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Effects of positive end-expiratory pressure on intracranial pressure during pneumoperitoneum and Trendelenburg position in a porcine model*

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Background/aim: This study was undertaken to evaluate the effects of positive end-expiratory pressure (PEEP) levels on intracranial pressure (ICP) and cerebral perfusion pressure (CPP) and to determine the appropriate PEEP level during steep Trendelenburg position combined with pneumoperitoneum.

Materials and methods: Ten pigs were included in this study. Pneumoperitoneum and Trendelenburg position were maintained and PEEP titration was initiated. Arterial pressure, heart rate, arterial blood gas, ICP, and CPP were recorded at the following time points: baseline (T0), 30 min after positioning and pneumoperitoneum (T1), PEEP 5 (T2), PEEP 10 (T3), PEEP 15 (T4), and PEEP 20 (T5).

Results: MAP significantly increased at T1 compared to T0 and decreased at T4 and T5 compared to T1. ICP was 9.5 mmHg and CPP was 69.3 mmHg at T0. CO_2 insufflation and steep Trendelenburg position did not cause any significant difference in ICP and CPP. ICP increased and CPP decreased significantly at T4 and T5 compared to both T0 and T1. PaO_2 and PaO_2/FiO_2 decreased significantly at T1 and T2 compared to T0, while both increased significantly at T3, T4, and T5 compared to T1.

Conclusion: PEEP of 10 cmH_2O was effective for providing oxygenation while preserving hemodynamic stability, ICP, and CPP in this model.

Key words: PEEP, intracranial pressure, Trendelenburg position, pneumoperitoneum

1. Introduction

Robot-assisted laparoscopic surgery has developed greatly and is becoming a standard technique for radical prostatectomy. It is widely preferred for pelvic surgeries because of its important advantages that minimize postoperative morbidity and mortality. Robotic surgeries in the pelvic region, including radical prostatectomy, rectum resection, and gynecologic procedures, usually require a steep Trendelenburg position and carbon dioxide pneumoperitoneum to secure the surgical field. Pneumoperitoneum combined with steep Trendelenburg position may cause significant changes in cardiovascular, respiratory, and neurophysiological parameters (1,2). Both the increase in abdominal pressure as a result of carbon dioxide insufflation and the head-down position have been shown to impair respiratory functions during the procedure by pushing the diaphragm upward and reducing lung volume and respiratory compliance, thus inducing atelectasis formation (3,4).

Application of positive end-expiratory pressure (PEEP) has been demonstrated to prevent atelectasis and provide gas exchange. Studies reported that PEEP applied during laparoscopy improved oxygenation and respiratory compliance (5–7). However, PEEP application causes a subsequent elevation of intrathoracic pressure, decreases cerebral venous return, increases intracranial blood volume and pressure, and possibly impairs cerebral blood flow. The effects of PEEP on ICP and cerebral perfusion pressure (CPP) have been the focus of several experimental and clinical studies, but these studies did not address the direct relationship between ICP, cerebral blood flow, and PEEP during steep Trendelenburg position combined with pneumoperitoneum (8–11).

Pneumoperitoneum alone has been shown to induce intracranial hypertension in animal models, which is magnified by the addition of Trendelenburg positioning (12). In addition, human studies showed

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that steep Trendelenburg position along with CO_2 pneumoperitoneum causes an increase in intraocular and intracranial pressure monitored noninvasively (13,14).

These findings suggest that PEEP application to patients undergoing robot-assisted radical prostatectomy and other robotic pelvic surgeries may cause a risk for increased ICP. The effects of different PEEP levels on ICP during the Trendelenburg position and CO_2 pneumoperitoneum have not been well quantified previously. This study was undertaken to evaluate the effects of different PEEP levels on ICP and to determine the optimum PEEP level during steep Trendelenburg position combined with pneumoperitoneum in an experimental porcine model.

2. Methods

2.1. Ethics

Ethical approval for this study was provided by the Institutional Review Committee on the Ethics of Animal Experiments of the Medical Faculty of Gazi University, Ankara, Turkey (Ethical Committee No: GUET-11.082). This study was conducted in accordance with the Institutional and International Animal Care and Use Committee guidelines. This study was undertaken according to the ARRIVE (Animal Research: Reporting of In Vivo Experiments) guidelines.

2.2. Animals, anesthesia, and instrumentation

Ten male Yorkshire pigs weighing 30 ± 5 kg were included in this study. Before the experiment, animals were housed for 5 days in individual cages in a temperature- and light-cycle-controlled environment with standard laboratory food and water ad libitum.

