Preoxygenation using invasive ventilator in volume control mode in patients with emergency intubation can shorten the time of preoxygenation and improve the quality of preoxygenation

A retrospective study

Hai Wang, MD, Jiang-Li Sun, MD, Zheng-Hai Bai, MD, Xiao-Bo Wang, MD, Zheng-Liang Zhang, PhD, Hong-Hong Pei, PhD

Abstract
Preoxygenation can rapidly improve oxygenation and enhance the security of endotracheal intubation, so it is very essential before endotracheal intubation. The conventional preoxygenation method self-inflating bag (SIB) is not very effective in case of emergency. So our study aims to find a more effective method of preoxygenation in a critical situation.

We retrospectively analyzed data of 105 patients in this study. A total of 49 patients with preoxygenation with invasive ventilator in volume control mode (VCM) and 56 patients with preoxygenation with SIB were included. No significant differences were detected in the baseline data of the 2 groups (P > 0.05). Time of preoxygenation (95%) was 174 (168–180) seconds in group VCM and 205 (199–212) seconds in group SIB (P < 0.05), and multifactor linear regression showed that its main risk factors were the methods of preoxygenation and PO2 before preoxygenation (P < 0.05). Immediate SPO2 after preoxygenation was 91 (89–92)% in group VCM and 85 (83–86)% in group SIB (P < 0.05). Total time of preoxygenation and intubation was 266 (252–280) seconds in group VCM and 318 (298–338) seconds in group SIB (P < 0.05). The 24-hour and overall survival rate in group SIB were lower than in group VCM (P > 0.05). Cox regression showed that SaO2 at 5 minutes after intubation was the major risk factor for the survival rate.

Invasive ventilator with volume control mode in patients with emergency control mode can shorten the time of preoxygenation and improve the quality of preoxygenation in patients with emergency intubation and may be a better method of preoxygenation in a critical situation.

Abbreviations: SIB = self-inflating bag, VCM = invasive ventilator in volume control mode.

Keywords: endotracheal intubation, invasive ventilator, preoxygenation, self-inflating bag, volume control mode

1. Introduction
Patients who need emergency rescues are often associated with hypoxemia; so it is quite essential to rapidly improve oxygenation and stabilize basic vital signs before endotracheal intuba-
I invasive ventilator is an indispensable equipment in the emergency department and ventilation equipment after endotracheal intubation. Almost all doctors and nurses in the emergency department are skilled in operating invasive ventilator. Consequently, there are related equipment and personnel in the emergency department. However, few relevant studies on the application of invasive ventilator for preoxygenation in emergency department have been reported yet. Therefore, we hypothesized that invasive ventilator in volume control mode (VCM) may be a better equipment of preoxygenation than SIB.

2. Materials and methods

2.1. Inclusion criteria

Patients met the diagnostic criteria of respiratory failure and patients with endotracheal intubation, adopting invasive ventilator, or SIB for preoxygenation.

2.2. Exclusion criteria

Pregnant women and patients aged less than 18 years, patients with oral and maxillofacial trauma or deformity, patients without effective preoxygenation (when performing tracheal intubation, the patients' SPO2 did not reach $95\%$)—there were 2 main reasons for this situation: 1 reason was that immediately endotracheal intubation must be given in the situation of mask ventilate failure or massive hemoptysis and another reason was that the patients’ SPO2 could not be up to $95\%$ because of the severe decline of lung function), and patients with key data missing in medical records.

2.3. Study population

Patients with respiratory failure and endotracheal intubation were retrospectively collected from the Emergency Department & Emergency Intensive Care Unit of our hospital from October 2013 to April 2016. Among 141 patients, 36 patients were excluded—3 cases of pregnant women, 7 cases with age <18 years, 11 cases with oral and facial trauma or deformity, 13 cases without effective preoxygenation, and 2 cases with incomplete medical records or record errors.

2.4. Grouping criterion

The 105 patients were divided into VCM (n=49) group and simple respirator group (SIB, n=56) according to the different methods of preoxygenation.

