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นิพนธ์ต้นฉบับ **Original Article**

Comparison of Different Rates of Artificial Ventilation for Preterm Neonates with Respiratory Distress Syndrome

เปรียบเทียบผลของการตั้งอัตราการช่วยหายใจที่ต่างกันในทารกคลอดก่อนกำหนดที่ป่วยด้วยโรค Respiratory Distress Syndrome

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ABSTRACT

The effectiveness of two different rates of artificial ventilation, 40 breaths per minute (bpm) and 70 bpm, were studied in twenty preterm infants weight from 740 to 1,620 grams. All of them suffered from respiratory distress syndrome (RDS) and needed mechanical ventilation shortly after birth. They were randomized into two groups, 10 patients in group A and 10 patients in group B and were ventilated at rate of 40 and 70 bpm respectively. The outcome was patients' respiratory pattern which was evaluated at 30 min, 8 hours, 16 hours and 24 hours after the intermittent mandatory ventilator (IMV) performing. The results showed that 5, 7, 9 and 10 patients in group A and 8, 9, 10 and 10 patients in group B breathed synchronously with ventilator at 30 min, 8 hours, 16 hours and 24 hours respectively. Patients in group B took less time than group A to synchronize but it was not significantly different ($p > 0.05$). In addition duration of intubation in group A (mean 7.71 ± 4.38 days) was longer than that in group B (mean 5.69 ± 1.86 days) but it was not statistically significant ($p = 0.27$). These results might suggest that in acute phase of RDS fast ventilator rate could minimize discomfort to the patients but both treatments were comparably effective to ventilate infants with RDS.

Keywords : preterm, respiratory distress syndrome, fast ventilator rate, conventional ventilator rate

บทคัดย่อ

ได้ทำการศึกษาเปรียบเทียบการใช้เครื่องช่วยหายใจที่อัตรา 40 และ 70 ครั้งต่อนาทีในเด็กทารกคลอดก่อนกำหนดที่มีน้ำหนักตัวตั้งแต่ 740 กรัมจนถึง 1,620 กรัมซึ่งป่วยด้วยโรค Respiratory distress syndrome (RDS) และมีความจำเป็นต้องใช้เครื่องช่วยหายใจเพื่อการรักษา ได้แบ่งผู้ป่วยออกเป็น 2 กลุ่ม กลุ่มละ 10 คนกลุ่ม A ตั้งเครื่องช่วยหายใจที่อัตรา 40 ครั้งต่อนาทีและกลุ่ม B ที่อัตรา 70 ครั้งต่อนาทีตามลำดับ ประเมินผลการหายใจเมื่อเวลา 30 นาที 8 ชั่วโมง 16 ชั่วโมง และ 24 ชั่วโมงภายหลังการใส่เครื่องช่วยหายใจ พบว่าผู้ป่วย 5 ราย 7 ราย 9 ราย และ 10 รายในกลุ่ม A และผู้ป่วย 8 ราย 9 ราย 10 ราย และ 10 รายในกลุ่ม B หายใจสัมพันธ์กับเครื่องช่วยหายใจได้ดีภายหลังการใส่เครื่องช่วยหายใจเมื่อเวลา 30 นาที 8 ชั่วโมง 16 ชั่วโมงและ 24 ชั่วโมงตามลำดับ แต่ไม่มีนัยสำคัญทางสถิติ ($p > 0.05$) ระยะเวลาเฉลี่ยของการใส่ท่อช่วยหายใจในกลุ่ม A เท่ากับ 7.71 ± 4.38 วัน ซึ่งยาวกว่าในกลุ่ม B ที่มีระยะเวลาเฉลี่ย 5.69 ± 1.86 วันแต่ไม่มีนัยสำคัญทางสถิติ ($p = 0.27$) ผลการศึกษาพบว่าในระยะแรกของ RDS การตั้งเครื่องช่วยหายใจในอัตราที่เร็วช่วยลดความทุกข์ทรมานต่อผู้ป่วย แต่ประสิทธิภาพการใช้เครื่องช่วยหายใจในผู้ป่วยทั้งสองกลุ่มได้ผลเท่าเทียมกัน