Animals were deprived of food supply 12 h before the experiment and premedicated with ketamine (10 mg kg^{-1}, intramuscular) and xylazine (2 mg kg^{-1}, intramuscular). After sedation, animals were placed on an operation table with a heating pad, an intravenous line was placed to the ear vein, and lactated Ringer solution was infused at a rate of 3 mL kg^{-1}. Anesthesia was induced with 5 mg kg^{-1} propofol and 5 µg kg^{-1} fentanyl intravenously and maintained by 2% isoflurane in an oxygen/air mixture and a fentanyl infusion at 0.1 µg kg^{-1} per minute. All animals were intubated with a 6.5 endotracheal tube and ventilated mechanically with a tidal volume of 7 mL. Respiratory rate was adjusted to maintain end-tidal CO_2 ($etCO_2$) in the range of 35 to 40 mmHg and an inspiratory : expiratory ratio of 1:2 with volume control mechanical ventilation. Inspired oxygen fraction was 0.4 in air, and PEEP was not applied before the onset of pneumoperitoneum and the Trendelenburg position.

A temperature probe was applied and body temperature was maintained between 36 and 37 °C. An arterial catheter was placed to one femoral artery for arterial blood pressure measurements and to obtain blood samples for blood gas analysis. A ventricular catheter device (Integra Camino Flex Ventricular Catheter Kit) was placed into the third ventricle through the bur hole as described by Kaiser and Frühauf (15) for the measurement of ICP. The catheter was fixed and connected to the pressure monitor. CPP was calculated via arterial pressure and ICP monitoring. The arterial transducer was zeroed at the heart level for MAP measurement, while the tragus of the ear was the level at which the pressure transducer was zeroed for the ICP measurement.

Pneumoperitoneum was maintained at a pressure of 15 mmHg and the animals were placed at 45 degrees of Trendelenburg positon and stabilized for a period of 30 min. PEEP titration was initiated at a level of 5 cmH_2O with a stepwise increase of 5 cmH_2O until a plateau PEEP level of 20 cmH_2O was achieved. This was followed by a stepwise reduction. At each step PEEP was applied for 3 min and the measurements detailed below were taken.

2.3. Measurements

Heart rate (HR), mean arterial blood pressure (MAP), $etCO_2$, and peripheral oxygen saturation (SpO_2) were monitored all throughout the procedure. Partial oxygen pressure (PaO_2) and partial carbon dioxide pressure ($PaCO_2$) monitored through blood gas analysis were obtained at every measurement time. Parameters of oxygenation [partial pressure of arterial oxygen/inspiratory fraction of oxygen ratio (PaO_2/FiO_2)] and ventilation [arterial and end tidal carbon dioxide ($PaCO_2$, $etCO_2$), arterial end tidal carbon dioxide gradient (P (a-et) CO_2)] were recorded and calculated. ICP was monitored by using a ventricular drainage system, and cerebral perfusion pressure (CPP = MAP – ICP) was calculated. All the measured and calculated parameters were compared at the following time points: baseline (T0), Trendelenburg position and pneumoperitoneum (T1), PEEP 5 (T2), PEEP 10 (T3), PEEP 15 (T4), and PEEP 20 (T5).

2.4. Statistics

Statistical analysis was performed with the GraphPad software package and $P < 0.05$ was regarded as statistically significant (SPSS 20; IBM Corp., Armonk, NY, USA). The Shapiro–Wilk normality test was used to evaluate the distribution of the data. Comparison of the nonnormally distributed data between measurement points was performed with the Friedman test, followed by Wilcoxon's signed-rank test. Results were expressed as median with interquartile range (25th–75th). For normally distributed data comparisons between measurement points were performed by two-way ANOVA and Tukey's honestly significant difference method.

3. Results

MAP and HR values are displayed in Table 1. MAP significantly increased at T1 compared to the baseline (T0) measurement ($P < 0.05$). The MAP value then significantly decreased at T4 and T5 compared to the T1 measurement ($P < 0.05$). HR was stable until the PEEP level reached 20 cmH_2O, but at this level (T5) HR decreased significantly compared to both T0 and T1 measurements ($P < 0.05$).

Oxygenation and ventilation parameters are shown in Table 2. The PaO_2 value and PaO_2/FiO_2 ratio decreased significantly at T1 and T2 compared to T0. Moreover, both the PaO_2 value and the PaO_2/FiO_2 ratio increased significantly at T3, T4, and T5 compared to T1 ($P < 0.001$). $P(a\text{-}et)CO_2$ did not show any significant change throughout the study ($P > 0.05$).

ICP and CPP values are shown in Figures 1 and 2. Baseline ICP and CPP values obtained at the T0 measurement were 9.5 mmHg and 69.3 mmHg, respectively, and were not significantly affected by intraabdominal CO_2 insufflation combined with steep Trendelenburg position ($P > 0.05$). ICP increased significantly while CPP decreased significantly at T4 and T5 compared to both T0 and T1 measurements ($P < 0.05$).