2.5. Preoxygenation and intubation approaches

Preparations: the ventilator and SIB were rightly connected and then tested; parameters adjusted: in group VCM, volume control mode, tidal volume = 8-10 ml/kg, respiratory frequency = 14 times/min, with oxygen concentration adjusted to 100%; in group SIB, oxygen source was connected through the oxygen catheter with oxygen flow of 10 L/min; and visual laryngoscope, lidocaine, and endotracheal catheter (according to gender, age, and height) were prepared for the patients. Preoxygenation and intubation: routine electrocardiograph and SPO2 monitoring were given to the patients, jaws of the patients were held by the intubation surgeon to tightly close the mask, and ventilator in group VCM was initiated for preoxygenation according to the adjusted parameters, in group SIB it was given by manual control of an assistant (respiratory frequency, 12/min; tidal volume, with thoracic fluctuation as standard) while preoxygenation. Endotracheal intubation was granted after preoxygenation for at least 3 minutes and SPO2 more than $95\%$.[12] Moderate sedation was given to the patients with fidget and inability to cooperate before and during intubation; preoxygenation with tightly holding the mask was continued in the patients with SPO2 less than $85\%$ during intubation, and endotracheal intubation was conducted after the SPO2 more than $95\%$; intubation was performed by another senior physician in the patients with intubation more than 3 times. Tracheotomy was conducted if the senior doctor also failed in intubation. After successful intubation, a ventilator was pursued with oxygen concentration of 100%, and ventilator parameters and inspiratory oxygen concentration were readjusted according to arterial blood gas in 5 minutes after intubation. In the process of preoxygenation and endotracheal intubation, we would use proper sedative drugs such as propofol, etomidate, or midazolam according to the condition of patients to reduce respiratory resistance and enhance compliance for the agitated.

2.6. Relevant outcome measures

Main outcome measures: time of preoxygenation (95%); secondary outcome measures: immediate SPO2 after intubation, interruption times of endotracheal intubation, total time of preoxygenation and endotracheal intubation, 24-hour survival and overall survival during hospitalization; and collection of relative adverse events.

2.7. Data source and measurement

All the data were retrospectively collected from the detailed and authentic records in our emergency department. Time of preoxygenation (95%) was defined as the time from the beginning of preoxygenation to patients' SPO2 up to 95%; total time of preoxygenation and endotracheal intubation was calculated from the beginning of preoxygenation to endotracheal intubation and to the end of intubation; baseline demographic data, arterial blood gas results, interruption times of endotracheal intubation, time of endotracheal intubation, 24-hour survival, survivals during hospitalization, and occurrence of adverse events were acquired according to the nursing or medical records.

2.8. Statistical analysis

Statistical analysis: a total of 105 cases of this study were included for statistical analysis. Mean ± standard deviation ($\mu$ ± $\sigma$) was used for continuous variables of baseline data in the 2 groups, and count data were shown by numerical values and percentages. Duration of preoxygenation and secondary indices including pulse oxygen saturation after intubation, total duration of endotracheal intubation, blood gas results at 5 minutes after intubation, interruption frequency of endotracheal intubation, and 24-hour survival were represented as mean and 95% confidence interval; the rest of the indices and adverse events were represented in numerical values and percentages. Continuous data meeting normal distribution and homogeneity of variance were subject to an independent sample t test, and the data that did not meet normal distribution or homogeneity of variance were subject to independent sample Wilcoxon rank sum test. Binary classification count was performed by using 4-fold table $\chi^2$ test or Fisher exact probability method; ranked data were tested by the
x² test of line x of list data or rank sum test. Comparison between groups was performed when \( P > 0.05 \) in the \( x² \) test of line x list data or rank sum test. In order to control the related confounding factors affecting the duration of preoxygenation, multifactor linear regression was applied to further analyze the influencing factors of duration of preoxygenation, and methods were as follows: whether data conformed to the suitable conditions of linear regression was tested by drawing a scatter plot, histogram of normalized residuals, and normal probability plot gradually. Survival during hospitalization was investigated by using Kaplan–Meier survival curve; due to relatively short follow-up time and a relatively large number of censored data, Cox regression was applied as follows: survival analysis test was conducted under method: LR, and relative risk (RR) value and 95% confidence interval were calculated. All statistical analyses were performed using SPSS software (version 22.0, International Business Machines [IBM] Corp, Armonk, New York, USA), and \( P < 0.05 \) was considered as a statistical difference. As for missing values, all missing records were compared and included to analyze and exclude whether analysis results of all missing records were consistent; consistency suggested reliable statistical conclusion, while inconsistency implicated unreliable statistical conclusion, with further analysis needed through stratified analysis or filling missing values.