Introduction

Mechanical ventilation is an invasive life support method in critical illness and preterm infant. Recent advances of technology have brought in new modes of mechanical ventilation.[1] Synchronous intermittent mandatory ventilation (SIMV) is useful for solving fighting the ventilator or asynchrony resulting from out of phase breathing with the ventilator inflation. This condition causes ineffective gas exchange and is a risk factor for pneumothorax and intraventricular hemorrhage. However when trigger sensitivity is set too low, the ventilator may frequently alarm. If trigger sensitivity is set too high, patients may not sense the ventilator (trigger asynchrony) and SIMV functions like conventional ventilation or intermittent mandatory ventilation (IMV). Sometimes auto trigger comes about causing desaturation or death to patients. Due to these disadvantages of SIMV, IMV which was first described in 1955 is still used by most pediatricians in many provincial hospitals in Thailand. For conventional setting, mechanical ventilator rate may start at 20-40 breaths per minute (bpm). Ventilation at rates greater than 60 bpm in spontaneously breathing infants with respiratory distress syndrome (RDS) may be advantageous since it could lower pneumothorax rate.[2-4] In addition, fast rate is most efficacious for preterm neonates and rarely associated with apnea.[2,5,6] In contrast, it was reported that ventilator rate at 30-40 bpm caused fewer infants died and fewer developed bronchopulmonary dysplasia (a form of chronic lung disease).[7] Furthermore, fast rate ventilation shows limited success in suppressing respiratory activity in infants actively expiring against the ventilator.[6] Increasing ventilator rate higher than 60 bpm in the infants is not helpful beyond the first week of life.[8] Accordingly, the regimen for ventilator rate use remains controversial. The objective of this study was therefore to investigate either the IMV rate at 40 or 70 bpm should be used for RDS patients in acute phase.

Subjects and Methods

The study was performed in neonatal intensive care unit at Banpong Hospital between January 2008 to September 2009. All ventilated preterm patients with a clinical and radiographic diagnosis of RDS were included into the study. Exclusion criteria were prenatal steroid administration, premature rupture of membrane and criminal abortion. Indications for IMV were clinical deterioration, persistent apnea and bradycardia, desaturation or cardiorespiratory collapse. The first patient who met criteria was randomized to group A or group B. Then the next patients were in the other group alternatively between group A and group B until the study was stopped.

After assignment to each group, the patient was placed on the chosen rate of one of these four types of ventilators : Bear Cup 750 PSV model 51-09654-00 class T type B serial no. AFC01296, Bear Cub BP 201 serial no. 52801332 Type BV 041, VIP Bird Model 15215 C serial KFJ 02519, Newport model E 150 serial no. 9301BBQ13. In addition, endotracheal tube number 2.5 and 3.0 mm were used for infants weighted below 1000 and over 1,000 g, respectively. The ventilation setting was as followed : inspiratory time (Ti) = 0.3 sec, a peak inspiratory pressure (PIP) = 15-20 cm H_2O, a positive end-expiratory pressure (PEEP) = 4 cm H_2O, an initial fraction of inspired oxygen (FiO_2) = 1.0. After wards, PIP was adjusted until good chest movement and good air entry of both lungs achieved. FiO_2 was gradually decreased until target oxygen saturation reached 88-96%. After initiation of ventilation for 30 min, 8 hr, 16 hr and 24 hr, pattern of respiration, synchrony or asynchrony, was observed for both groups. Asynchrony was defined as times that patients breathed against inspiration phase of ventilator divided by total infant respiratory rate more than 10%. Oxygen saturation was continually measured with Nihon Kohden OPV-1500K. Incubator was used to maintain neutral thermal environment to the infant. Because clinical and radiographic features of pneumonia may be indistinguishable from RDS, all infants received empiric antibiotic therapy until the clinical symptoms were improved. After 24 hours, ventilation management was adjusted depending on patients' clinical. Any complication such as intraventricular hemorrhage, patent ductus arteriosus, necrotizing enterocolitis and pneumothorax were observed.

Categorical variables were expressed as percentage and compared between the two groups using the Chi-Square test. Continuous variables were expressed as mean and compared between the two groups using the Studentís t-test. All tests were two tailed. A p-value less than 0.05 was considered significant. SPSS version 10 statistic software was used for statistical analysis.

Results

Data of 20 patients were recruited in this study. Baseline characteristics of patients were shown in Table 1. Birth weight, gestational age, sex, maternal age, antenatal care and mean airway pressure were compatible in the two groups ($p > 0.05$). According to Apgar score, patients in group B had more incidence of birth asphyxia compared to those in group A ($p < 0.05$). Table 2 shows the number of

Table 1 Baseline characteristics of patients.

	Group A (n = 10)	Group B (n = 10)	p-value
Birth weight (g), mean ± SD	1,127.00 ± 276.85	1,172.00 ± 286.43	0.73
Gestation (weeks), mean ± SD	28.1 ± 2.47	28.1 ± 2.73	1.00
Boys, n (%)	6 (60)	6 (60)	1.00
Girls, n (%)	4 (40)	4 (40)	1.00
Apgar score < 7 at 5 minutes, n (%)	1 (10)	5 (50)	0.05
Maternal age (year)	26.4 ± 6.59	26.1 ± 8.17	0.93
Antenatal care (ANC), n (%)	8 (80)	7 (70)	0.61
Mean airway pressure (cm H_2O), mean ± SD	10.72 ± 0.85	10.88 ± 0.99	0.70

Table 2 Number of patients obtaining synchronized ventilation at various times, number of intubation days and death of patients in each group.