Table 1. Hemodynamics of swine with respect to positive end-expiratory pressure (PEEP) levels.

	T0	T1	T2	T3	T4	T5
MAP mmHg	78.7 ± 12.1	105.2 ± 14.3*	90.1 ± 13.1	89.6 ± 15.1	82.7 ± 16.1^β	79.6 ± 12.2^β
HR min^{-1}	94.7 ± 15.1	96.5 ± 13.4	95.4 ± 15.2	93.4 ± 17.2	81.6 ± 16.1	66.5 ± 13.3^{*β}

MAP: Mean arterial pressure; HR: heart rate. * $P < 0.05$ compared to T0 measurement time. ^{β} $P < 0.05$ compared to T1 measurement time.

Table 2. Oxygenation and ventilation parameters of swine with respect to PEEP levels.

	T0	T1	T2	T3	T4	T5
PaO_2/FiO_2	468 (375–510)	310* (243–356)	318* (265–398)	432^β (376–437)	438^β (395–462)	487^β (450–541)
$P(a\text{-}et)CO_2$	5 (3–7)	6 (5–8)	7 (5–8)	5 (4–8)	6 (5–7)	5 (5–6)
PaO_2 mmHg	190 ± 43	149 ± 37*	152 ± 40*	178 ± 38^β	185 ± 34^β	198 ± 43^β
$PaCO_2$ mmHg	33.5 ± 2.1	43.7 ± 4.1	42.2 ± 4.3	42.1 ± 3.2	38.2 ± 1.4	34.5 ± 2.8

$etCO_2$: End tidal carbon dioxide; SpO_2: peripheral oxygen saturation; PaO_2: partial oxygen pressure; $PaCO_2$: partial carbon dioxide pressure; P(a-et) CO_2: arterial end tidal carbon dioxide gradient. * $P < 0.05$ compared to T0 measurement time. ^{β} $P < 0.05$ compared to T1 measurement time.

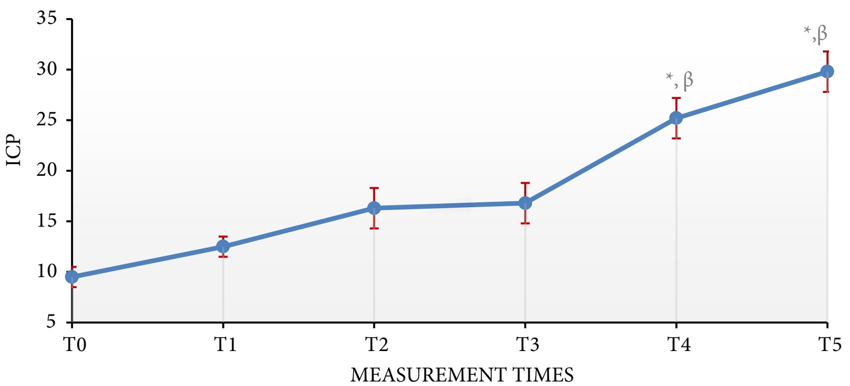

Figure 1. Changes in intracranial pressure (ICP) with respect to positive end-expiratory pressure (PEEP) are shown.
* $P < 0.05$ compared to T0 measurement time. ^{β} $P < 0.05$ compared to T1 measurement time.

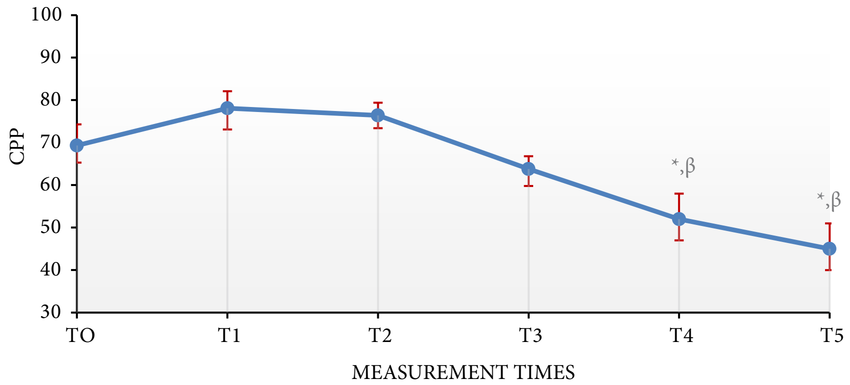

Figure 2. Changes in cerebral perfusion pressure (CPP) with respect to positive end-expiratory pressure (PEEP) are shown.
* $P < 0.05$ compared to T0 measurement time. $^{\beta}$ $P < 0.05$ compared to T1 measurement time.

