EFFECT OF PERIOPERATIVE LUNG PROTECTIVE VENTILATION ON PATIENTS WITH SEPSIS IN THE ABDOMINAL CAVITY

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ABSTRACT

Introduction*: Severe abdominal infections often induce sepsis, and the lung is one of the organs that are frequently affected by sepsis. Many patients with sepsis caused by abdominal infections, but no clinical study on whether these patients should receive ventilation strategies has been reported. This study aims to investigate the effects of different mechanical ventilations on patients with sepsis in the abdominal cavity.*

Materials and methods*: A retrospective analysis was conducted on data obtained from 296 patients with sepsis in the abdominal cavity, who were admitted in our hospital, in order to evaluate the effects of mechanical ventilations with different tidal volumes. Carbon dioxide partial pressure, oxygenation index and mean airway plateau pressure at different time points after mechanical ventilation, the tracheal extubation rate within two hours after surgery, the incidence of atelectasis within 24 hours after surgery, and mortality within 28 days after surgery were compared between the two groups.*

Results*: Differences in the basic situations of patients upon entering the operating room between the two groups were not statistically significant. At 10, 30 and 60 minutes after mechanical ventilation, and at the end of the operation, differences in arterial blood pH value, oxygenation index, extubation rate within two hours after surgery, and the incidence of atelectasis within 24 after surgery between the two groups were not statistically significant ($P>0.05$). Ventilation was obviously excessive and airway plateau pressure was higher in group I, while patients had mild CO_2 retention in group II; and the difference was statistically significant ($P<0.05$). Furthermore, differences in the incidence of acute respiratory distress syndrome and 28-day mortality between the two groups were statistically significant ($P=0.04$).*

Conclusion*: Lung protective ventilation can reduce the incidence of acute respiratory distress syndrome and 28-day mortality.*

Keywords*: Intraoperative lung protection ventilation, sepsis, intra-abdominal infection, Acute Respiratory Distress Syndrome, pulmonary complication.*

DOI: 10.19193/0393-6384_2018_6_259

Received *January 30, 2018;* ***Accepted*** *March 20, 2018*

Introduction

Severe abdominal infections often induce sepsis, and the lung is one of the organs that are frequently affected by sepsis. Postoperative pulmonary complications can increase the mortality of patients and prolong hospitalization time. Different mechanical ventilation methods during operation under general anesthesia have different effects on the prognosis of patients. It has been widely recognized that inappropriate mechanical ventilation can induce or aggravate lung injury. Lung protective ventilation was mainly applied in acute respiratory distress syndrome (ARDS) patients in the past. Recently, some retrospective and prospective studies have indicated that low tidal volume also brought about beneficial effects, even for patients who require short-term mechanical ventilation(1). Many scholars have applied the lung protective ventilation strategy including low tidal volume, positive end-expiratory pressure (PEEP) and recruitment maneuver (RM) in the operation process, in order to reduce lung injury and improve postoperative respiratory function(2-5). Lellouche(6) even believes that low tidal volume ventilation can be recommended for all non-ARDS patients who require mechanical ventilation. However, some studies have drawn quite different findings(7), while the specific methods of lung protection are also inconclusive(8-11).

In particular, for patients with sepsis caused by abdominal infections, no clinical study on whether these patients should receive ventilation strategies has been reported. A retrospective analysis was conducted on data obtained from 296 patients with sepsis in the abdominal cavity. These patients had complete monitoring data and were treated under general anesthesia from May 2008 to August 2015, in order to investigate the effects of mechanical ventilation on patients with sepsis in the abdominal cavity.

Clinical Data

General information

From May 2008 to August 2015, 968 surgical patients with sepsis in the abdominal cavity were included into this study. The diagnosis of sepsis was based on the criteria established in the International Sepsis Definition Conference in 2001[12]. Based on the exclusion of patients who had severe cardiac and pulmonary diseases, patients who did not undergo general anesthesia, patients who used a large dose of cardiovascular drugs, and patients who did not have complete follow-up data, a total of 296 patients who had complete clinical data and underwent total intravenous anesthesia were included into this study.