2.9. Ethical approval
The data of statistical analysis in this study were all adopted by anonymous analytics, and the related data were strictly confidential and only used for academic research, with the approval of ethical review obtained (ethical approval number: LLGZB-FS-003-01).

3. Results
A total of 105 patients were involved in statistical analysis, and no significant differences were found in the baseline data (Table 1). Time of preoxygenation (95%) was 174 (168–180) seconds in group VCM and 205 (199–212) seconds in group SIB (\( P < 0.05 \)) (Table 2). Multifactor linear regression equation: \( \text{y} = 241.37 + 33.45 \times x_1 - 2.04 \times x_2 \), \( x_1 = \text{time of preoxygenation, } x_2 = \text{preoxygenation method (group VCM, 1; group SIB, 2)} \), before preoxygenation \( (P < 0.05) \) (Table 3). Immediate SPO2 after endotracheal intubation was 91 (89–92)% in group VCM and 85 (83–86)% in group SIB \( (P < 0.05) \) (Table 2). Total time of preoxygenation and intubation was 266 (252–280) seconds in group VCM and 318 (298–338) seconds in group SIB \( (P < 0.05) \) (Table 2). Group VCM had fewer interruption times of intubation than group SIB \( (P < 0.05) \) (Table 5). Arterial blood gas at 5 minutes after intubation revealed that power of hydrogen (PH) value was 7.33 (7.31–7.35) and 7.29 (7.27–7.31), respectively, in group VCM and group SIB \( (P < 0.05) \); PO\(_2\) was 144 (128–162) and 98 (87–110) mm Hg, respectively, in group VCM and group SIB \( (P < 0.05) \) (Table 2). Survival analysis during hospitalization: Kaplan–Meier survival analysis revealed that 24-hour survival rate and total survival rate in group SIB were lower than those in group VCM \( (P > 0.05) \) (Fig. 1); Cox regression showed that the regression coefficient of SaO2 at 5 minutes after intubation was \(-0.14 \) (RR = 0.87 [0.78, 0.95]) \( (P < 0.05) \) (Table 4). Sensitivity analysis for the data containing missing values and outlier revealed that the former and latter statistical results of the included and excluded missing values were in accordance, suggesting a reliability. Adverse events: as for hypoxemia, there were 3 cases (6%) in group VCM and 12 cases (21%) in group SIB \( (P < 0.05) \) (Table 5); no statistically significant differences were detected in aspiration pneumonia, hypotension, hypertension, arrhythmia, laryngospasm or bronchospasm, endotracheal catheter into the esophagus, vomit or aspiration pneumonia.