	Group A (n = 10)	Group B (n = 10)	p-value
Synchronization at 30 min, n (%)	5 (50)	8 (80)	0.16
Synchronization at 8 hr, n (%)	7 (70)	9 (90)	0.26
Synchronization at 16 hr, n (%)	9 (90)	10 (100)	0.31
Synchronization at 24 hr, n (%)	10 (100)	10 (100)	-
Number of intubation days, mean ± SD	7.71 ± 4.38	5.69 ± 1.86	0.27
Number of dead, n (%)	5 (50)	3 (30)	0.36

patients that breathed synchronized to the ventilator. Patients in group B took less time to breath synchronize than patients in group A but no statistically significant difference.

Period of IMV was 7.71 ± 4.38 days in group A which was not significantly longer than that of group B 5.69 ± 1.86 days ($p = 0.27$). No complication was detected in both groups in first 24 hours

but it occurred later. Patent ductus arteriosus (PDA) detected by bounding pulse and systolic murmur was found in 3 and 1 patients in group A and B, respectively. All patients with PDA were treated by oral ibuprofen 10 mg/kg, followed by 5 mg/kg after 24 and 48 hours. Three patients in group A died from intraventricular hemorrhage, pulmonary hemorrhage and sepsis and 2 patients from respiratory failure. Three patients in group B were dead from intraventricular hemorrhage, sepsis and necrotizing enterocolitis ($p = 0.36$).

Discussion

The results of this study showed that high ventilation and conventional rate had comparable efficacy in preterm ventilation as shown in time for patients to obtain synchronized ventilation with IMV and number of intubation days (Table 2). Although patients in group A took more time to synchronize, all patients in this group obtained synchronized time in 24 hrs without any complication observed. Numbers of intubation days for patients in group B were less than those in group A, although it was not statistically different. According to Apgar score, numbers of critical patients in group B were higher than that in group A. This suggested that high ventilation rate was well tolerated and more preferably used.

At the present time, RDS is still a medical problem required substantial attentions from pediatricians. Mechanical ventilation is one of life saving equipment in severe case. Asynchronous breathing has been demonstrated to be associated with short-term adverse effects such as delivery of inconsistent tidal volume and minute ventilation, hypercarbia, hypoxemic episodes. Also it increases energy expenditure, need for sedation and paralysis, intraventricular hemorrhage, decreases venous return, caused fluctuation in blood pressure. However, mechanical ventilation has changed considerably over the past few years with the advance of technology. Pressure-limited ventilation modes such as SIMV are routinely used as a result of its simple use,[9] safety and can deliver synchronized breaths to the RDS patient. Nevertheless, many pediatricians face problems of SIMV such as frequent alarm and auto trigger that causes high ventilator rate and desaturation to patient. Due to problems occurring with SIMV and most ventilators in Banpong Hospital are IMV, this mode of IMV is mainly used in the hospital.

Many studies have shown that fast rate of ventilator is more effective than slow rate. Tarnow-Mordi W0, et al[2] had studied 237 premature infants with RDS aged less than 72 hours. The incidence of pneumothorax was lower in high frequency positive pressure ventilation group compared to low frequency positive pressure ventilation group (18% vs 33%, $p = 0.013$).[2] Hird and Greenough had studied twelve preterm infants with RDS, median age 25 hours. They found that fast ventilator rate, 60 to 105 bpm (median 90 bpm) and short inflation time could improve oxygenation from a median of 66 mmHg (range 43-86 mmHg) to a median of 77 mmHg (range 60-105 mmHg), ($p < 0.01$) and decreased in $PaCO_2$ from 42 mmHg (range 30-46 mmHg) to a median of 37 mmHg (range 25-45 mmHg), ($P < 0.05$).[5]

Most RDS patients have breath rates more than 70 bpm. This fast rate of IMV will more easily

capture the respiratory rate of the baby than rate at 40 bpm. As seen in patients group B, fast rate ventilation took less time to capture infant' s respiratory rate. Focused to intubation days, the duration of endotracheal intubation was shorter in group B than group A. As observed in this study, patients in group B could wean from IMV earlier than group A. This might due to lung compliance in group B could get to normal faster than that in group A. Subsequently, intubation days were lower and group B patients had less death rate and complication rate than group A. It is known that if ventilator setting is not weaned rapidly, the patientís lung may undergo traumatic injury.[10, 11] Concerning this issue, the patient care team had conference two times a day to plan for gradually weaning ventilator setting along 24 hours for individual infant. To avoid ischemic brain injury secondary to hyperventilation,[12] PIP 1 cm H_2O or rate 5 bpm was slightly decreased in the following day to allow the patients having spontaneous breathing 1 or 2 times per minute. Another setting was also adjusted when appropriate until weaning occurred. Limitations of this study included too many types of ventilators using which might affect results of the study, also sample size was too small to give good statistic value.

Conclusion

In summary, in this study, IMV at fast rate was comparably effective to conventional rate. However, in view of patient's comfortable fast rate may be used.

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