The causes of the diseases in these patients were as follows: peptic ulcer perforation (119 patients), carcinomatous obstruction of the colon with perforation (75 patients), fecal ileus followed by perforation (44 patients), traumatic gastrointestinal perforation (11 patients), hemorrhagic necrotic enteritis (six patients), gangrenous cholecystitis (21 patients), acute obstructive suppurative cholangitis (11 patients), and pelvic abscess(9 patients).

Induction and maintenance of anesthesia:

Approximately 0.2-0.5 mg of penehyclidine hydrochloride was used to inhibit airway and gastrointestinal secretions, in order to completely remove oxygen and nitrogen. Anesthesia was induced with the intravenous injection of 0.01-0.02 mg/kg of midazolam, 1-3 µg/kg of fentanyl, 0.5-2 mg/kg of propofol or 0.2-0.3 mg/kg of etomidate, and 0.05-0.1 mg/kg of vecuronium. Then the endotracheal intubation was rapidly conducted and the Dräger Fabius Plus machine was used to control respiration. Oxygen concentration was set at 100% for all patients. Respiratory parameters are shown in the next paragraph.

During the operation, propofol at a dose of 2-5 mg/Kg/h and remifentanil at a dose of 0.2-0.5 µg/kg/min were continuously infused to maintain the adequate depth of anesthesia, and fluid was fully supplemented at a crystal/binder ratio of 2:1 to maintain circulation stability.

Grouping

The conventional mechanical ventilation group (group I): number of patients, 181; tidal volume, 8-10 ml/kg; respiration frequency (RR), 10-14 times/min; inspiratory-to-expiratory ratio (I:E), 1:2-2.5. PEEP and pulmonary rehabilitation techniques were not used. The lung protective mechanical ventilation group (group II): number of patients, 115; tidal volume, 6-8 ml/kg; RR, 12-18 times/min; I:E, 1:2-2.5. PEEP of 5-10 cmH_2O was applied, and balloon compression was intermittently applied for RM. During the operation, RR, I:E and PEEP values were adjusted at any time according to the blood gas of patients.

Evaluation indexes

Carbon dioxide partial pressure ($PaCO_2$), oxygenation index ($OI=PaO_2/FiO_2$) and airway plateau pressure (Pplat) mean values at 10, 30 and 60 minutes after mechanical ventilation in the two groups; extubation rate at two hours after the end of the operation; the incidence of atelectasis within 24 hours; and mortality rate within 28 days after operation.

1.5 Statistical methods: Data were analyzed using statistical software SPSS 10.0. Measurement data were expressed as mean ± standard deviation ($\bar{x}$± SD). Count data were compared using Chi-square test. $P<0.05$ was considered statistically significant.

Results

Basic situations

Differences in age, body mass, APACHE II score when entering the operation room, blood lactate, perioperative fluid resuscitation, and blood transfusion volume between these two groups were not statistically significant ($P>0.05$, Table 1).

Perioperative situations

At 10, 30 and 60 minutes after mechanical ventilation, and at the end of the operation, differences in arterial blood pH value, oxygenation index, extubation rate within two hours after surgery, and incidence of atelectasis within 24 after surgery between the two groups were not significantly different (P>0.05). Ventilation was obviously excessive in group I, while patients had mild CO_2 retention in group II; and the differences between these two groups were statistically significant. Pplat at each time period after ventilation was higher in group I, and the difference was statistically significant compared with group II (P<0.05). This suggests that the effect of appropriate PEEP on airway pressure may be less than that of the tidal volume (Table 2).

group	Age(year)	body mass (Kg)	perioperative fluid resuscitation and blood transfusion volume (ml)	APACHE II score when entering the operation room	blood lactate when entering the operation room (mmol/L)
I	66.62±16.22	59.03±13.96	2579.12±1151.76	11.3.5 ±5.14	4.95±3.32
II	67.18±18.58	58.12±12.55	2898.79±1625.22	12.03±5.25	6.26±3.76
P value	0.89	0.78	0.36	0.59	0.135775

Table 1: Basic situations of each group when entering the operation room.