### Table 1
Baseline data of studied cases.

|                     | VCM group (n = 49) | SIB group (n = 56) | P   |
|---------------------|-------------------|-------------------|-----|
| Age, y              | 63.61 ± 18.33     | 67.89 ± 16.42     | 0.21|
| Sex, F/M            | 29/20             | 35/21             | 0.73|
| Height, cm          | 166.18 ± 7.54     | 167.89 ± 6.63     | 0.86|
| Weight, kg          | 88.44 ± 10.77     | 68.66 ± 9.94      | 0.91|
| BMI, kg/m²          | 24.33 ± 3.30      | 24.40 ± 3.54      | 0.92|
| Diagnosis           |                   |                   | 0.39|
| ICH, n (%)          | 17 (35)           | 11 (21)           |     |
| Cerebral infarction, n (%) | 5 (10)  | 11 (20)          |     |
| Cardiac insufficiency, n (%) | 3 (6)  | 6 (11)           |     |
| COPD, n (%)         | 4 (8)             | 8 (14)            |     |
| Pneumonia, n (%)    | 8 (16)            | 4 (7)             |     |
| Shock, n (%)        | 3 (6)             | 7 (13)            |     |
| Drug poisoning, n (%) | 4 (8)      | 6 (11)           |     |
| Others, n (%)       | 5 (10)            | 3 (6)             |     |
| Cormack–Lehane classification* | 0.84  |                   |     |
| Grade I, n (%)      | 19 (39)           | 24 (43)           |     |
| Grade II, n (%)     | 15 (31)           | 16 (29)           |     |
| Grade III, n (%)    | 11 (22)           | 11 (20)           |     |
| Grade IV, n (%)     | 3 (6)             | 5 (9)             |     |
| Blood gases         |                   |                   | 0.24|
| PH                  | 7.26 (7.24–7.28)  | 7.27 (7.26–7.29)  |     |
| PO\(_2\), mm Hg     | 49 (47–51)        | 50 (48–52)        | 0.46|
| PCO\(_2\), mm Hg    | 61 (58–64)        | 64 (61–67)        | 0.19|
| SaO\(_2\), %        | 83 (77–83)        | 81 (80–83)        | 0.47|

**Table 2**
Main outcome measures, secondary outcome measures, and relevant outcome measures.

|                     | VCM group (n = 49) | SIB group (n = 56) | P   |
|---------------------|-------------------|-------------------|-----|
| Time of preoxygenation (95%), s | 174 (168–180) | 205 (199–212) | <0.05|
| Immediate SPO\(_2\) after ETI, % | 91 (89–92)   | 85 (83–86)      | <0.05|
| Total time of preoxygenation and ETI, s | 266 (252–280) | 318 (296–338) | <0.05|
| Intubation interruption* |                   |                   | <0.05|
| Zero time, n (%)    | 37 (76)           | 30 (54)           | <0.05|
| 1 time, n (%)       | 7 (20)            | 13 (25)           | >0.05|
| 2 times, n (%)      | 3 (6)             | 4 (13)            | >0.05|
| 3 times or more, n (%) | 2 (4)     | 9 (9)            | <0.05|
| Death case in 24 h  | 5 (10)            | 13 (22)           | >0.05|
| 5 min blood gases after ETI |                   |                   |     |
| PH                  | 7.30 (7.27–7.32)  | 7.28 (7.27–7.30)  | >0.05|
| PO\(_2\), mm Hg     | 144 (128–162)     | 98 (87–110)       | <0.05|
| PCO\(_2\), mm Hg    | 56 (54–59)        | 62 (59–65)        | <0.05|
| SaO\(_2\), %        | 94 (93–95)        | 92 (91–93)        | <0.05|

**Table 2**

* Cormack–Lehane classification: according to the results of the throat exposed under laryngoscope: grade I, the glottis was exposed fully; grade II, the arytenoid cartilage and the latter part of the glottis were detected; grade III, only the epiglottis was observed; grade IV, the epiglottis was undetectable.

ETI = endotracheal intubation, SPO\(_2\) after ETI = immediate pulse oxygen saturation after endotracheal intubation, VCM = inverse ventilator in volume control mode.
oropharyngeal mucosa, and teeth injury between the 2 groups ($P>0.05$) (Table 5).