4. Discussion

The results of this experimental study showed that PEEP of 10 cmH_2O was an efficient PEEP level to ameliorate oxygenation and hemodynamic stability while preserving ICP and maintaining adequate CPP even in the presence of pneumoperitoneum and steep Trendelenburg positon. PEEP levels higher than 10 cmH_2O increased ICP and had a hazardous effect on cerebral perfusion.

Minimally invasive surgery is a worldwide preferred technique as it brings many advantages. The steep Trendelenburg position accompanied by pneumoperitoneum is essential for pelvic robotic surgeries, but this combination is a challenge for respiratory mechanics and cerebrovascular hemostasis (1,2). A minimally invasive technique reduces surgical complications and improves outcomes and patient comfort; thus, the patient profile is expanded and more patients with significant comorbidities are being offered robotic surgeries. In addition, more complicated surgical procedures began to be implemented via the robotic surgical approach, which means longer operating times in these nonphysiological circumstances. Clinical and experimental studies showed that pneumoperitoneum and Trendelenburg position cause hemodynamic perturbations and gas exchange disturbances, and they have effects on cerebrovascular hemostasis (13,16–18). Likewise, in this study, MAP increased and oxygenation was disturbed in pigs that were exposed to the steep Trendelenburg position and pneumoperitoneum.

In the literature, several ventilation strategies including volume control ventilation, pressure control ventilation, recruitment maneuvers, and PEEP application are discussed for the management of ventilation and oxygenation problems caused by increased intraabdominal pressure and head-down position (19–23). The importance of PEEP application for maintaining adequate gas exchange while preventing ventilator-induced lung injury is especially emphasized (7,10,22,23). Many studies suggested that PEEP and the alveolar recruitment maneuver application improved ventilation-perfusion and gas exchange (7,24,25). In a clinical trial it was demonstrated that a PEEP of 10 cmH_2O produced beneficial effects on the impaired elastance of the respiratory system caused by pneumoperitoneum in patients undergoing laparoscopic cholecystectomy (5). Futier et al. (24) reported that recruitment maneuvers combined with 10 cmH_2O of PEEP were effective for oxygenation and restoring respiratory dynamics in obese patients. In a clinical study, Cinnella et al. (7) applied lung recruitment followed by PEEP of 5 cmH_2O in patients undergoing laparoscopic surgery at 20 degrees of Trendelenburg position. They concluded that this approach led to alveolar recruitment and improved gas exchange. Despite this conclusion, they added that this level of PEEP was not enough to maximize alveolar recruitment and recommended further studies to determine the optimum PEEP level.

However, these suggestions may create a challenge in situations in which ICP increase has already been initiated by increased intraabdominal pressure, etCO_2 changes, and steep Trendelenburg position. PEEP application may reduce cardiac output and blood pressure may produce reduction in CPP that may lead to cerebral ischemia. However, the effects of PEEP on ICP and CPP in patients undergoing laparoscopic surgery needing steep Trendelenburg position have not been well quantified.

Recent human studies investigated the effects of Trendelenburg positioning and CO_2 pneumoperitoneum on ICP measured by noninvasive methods. Results showed that patients undergoing robotic radical prostatectomy might be at risk for increased ICP even without PEEP application (13,14). In the present study, an experimental model was prepared to simulate nonphysiological conditions of robotic prostatectomy and we evaluated the effects of PEEP on ICP under these conditions. In this study, ICP was measured directly and $PaCO_2$ was normalized by increasing minute ventilation in order to isolate the effects of PEEP independent of the effects of hypercapnia. Our results showed that steep Trendelenburg positioning combined with pneumoperitoneum did not cause a significant increase in ICP, while high PEEP levels resulted in increased ICP.

Muench et al. (10) studied the effects of high PEEP levels (25 cmH_2O) on ICP both in healthy pigs and in patients suffering from subarachnoid hemorrhage. They reported that ICP increase would be most relevant in patients with a preexisting increase in ICP. Moreover, they concluded that PEEP and ICP interaction depended on hemodynamic stability. In the present study, we evaluated the relation between PEEP and ICP in pigs without preexisting increased ICP, and our results showed that ICP was affected by PEEP at 15 and 20 cmH_2O levels, even though the MAP values of the pigs were maintained at baseline levels.

In conclusion, this experimental model was applied to simulate decreased lung compliance and increased cerebral blood flow conditions in pigs without any cerebral or respiratory pathology; our results showed that PEEP of 10 cmH_2O was an effective level to manage alveolar recruitment during pneumoperitoneum and Trendelenburg position while preserving ICP and CPP. The application of high PEEP levels may cause problems related to decreased CPP and patients must be treated cautiously in these conditions.

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