	10 min		30 min		60 min		After surgery	
	Group I	Group II	Group I	Group II	Group I	Group II	Group I	Group II
PH value	7.32±0.13	7.24±0.14	7.28±0.13	7.27±0.12	7.32±0.08	7.29±0.09	7.33±0.08	7.30±0.09
P value	0.05		0.65		0.34		0.19	
OI value (mmHg)	283.56±71.03	266.42±75.16	281.21±68.68	270.97±60.25	308.56±61.3	302.03±63.89	302.62±55.85	281.61±78.49
P value	0.34		0.55		0.49		0.21	
$PaCO_2$ (mmHg)	29.12±4.85	36.97±6.17	29.09±4.76	35.94±5.62	30.53±4.84	35.12±5.24	31.50±4.9	34.88±4.75
P value	0		0		0		0.01	
Pplat (cmH_2O)	22.97±4.95	19.48±5.92	22.06±4.13	19.27±5.76	21.03±3.69	18.64±5.46	21.29±3.92	18.79±5.35
P value	0.01		0.03		0.04		0.03	

Table 1: Index changes at 10, 30 and 60 minutes after mechanical ventilation, and at the end of the operation.

Postoperative situations

Extubation rates within two hours after the operation between these two groups were 92.27% and 94.78%, respectively (P=0.40). The incidences of atelectasis within 24 hours between these two groups were 2.21% (four patients) and 1.74% (two patients), respectively; and the difference was not statistically significant (P=0.78). The incidences of ARDS between these two groups were 12.15% (22 patients) and 4.35% (five patients), respectively; and the difference was statistically significant (P=0.02). The 28-day mortality rates between these two groups were 8.29% (15 patients) and 2.61% (three patients), respectively, the difference was also statistically significant (P=0.04).

Discussion

Acute abdomen caused by gastrointestinal perforation can often lead to sepsis. When severe infection occurs, the incidence of acute lung injury (ALI)/ARDS can be as high as 25-50%[13,14]. ARDS is the result of multiple organ failure (MOF), and may also be the cause of MOF[15]. A number of studies have revealed that the time of ventilator therapy was the shortest and the incidence of pulmonary infection was low in patients who underwent lung protective ventilation (low tidal volume combined with PEEP and RM)[16,17]. However, determining the ventilation method to be applied on selective operation patients without lung injury remains unconclusive. It is not easy to choose an appropriate PEEP during operation, and high PEEP should also be avoided[9].

Under general anesthesia, 90% of normal selective operation patients will have atelectasis/small airway closure, decreased functional residual capacity, and increased alveolar-arterial PO_2 difference. It remains unknown whether the application of mechanical ventilation often applied on ARDS patients is beneficial.

After inappropriate mechanical ventilation, acute lung injury caused by ventilator-related factors, specifically ventilator induced lung injury (VILI), may also occur in patients without previous lung injury[18]. For surgery/ICU patients without lung injury, the application of low tidal volume ventilation can reduce the incidence of postoperative complications[17]. Through an analysis on literatures on low tidal volume ventilation, Lellouche et al.[6] believed that healthy patients undergoing routine selective operation may not benefit from ventilation with low tidal volume. However, ventilation with low tidal volume could be recommended for almost all non-ARDS patients requiring mechanical ventilation. Furthermore, very low tidal volumes can easily cause complications such as hypoventilation, alveolar collapse, increased intrapulmonary shunt and VILI.

The incidence of atelectasis after surgery was obviously decreased in patients receiving lung protective ventilation (low tidal volume) than in patients receiving traditional tidal volume ventilation. However, it does not form a convincing evidence[19,20]. At 10, 30 and 60 minutes after mechanical ventilation, and at the end of the operation, differences in arterial blood pH value and oxygenation index between the two groups were not significantly different (P>0.05). This suggests that mechanical ventilation in patients without obvious lung injury do not need a large tidal volume. In group I, patients received traditional ventilation and had obvious hyperventilation; and the Pplat was higher in each time period after ventilation. In group II, patients received lung protective ventilation with low tidal volume, had mild CO_2 retention, and Pplat was lower in each time period after ventilation.

Differences between these two groups were statistically significant (P<0.05). This suggests that the influence of an appropriate PEEP on airway pressure was smaller than an increase in tidal volume. Permissive hypercapnia ventilation can be used in critical patients and ARDS patients, which is therapeutic. In practice, $PaCO_2$ in critical patients can reach up to 100 mmHg. Therefore, a slight increase in hypercapnia compared with normal people is also acceptable. In addition, for the patients with sepsis caused by gastrointestinal perforation, high $PaCO_2$ level (but lower than 70 mmHg) not only stimulates the release of catecholamine to strengthen the heart, but also expands peripheral blood vessels and improve microcirculation; which may improve the prognosis.

