and p_aO_2 will not be affected [6, 8], as observed in the 8 cmH$_2$O PEEP group (Fig. 2). These findings are in concordance with a study in pigs by Loeckinger et al. [7] in which they conclude that application of PEEP during intraperitoneal CO_2 insufflation can improve pulmonary gas exchange. One of the main differences between the study by Loeckinger et al. and our study is that they evaluated different levels of PEEP during intraperitoneal CO_2 insufflation on the lung's ventilation–perfusion, whereas we studied the effect of mechanical ventilation with a constant level of PEEP during pneumoperitoneum. To mimic clinically relevant settings we kept PEEP levels constant and applied the pneumoperitoneum and PEEP levels during a 180-min study period, thus simulating prolonged laparoscopic procedures.

In our second experiment, we studied the effects of release of intraabdominal pressure on pulmonary gas exchange. This study design is more representative for clinical laparoscopic procedures since abdominal desufflation occurs during inadvertent removal of laparoscopic instruments and because of deflation of electrocautery smoke. Although moments of intraabdominal pressure release are often incomplete and may occur randomly in clinical practice, procedures of abdominal desufflation were of the same length and were performed at defined time points to prevent any bias among the experimental groups. In rats ventilated with and without PEEP, p_aO_2 levels did not significantly change after 60 min or during the first abdominal desufflation procedure (Fig. 4). However, after 120 min, p_aO_2 was significantly decreased in animals ventilated without PEEP. At this time, abdominal desufflation led to an increase in p_aO_2, suggesting that release of pneumoperitoneum improves ventilation–perfusion mismatch. After 180 min, p_aO_2 levels were decreased again and remained significantly decreased after final abdominal desufflation. These findings suggest that there is a beneficial effect on pulmonary gas exchange caused by abdominal desufflation. However, this effect appears to be temporary since installation of pneumoperitoneum caused a further decrease in arterial oxygenation.

The use of PEEP in the presence of pneumoperitoneum has been controversial due to the decrease of venous return with subsequent reduced cardiac output [5]. However, others conclude that simultaneous application of PEEP and increased intraabdominal pressure results only in modest hemodynamic depression [7] or can be

performed without adverse cardiovascular effects [1]. In our study, we did not measure cardiac output because accurate measurement of cardiac output in rodents requires placement of a flow probe around the aorta by thoracotomy. Therefore, we measured MAP to investigate the effect of pneumoperitoneum on hemodynamic function. As shown by Pizov et al., [9] measuring arterial blood pressure changes allows sufficient assessment of hemodynamic changes in the absence of cardiac output measurement. Our study revealed a significant decrease in blood pressure during ventilation with PEEP in only two instances. This suggests that the adverse hemodynamic effects of PEEP during pneumoperitoneum are limited.

It is well recognized that as laparoscopic procedures become longer and more complex, the altered physiology due to pneumoperitoneum becomes more important [2]. Therefore, insight into the potential side effects inherent to laparoscopic surgery is mandatory.

Information concerning the use of PEEP in patients undergoing mechanical ventilation during pneumoperitoneum is scarce. However, Neumann et al. [8] showed that during general anesthesia, a PEEP level of 10 cmH_2O could prevent atelectasis formation in patients undergoing elective surgery, demonstrating that a PEEP level of at least 10 cmH_2O is required to prevent atelectasis formation in healthy lungs. In addition, prevention of atelectasis formation can reduce postsurgery respiratory morbidity [12, 16]. Our study demonstrates that pulmonary atelectasis formation, as measured by arterial oxygenation, induced by abdominal gas insufflation can be prevented by adding PEEP to mechanical ventilation. Issues concerning the pathophysiological consequences of PEEP ventilation during laparoscopic surgery should therefore be addressed in clinical trials.

We conclude that application of PEEP preserves arterial oxygenation during prolonged pneumoperitoneum in mechanically ventilated rats. In the current study, application of 8 cmH_2O of PEEP was feasible with minimal hemodynamic changes. Our data indicate that PEEP can be used to prevent pulmonary atelectasis formation during laparoscopic surgery.

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