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Research Paper

The effects of inverse ratio ventilation on cardiopulmonary function and inflammatory cytokine of bronchoaveolar lavage in obese patients undergoing gynecological laparoscopy

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ABSTRACT

Background: High peak airway pressure (Ppeak) and high end-tidal carbon dioxide tension ($P_{ET}CO_2$) are the common problems encountered in the obese patients undergoing gynecological laparoscopy with conventional volume-controlled ventilation. This study was designed to investigate whether volume-controlled inverse ratio ventilation (IRV) with inspiratory to expiratory (I:E) ratio of 2:1 could reduce Ppeak or the plateau pressure (Pplat), improve oxygenation, and alleviate lung injury in patients with normal lungs.

Methods: Sixty obese patients undergoing gynecological laparoscopy were enrolled in this study. After tracheal intubation, the patients were randomly divided into the IRV group ($n = 30$) and control group ($n = 30$). They were ventilated with an actual tidal volume of 8 mL/kg, respiratory rate of 12 breaths/min, zero positive end-expiratory pressure and I:E of 1:2 or 2:1. Arterial blood samples, hemodynamic parameters, and respiratory mechanics were recorded before and during pneumoperitoneum. The concentrations of tumor necrosis factor-α, and interleukins 6 and 8 in bronchoalveolar lavage fluid were measured immediately before and 60 minutes after onset of CO_2 pneumoperitoneum.

Results: IRV significantly increased arterial partial pressure of oxygen, mean airway pressure, and dynamic compliance of respiratory system with concomitant significant decreases in Ppeak and Pplat compared to conventional ventilation with I:E of 1:2 ($p < 0.05$). Additionally, the levels of tumor necrosis factor-α, and interleukins 6 and 8 were significantly lower than those in control group ($p < 0.05$).

Conclusion: Volume-controlled IRV not only reduces Ppeak, Pplat, and the release of inflammatory cytokines, but also increases mean airway pressure, and improves oxygenation and dynamic compliance of respiratory system in obese patients undergoing gynecologic laparoscopy without adverse respiratory and hemodynamic effects. It is superior to conventional ratio ventilation in terms of oxygenation, respiratory mechanics and inflammatory cytokine in obese patients undergoing gynecologic laparoscopy.

1. Introduction

Laparoscopy is associated with increases peak airway pressure (Ppeak) and high end-tidal carbon dioxide tension ($P_{ET}CO_2$) with conventional ratio ventilation mode, especially in obese patients. Laparoscopic gynecologic surgery usually requires steep lithotomy or Trendelenburg position, demanding additional ventilatory adjustments to maintain oxygenation and normocapnia.[1,2] It is difficult to improve the hypercapnia by increasing the respiratory rate or tidal volume, as the high airway pressure may not allow a further increase in tidal volume, and increasing respiratory rate sometimes fails to correct hypercapnia. Applying positive end-expiratory pressure (PEEP) might improve oxygenation and be accompanied with an increase in Ppeak. Furthermore, high tidal volume and high airway pressure may lead to lung barotrauma and volutrauma. It is reported that pressure-controlled inverse ratio ventilation (IRV) can successfully recruit collapsed alveoli and has improved oxygenation at lower Ppeak.[3–7] However, its use is sometimes limited by the significant elevation in Ppeak with increasing the risk of barotrauma[3,4] and a decrease in tidal volume. Prolonging inspiratory time with inspiratory to expiratory (I:E) ratio more than 3:1 might affect cardiac output, and the optimal I:E

Conflicts of interest: There are no conflicts of interest in connection with this article.

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of IRV is 2:1,[8] so we investigated whether volume-controlled IRV (I:E = 2:1) was superior to conventional ratio ventilation in terms of oxygenation and respiratory mechanics in obese patients undergoing laparoscopic gynecologic surgery.

2. Methods

This study was approved by the Hospital Ethics Committee of Jinxing maternity and child health care hospital and registered in the protocol registration system (www.chictr.org.cn, registration number:ChiCTR-IPC-15006522). Informed consent was signed by the patients. From May 2014 to June 2015 we chose a total of 60 obese patients of elective major gynecologic laparoscopy, ASA grade I or II, age 34–61 years, body mass index 30–35 kg/m^2 (weight 71–87 kg), and expected duration of surgery > 1 hour. We excluded patients with cardiopulmonary disease and age > 65 years or < 18 years. The 60 patients were randomly divided into the IRV group (n = 30) and control group (n = 30), based on a computer-generated randomization list.

All patients were premedicated with 5 mg midazolam and 0.5 mg atropine intramuscularly 30 minutes before arrival at the operating room. After entering the operating room, monitoring, including electrocardiogram, noninvasive blood pressure, heart rate, cardiac output, stroke volume index, systemic vascular resistance, and other indicators, was applied with BioZ.com noninvasive hemodynamic (Cardio Dynamics company, USA) and venous access was established. After preoxygenation, anesthesia was induced with intravenous fentanyl 4 μg/kg, propofol 2 mg/kg given over 15 s, and *cis*-atracurium 0.15 mg/kg. After tracheal intubation using direct laryngoscope, the patients were randomly divided into of two groups with volume-controlled ventilation mode. Lungs were ventilated with Datex-Ohmeda Aspire anesthesia ventilator. Respiratory parameters were set as: actual tidal volume 8 mL/kg actual body weight, respiratory rate 12 breaths/min, PEEP of zero, oxygen flow 1 L/min, fraction inspired oxygen (FiO_2) 1.0, and I:E ratio of 2:1 (in the IRV group) or 1:2 (in control group).