A clinical control study on lung protective ventilation in elderly patients undergoing spinal surgery in the prone position revealed that lung protective ventilation could decrease inflammatory reaction in the lung and improve postoperative oxygenation. However, this did not have a serious impact on hemodynamics, and CO_2 retention was not obvious[3]. The results of this study also revealed that there was no significant difference in extubation rate within two hours after surgery between traditional ventilation and lung protective ventilation during the operation (92.27% vs. 94.78%, P=0.40), and there was no significant difference in the incidence of atelectasis within 24 hours after surgery between these two groups (2.21% vs. 1.74%, P=0.78). However, differences in the incidence of ARDS between these two groups was statistically significant (12.15% vs. 4.35%, P=0.02). In addition, the difference in mortality within 28 days after surgery between these two groups was statistically significant (8.29% vs. 2.61%, P=0.04). This suggests that different mechanical ventilations have no influence on extubation rate, and the incidence of atelectasis and the use of lung protective ventilation with low tidal volume may decrease the incidence of postoperative pulmonary complications.

PEEP can not only prevents the occurrence of atelectasis and recurrent alveolar closure during surgery, but also reduces the occurrence of pulmonary inflammatory reaction. Thus, it has a certain lung protective effect[7]. A study revealed that a high PEEP of even up to 10 cmH_2O did not increase hemodynamic impairment, and did not increase fluid requirement and perioperative bleeding volume[21].

This study also revealed that lower tidal volume and the RM method could safely and effectively reduce postoperative complications. However, a suitable PEEP is hard to obtain. This was consistent with the results of other studies[2, 22]. Finally, the specific value of PEEP was also not determined. Clinical studies have revealed that mechanical ventilation with low tidal volume and PEEP with ≥5 cmH_2O could significantly reduce the incidence of pulmonary collapse and lung injury in patients with pulmonary edema and atelectasis[8]. Furthermore, a meta-analysis revealed that this method could also improve the in-hospital survival rate of ARDS patients[10].

However, an international multi-center randomized controlled study has recently revealed that the incidences of perioperative hypotension and postoperative pulmonary complications were higher in patients who underwent abdominal surgery under high levels of PEEP (12 cmH_2O)[11].

In this study, the application of 5-10 cmH_2O of PEEP in patients was able to meet the demand of oxygenation improvement, which was different from ARDS patients who required higher PEEP.

Recently, through multivariate regression analysis, a scholar suggested that the protective ventilation for patients during the operation could reduce the risk of postoperative pulmonary complications. It was also revealed that the PEEP values required by patients with normal lung tissue were not the same with that by ARDS patients[23]. Furthermore, another researcher considered that low tidal volume combined with low PEEP may induce lung inflammatory response[24].

In mechanical ventilation, intermittent pressure, which is higher than the normal airway pressure, is given and persists for a period of time; which can recruit more collapsed alveoli and prevent secondary atelectasis cause by low tidal volume ventilation. This is an important means to ensure the effect of PEEP[25]. This RM strategy has a positive effect in promoting part of the collapsed alveoli to recover and improving ventilation/blood flow ratio and oxygenation. During the operation, the simplest and most practical RM approach is balloon extrusion, where the breathing bag is intermittently compressed to keep the airway pressure within 35-40 cmH_2O for more than 15 seconds. Other ventilation methods with progressively increased PEEP or progressively increased tidal volume need deeper anesthesia, which has a great influence on the systemic circulation system and may bring about related adverse reactions. However, it should be noted that RM is more effective in patients with low elastic resistance in the chest wall and lung, and good compliance of the respiratory system. In addition, physicians should be particularly cautious when RM is applied on patients with dysfunction of the other organs, patients with an unstable circulatory system, and patients with poor compliance of the respiratory system.

Furthermore, a study[26] revealed that postoperative pulmonary complications were related to age, preoperative low blood oxygen saturation, acute pulmonary infection and operative time of more than two hours. It is inevitable that this study has a certain bias, since this study is retrospective in nature. Lung protective ventilation, which is presently widely recommended, has a good effect on sepsis caused by gastrointestinal perforation. However, further observation is required to determine whether lung protective ventilation would be suitable for all patients with relatively normal lungs.

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