Prone Position Impairs Oxygen Supply-Demand Balance During Systemic Hypoxia in Rabbits

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ABSTRACT
Ventilation in the prone position improves the prognosis of patients with severe acute respiratory distress syndrome (ARDS). Contraindications to ventilation in this position include unstable systemic circulation. Only a few reports exist on the effects of prone ventilation in respiratory failure on systemic circulation. This animal study compared systemic hemodynamic changes between supine and prone positions in anesthetized rabbits under acute systemic hypoxia (breathing 15% O2). Cardiac output and the systemic O2 extraction ratio increased under the hypoxia, but only in the supine group. Besides, the rate pressure product was higher in the prone group than in the supine group. This study showed that prone ventilation increases myocardial O2 consumption and suppresses compensatory mechanisms to maintain aerobic metabolism during systemic hypoxia. First of all, it will be necessary to examine the effect of prone ventilation on the O2 supply-demand balance in the ARDS model.

Key words hypoxia; oxygen consumption; prone position; respiratory distress syndrome

In 1974, Bryan first proposed that the prone position effectively improves oxygenation in acute respiratory failure because it improves regional ventilation in the dorsal lung and reduces atelectasis.1 A multicenter study in France showed that starting ventilation in the prone position early in the course of severe acute respiratory distress syndrome (ARDS) and continuing for 16 hours in combination with low tidal volume ventilation and the use of muscle relaxants markedly improved the prognosis of these patients.2 Contraindications to prone ventilation include cases with an unstable systemic circulation.2 In severe ARDS, systemic circulation is rather unstable.3 Only a few studies have examined the effect of ventilation in the prone position for ARDS on systemic circulation.4 In ARDS patients with preload reserve, the prone position reduces right ventricular afterload by improving oxygenation and increasing cardiac output (CO).4 To further improve the prognosis of severe ARDS, it is essential to investigate the effect of prone ventilation on systemic circulation. In an experiment with healthy adult volunteers under conscious and spontaneous breathing, the lateral position decreased myocardial O2 consumption by reducing gravitational stress, resulting in a decrease in the O2 consumption of the body as a whole.5 Prone ventilation may also alter the O2 supply-demand balance.

Severe ARDS is caused by a variety of factors and has a complex pathogenesis that can lead to systemic hypoxemia if not properly managed.3 In this short communication, as a preliminary study, we examined the effect of prone position on the systemic circulation in a simple experimental model in which systemic hypoxemia was induced by inhalation of a low concentration of O2. We presented the O2 supply-demand balance in the prone position in anesthetized rabbits under acute systemic hypoxia (breathing 15% O2).

MATERIALS AND METHODS
This protocol was approved by the Laboratory Animal Care Committee of the Faculty of Medicine at Tottori University (approval number 08-Y-59).

Experimental setting
Adult male Japanese white rabbits were anesthetized with 30 mg/kg pentobarbital administered via the ear vein and placed in the supine position. After local anesthesia of the anterior neck region with 1% lidocaine, the rabbits were tracheotomized and ventilated with...
Experimental protocol

We studied 18 rabbits (body weight, 2.2–2.7 kg) equally randomized to the prone (9) and supine (9) positions, respectively. Thirty minutes after the end of the surgical procedures, animals in the prone group were changed from the supine to the prone position. The position of the supine group was not changed from the onset of the surgical procedure. The inhaled gas was then switched to 15% O₂ in balance N₂ in both groups, and systemic hemodynamic changes were measured for 6 hours. In the prone position, rabbits were placed on a handmade styrofoam table that was hollowed out where the anterior chest and abdomen rested. In both groups, a small-animal warmer/thermometer system (BWT-100, Bio Research Center, Nagoya, Japan) was placed under the rabbit’s trunk to control the blood temperature at the base of the aorta to 38–39 °C. In both groups, CO measurements were made while breathing room air (baseline) and after 1.5, 3.0, 4.5, and 6.0 hours of hypoxia. Blood gas analysis was also performed at each interval, except for the 4.5-hour measurement.

Statistical analysis

All data are expressed as the mean ± SE. GraphPad Prism ver. 4 software (GraphPad Software, San Diego, CA) was used for statistical analysis. Two-way ANOVA was used for between-group comparisons and one-way ANOVA for within-group comparisons. Bonferroni’s test was used for both post hoc tests. Statistical significance was accepted at P < 0.05.

RESULTS

In both groups, the PaO₂ at 1.5, 3.0, and 6.0 hours of hypoxia was significantly lower than the baseline value (Fig. 1A). In both groups, the mean arterial pressure at 6.0 hours of hypoxia was significantly lower than the baseline value (Fig. 1B). The heart rates (HR) at 1.5, 3.0, and 4.5 hours of hypoxia were 262.8 ± 10.4, 264.5 ± 10.4, and 265.8 ± 11.4 (beats/min) in the prone group, and 240.6 ± 7.3, 238.5 ± 8.9, and 241.1 ± 9.9 (beats/min) in the supine group, respectively. The HR at 1.5, 3.0, and 4.5 hours of hypoxia was significantly higher in the prone group than in the supine group. The rate pressure product (RPP) at 1.5, 3.0, and 4.5 hours of hypoxia was significantly higher in the prone group than in the supine group (Fig. 1C). At all measurement times, the mean pulmonary arterial pressure was not significantly different between the two groups (Fig. 1D). In the supine group, the CO at 4.5 and 6.0 hours of hypoxia was significantly higher than the baseline value (Fig. 1E). In both groups, the O₂ delivery at 1.5, 3.0, and 6.0 hours of hypoxia was significantly lower than the baseline value (Fig. 1F). In the supine group, the systemic O₂ extraction ratio (O₂ER) at 1.5, 3.0, and 6.0 hours of hypoxia was significantly higher than the baseline value (Fig. 1G).