4. Discussion

Through this retrospective study, we found that application of invasive ventilator for preoxygenation could shorten the time of preoxygenation (95%), increase immediate SPO2 after intubation, and shorten total time of preoxygenation and endotracheal intubation, compared with SIB. The linear regression equation revealed that the influencing factors of the time of preoxygenation included preoxygenation method and PO2 before preoxygenation, and the former had a greater effect than the latter on the time of preoxygenation, suggesting that application of invasive ventilator for preoxygenation had higher efficacy than SIB. In addition, in contrast with using SIB for preoxygenation, using invasive ventilator had fewer intubation interruptions and higher quality of preoxygenation, as well as could increase alveolar oxygen concentration during the same period of time, prolong tolerant ventilation time, and reduce the incidence of hypoxemia. Furthermore, Kaplan–Meier survival analysis revealed that 24-hour survival rate and total survival rate of SIB group were lower than those in VCM group ($P>0.05$), and Cox regression showed that SaO2 at 5 minutes after intubation was the main risk factor for the survival rate ($P<0.05$). Kaplan–Meier curve implied a higher 24-hour survival rate in VCM group than in SIB group, which may be associated with the urgency and rapid development of acute critical illness[13] and may also be related to that invasive ventilator for preoxygenation, is able to improve hypoxemia in a relatively short period of time and reduce the time of endotracheal intubation and the incidence of severe hypoxemia during intubation[14]. Multifactor Cox analysis for total survival during hospitalization revealed that PO2 at 5 minutes after intubation was related to survival during hospitalization; different preoxygenation methods had no influences on patients’ prognosis; meanwhile, the effects of age and causes of disease on the prognosis had no statistical significance. Generally speaking, more severe condition is positively associated with more severe hypoxia and harder correction of anaerobic condition,[15] and PO2 can indirectly reflect oxygenation in vivo[16]; therefore, PO2 at 5 minutes after intubation could be used to predict patients’ prognosis. In addition, Cox analysis showed that preoxygenation method, age, and pathogeny were not related to patients’ prognosis, which may be caused by relatively small sample size, relatively short follow-up time, and a relatively large number of missing values.[17]

Preoxygenation can increase oxygen/nitrogen ratio of pulmonary functional residual capacity, enhance functional residual capacity, and facilitate the rapid improvement on oxygenation[18] and stabilization of basic vital signs, thereby providing precious time for clinicians to establish airway or recover effective ventilation during apnea[19]. Moreover, the key factors affecting preoxygenation efficacy are inspiratory oxygen concentration and ventilator capacity per unit time.[20] Enhancing inspiratory oxygen concentration can rapidly increase oxygen concentration of lung functional residual capacity[21]; meanwhile, only more effective ventilation during a relatively short period of time can result in more nitrogen replaced from the alveolus.[22] Furthermore, rapid enhancement of oxygen/nitrogen ratio of pulmonary functional residual capacity can further increase oxygen concentration in lung functional residual capacity, increase oxygen reserves[23] and provide additional time for subsequent life support.

SIB connects with oxygen source through the catheter and provides breath support by manually squeezing a respirator, and excess oxygen can be stored in a gas storage bag.[24] Due to its own structure problem, it cannot reach the oxygen concentration of 100%[25]; in addition, its ventilatory capacity and ventilation frequency are completely dependent on operator’s manual control,[26] so it is easily affected by the operator and resulting

### Table 3

| Predictor variable          | Coefficient | Standard error | t value | P     |
|-----------------------------|-------------|----------------|---------|-------|
| Methods of preoxygenation    | 241.37      | 33.45          | 7.25    | <0.05 |
| PO2 before preoxygenation    | 241.37      | 33.45          | 7.25    | <0.05 |