Anesthesia was maintained with propofol 4–6 mg/kg/h and 1.5–2.5% end-tidal sevoflurane to keep the bispectral index value between 45 and 55 (BIS monitor Model A2000; Aspect, USA) and control the hemodynamic response to the surgical procedure within a 20% range of the preoperative value. Muscle relaxation was monitored by the train-of-four (TOF) stimulation on the ulnar nerve (Type TOF-Watch SX; Organon, Oss, The Netherlands). Continuous infusion of *cis*-atracurium (0.08–0.1 mg/kg/h) was performed to keep TOF value below 5%. Respiratory parameters were kept constant if $P_{ET}CO_2$ was <50 mmHg. When $P_{ET}CO_2$ exceeded 50 mmHg, respiratory rate or tidal volume was adjusted to maintain $P_{ET}CO_2$ below 50 mmHg. Spirometry readings included Ppeak, plateau pressure (Pplat), mean airway pressure (Pmean), PEEP (auto-PEEP), and dynamic compliance of the respiratory system (CL) using a side-stream spirometry device (Anesthesia Monitor D-FPD15-00; GE, Taipei, Taiwan). CO_2 pneumoperitoneum tension was set at 15 mmHg. Throughout the study period, lactated Ringer's solution was infused at rate of 6–8 mL/kg/h.

The patients were put in a 30° Trendelenburg position after trocars were placed and in the supine position again at the end of pneumoperitoneum. Hemodynamic parameters were monitored at 5 minutes before anesthesia induction (T0), immediately before onset of pneumoperitoneum (T1), 60 minutes after onset of pneumoperitoneum (T2), and the end of surgery (T3). Arterial blood gas was analyzed using a blood gas analyzer (ABL8000A; Denmark) at T1 and T2. Postoperative complications were observed, such as discharge time in the postanesthesia care unit (PACU), hypoxemia [defined as arterial partial pressure of oxygen (PaO_2) < 80 mmHg], and other pulmonary complications. The patients could be discharged from PACU when modified Aldrete score was 9 or above.

Before and during pneumoperitoneum, we collected respectively right bronchoalveolar lavage fluid soaked in 20 mL normal saline for 5 minutes with a fiber bronchoscope (Olympus, Tokyo, Japan), and 20–30% of this fluid was recovered. The samples were centrifuged (3000 r/min, r = 16 cm) for 15 minutes at 4°C and the supernatant stored at 70°C. Tumor necrosis factor (TNF)-α, interleukin (IL)-6, and IL-8 levels were detected with enzyme-linked immunosorbent assays (Boshide Biotechnology, China), using a microplate reader (Hyperion MRIII, USA) according to the manufacturer's instruction.

2.1. Statistical analysis

All data were analyzed with SPSS 19.0 statistical software (SPSS Inc, Chicago, IL, USA). Descriptive statics and compliance with normal distribution was examined with one-sample Kolmogorov–Smirnov test. Between the two groups, two-tailed Student t test and Mann–Whitney U test were used. Categorical variables were evaluated with the Chi-square test. All quantitative data were expressed as mean ± standard deviation. A value of $p < 0.05$ was considered statistically significant.

The sample sizes of this study were determined based on the following considerations. The main variable was PaO_2 in this study, which had a standard deviation of 38.6 from the pilot study done in 10 patients. *A priori* power analysis using two-sided analysis with α error of 0.05 and a power of 1.1 showed that 54 patients were needed for this study.

3. Results

Sixty patients were recruited into the study. No patient was excluded for any reason. All the patients were adult women with a mean age of 55.6 ± 5.8 years and a mean body mass index of 33.1 ± 1.9 kg/m^2. The mean duration of surgery was 118.5 ± 26.8 minutes. No significant differences were found in age, body mass index, or duration of surgery between groups ($p > 0.05$; Table 1). PaO_2 increased significantly at T2 than at T1 in both groups, and PaO_2 was higher in the IRV group than those in the control group at T2 (502.73 ± 52.54 vs. 466.51 ± 45.37; $p < 0.05$; Table 2). $PetCO_2$ values were all < 50 mmHg before T2, and $PaCO_2$ was increased obviously at T2 than at T1 in both groups, but there was no statistically significant difference between the two groups at T2. On comparison of pH, $PaCO_2$, HCO^{3-} and SaO_2 at T1 or T2 in both groups, there were no statistical significance ($p > 0.05$). The patients were showed a moderate hypercapnia (defined as $PaCO_2$ > 45 mmHg) during pneumoperitoneum in both groups. At T2, the Ppeak and Pplat were lower in the IRV group than those in control group (28.8 ± 2.3 vs. 32.3 ± 2.9, 27.5 ± 1.9 vs. 30.7 ± 2.2, respectively; $p < 0.001$), but the Pmean and auto-PEEP were higher in the IRV group than in the control group. There were statistically significant differences in Pmean and auto-PEEP (17.1 ± 1.8 vs. 12.3 ± 1.6, 4.3 ± 1.1 vs. 2.9 ± 0.8, respectively; $p < 0.01$), and CL was improved significantly compared to the control group (21.2 ± 1.5 vs. 19.6 ± 1.2; $p < 0.001$; Table 2).

BioZ.com noninvasive hemodynamic monitoring reflected the hemodynamic changes in the two groups. In the condition of anesthesia and pneumoperitoneum, mean arterial blood pressure fell, and gradually increased after the end of pneumoperitoneum. Intragroup comparison indicated that the blood pressure, heart rate, cardiac output, stroke volume index, and systemic vascular resistance were higher at T2 than T1, ($p < 0.05$), but comparison of hemodynamic parameters between the two groups found no statistical significance ($p > 0.05$; Figure 1). The levels of TNF-α, IL-6,