DISCUSSION

This study compared changes in the systemic circulation between supine and prone positions in anesthetized rabbits under systemic hypoxia. Notable differences were that CO and the systemic O₂ER increased during the hypoxia in the supine group but not in the prone group. Besides, RPP was higher in the prone group than in the supine group.

During systemic hypoxia, several compensatory mechanisms maintain aerobic metabolism. These include an increase in HR and CO via medullary and peripheral chemoreceptors, redistributions of blood flow to vital organs, and an increase in O₂ extraction ability. Because the prone position decreases venous return due to compression of the inferior vena cava, air using a Harvard Rodent Ventilator 683 (Harvard Apparatus, Holliston, MA). The positive end-expiratory pressure (PEEP) was set to 3 cmH₂O and the tidal volume to 6 ml/kg. The respiratory rate was adjusted so that the PaCO₂ value was in the normal range. Pentobarbital (10 mg/kg/h), pancuronium bromide (3 mg/kg/h), and lactated Ringer’s solution (10 ml/kg/h) were administered continuously via the ear vein. A preliminary experiment investigated the level of inhaled O₂ required to induce acute systemic hypoxia. Rabbit survival was examined while low concentrations of O₂ were administered. At 10% O₂, four animals died consecutively within 6 hours; at 15% O₂, no animals died within 6 hours, but some animals died after 9 hours. In this study, 15% O₂ was thus administered, and the animals were monitored for 6 hours.
Prone ventilation affects RPP and $O_2$ER

Fig. 1. Comparison of hemodynamics between the supine (●) and prone (□) groups under acute systemic hypoxia. (A) PaO$_2$. (B) mAP. (C) RPP. (D) mPAP. (E) CO. (F) DO$_2$. (G) O$_2$ER.

Data are mean ± SE ($n = 9$ per group). *$P < 0.05$ versus baseline value. †$P < 0.05$ versus prone group. RPP was calculated as heart rate × systolic arterial pressure. DO$_2$ was calculated as CaO$_2$ × CO. $O_2$ER was calculated as (CaO$_2$ – CvO$_2$) ÷ CaO$_2$. CO and DO$_2$ were normalized by body weight. CO, cardiac output; DO$_2$, O$_2$ delivery; mAP, mean arterial pressure; mPAP, mean pulmonary arterial pressure; $O_2$ER, O$_2$ extraction ratio; PaO$_2$, arterial oxygen tension; RPP, rate pressure product.
the CO may not have increased even with systemic hypoxia in the prone group in this study. The redistribution of blood flow from the abdominal organs to the heart and brain results in the transfer of blood flow from organs with a low O2 extraction ability to organs with a high O2 extraction ability, thus increasing the O2 extraction ability of the body as a whole.15, 16 Systemic O2ER is the sum of the O2ER of all tissues, and the ratio at rest is 0.25–0.35.17 In anesthetized dogs with acute systemic hypoxia, phenoxybenzamine, an alpha-adrenergic blocker, reduced systemic O2ER from 0.87 to 0.46 by inhibiting redistribution of blood flow, and consequently impaired aerobic metabolism.18 In this study, the fact that systemic O2ER in the prone position did not increase under systemic hypoxia may suggest an impaired redistribution of blood flow to vital organs. However, further studies are required to confirm this mechanism.

RPP correlates with myocardial O2 consumption.19, 20 Under spontaneous breathing in healthy human adults, the lateral position decreased myocardial O2 consumption via reduction of gravitational stress.5 In this study, the RPP was greater in the prone position because the HR, not the arterial pressure, was greater in the prone position. Compared to the supine position, the prone position was more deleterious in the balance of myocardial O2 supply and demand. In patients under general anesthesia, the prone position itself has been reported to slightly increase HR compared to the supine position.14

This study showed that prone ventilation increases myocardial O2 consumption and suppresses compensatory mechanisms to maintain aerobic metabolism during systemic hypoxia. In ARDS, systemic hypoxia as in this study can be avoided by increasing the inspired O2 concentration or applying PEEP. Therefore, there are difficulties in applying the results of this study to ARDS. However, in endotoxemia, even if the O2 supply is maintained at a high level, the prognosis is not improved because the ability of O2 uptake at the organ or cellular level is impaired.21 First of all, it will be necessary to examine the effect of prone ventilation on the O2 supply-demand balance in the ARDS model.

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The authors declare no conflict of interest.

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