### Table 4

| Predictor variable          | Coefficient | Standard error | RR (95% CI) | P     |
|-----------------------------|-------------|----------------|-------------|-------|
| Age                         | 0.04        | 0.01           | 1.00 (0.97, 1.04) | >0.05 |
| Methods of preoxygenation    | 0.06        | 0.02           | 0.94 (0.34, 2.63) | >0.05 |
| Diagnosis                   |             |                |             | >0.05 |
| PO2 before preoxygenation    | 0.08        | 0.07           | 1.08 (1.04, 1.26) | >0.05 |
| SaO2 before preoxygenation   | –0.11       | 0.07           | 0.90 (0.79, 1.03) | >0.05 |
| Cormach–Lehane classification| –           |                |             | >0.05 |
| Time of preoxygenation       | –           |                | 1.00 (0.97, 1.03) | >0.05 |
| Intubation interruption      | –           |                |             | >0.05 |
| 5 min SaO2 after ETI         | –0.14       | 0.05           | 0.87 (0.78, 0.95) | <0.05 |
| Total time of preoxygenation and ETI | 0.002      | 0.005          | 1.00 (0.99,1.01) | >0.05 |

ETI=endotracheal intubation.

* Cormach–Lehane classification: according to the results of the throat exposed under laryngoscope: grade I, the glottis was exposed fully; grade II, the arytenoid cartilage and the latter part of the glottis were detected; grade III, only the epiglottis was observed; grade IV, the epiglottis was undetectable.
in inadequate or excessive ventilator capacity, too fast respiratory rate, too high airway pressure, leakage, and others. Among the patients with acute critical illness always accompanied with hypoxemia and hypokniaemia, inadequate ventilator capacity during preoxygenation may further aggravate hypoxemia, leading to the deterioration of the condition; while excessive ventilator capacity during preoxygenation may cause hypocapnia, leading to cerebral vasocostriction, and further aggravating cerebral ischemia and hypoxia under hypokniaemia. Because of lack of effective monitoring means for respiratory parameters and great effect from operator in SIB for respiratory support, the rescue for patients with acute critical illness is greatly affected.

As compared with SIB, the oxygen concentration of invasive ventilator can reach 100%; meanwhile, reasonable respiratory parameters can be set via breathing machine, and related respiratory parameters can be monitored dynamically, contributing to timely detection of inadequate ventilator capacity, excessive ventilator capacity, and too high airway pressure. Invasive ventilator is useful to adjust the ventilation strategy in time and avoid the respiratory support completely dependent on the operator. Therefore, compared with SIB, invasive ventilator can provide respiratory support more effectively, reduce insufficient ventilation, excessive ventilation and air pressure injury, increase oxygen concentration in lung functional residual capacity and alveolar oxygen/nitrogen ratio in a relatively short period of time, reduce the time of preoxygenation and improve preoxygenation efficacy, reduce the incidence of hypoxemia during intubation, and further reduce the interruption rate of endotracheal intubation, improving the safety of intubation in the patients with acute critical illness.

Comparison of pressure-control mode and pressure-control mode for preoxygenation shows that pressure-control mode is able to ensure ventilator capacity and also can facilitate earlier related interventions to airway obstruction or leakage in breathing loop, which may affect ventilation; while the ventilator capacity of pressure control mode is affected by many factors, such as airway condition, thorax and lung compliance, and others, pressure-control mode has a relatively low sensitiveness to airway obstruction or leakage in breathing loop. Therefore, application of invasive ventilator for preoxygenation can more effectively ensure ventilator capacity and increase oxygen/nitrogen ratio in pulmonary functional residual capacity and can rapidly improve oxygenation in patients with acute critical illness, thereby providing more time for further life support.

4.1. Limitations of this study

A relative short follow-up resulted in no statistical significance in some important prognostic factors; due to greater potential short-term effect of preoxygenation on patients, the feasibility of follow-up, and economic consideration, long-time follow-up was not conducted. This study is a retrospective observational study, intensity of evidence of which is weaker than RCT test, so it is necessary to carry out further studies on preoxygenation methods for acute critical illness to obtain better preoxygenation methods.

5. Conclusion

Invasive ventilator with volume control mode can shorten the time of preoxygenation and improve the quality of preoxygenation in patients with emergency intubation and may be a better method of preoxygenation in a critical situation.

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