Bi-level Positive Airway Pressure Versus Nasal CPAP for the Prevention of Extubation Failure in Infants After Cardiac Surgery

Yi-Rong Zheng, Wen-Hao Lin, Shi-Hao Lin, Ning Xu, Hua Cao, and Qiang Chen

BACKGROUND: Extubation early in the postoperative period is beneficial to the recovery and rehabilitation of patients. This study compared the postoperative extubation failure rates among infants who received postextubation respiratory support by either bi-level positive airway pressure (BPAP) or nasal CPAP following cardiac surgery. METHODS: This was a single-center randomized controlled trial registered at the Chinese Clinical Trial Registry (number ChiCTR2000041453) and was conducted between January 2020 and March 2021. Ventilated infants who underwent cardiac surgery were randomized to either a BPAP or a nasal CPAP group for ventilatory support following extubation. The primary outcome measure was the extubation failure rate within 48 h. RESULTS: The analyses included 186 subjects. Treatment failure necessitating re-intubation was noted in 14 of the 93 infants (15%) in the BPAP group and in 11 of the 93 infants (12%) in the nasal CPAP group ($P = .52$). Moreover, there were no statistically significant differences between the 2 groups regarding the duration of noninvasive ventilation ($P = .54$), total enteral feeding time ($P = .59$), or complications ($P = .85$). We found that both the BPAP group and the nasal CPAP group showed significantly improved oxygenation and relief of respiratory distress after treatment. However, the P_{aCO_2} level within 24 h was significantly lower in the BPAP group ($P = .001$) than in the CPAP group. Additionally, the P_{aO_2}/F_{IO_2} in the BPAP group was significantly higher than in the nasal CPAP group at 6 h, 12 h, and 24 h after treatment ($P < .001$). CONCLUSIONS: The introduction of BPAP for postextubation respiratory support was not inferior to nasal CPAP in infants after cardiac surgery. Moreover, BPAP was shown to be superior to nasal CPAP in improving oxygenation and carbon dioxide clearance. *Key words: BPAP; nasal CPAP; congenital heart surgery; cardiopulmonary bypass; postoperative care.* [Respir Care 2022;67(4):448–454. © 2022 Daedalus Enterprises]

Introduction

Infants with congenital heart disease (CHD) with comorbid or preexisting conditions often require respiratory support after cardiac surgery. Pediatric cardiac ICUs increasingly use noninvasive modalities to support respiratory function in children with critical cardiovascular disease. Noninvasive respiratory support has been proven to be useful in providing respiratory support to pediatric patients and can effectively reduce the extubation failure rate in high-risk infants.[1-5] Previous single-center studies have demonstrated the safety and effectiveness of noninvasive support in the management of respiratory insufficiency in infants and young children, including those undergoing cardiac surgery.[6-10]

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The authors have disclosed no conflicts of interest.

There was no funding for this research.

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This trial was registered at the Chinese Clinical Trial Registry; number: ChiCTR2000039457.

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DOI: 10.4187/respcare.09408

In recent years, noninvasive respiratory support has become increasingly sophisticated, especially the application of bi-level positive airway pressure (BPAP) and nasal CPAP, which have significantly reduced the use of invasive ventilation and have shortened the duration of mechanical ventilation. Noninvasive respiratory support has been widely used in the care of premature infants and neonates. Studies have confirmed that BPAP and nasal CPAP can be used to treat neonatal respiratory failure and respiratory distress syndrome, and their use can reduce the incidence of bronchopulmonary dysplasia.[2,5-13] However, few studies have focused on the application of noninvasive support in infants with CHD postextubation. In particular, very little is known about the contribution of different noninvasive modalities to respiratory support in children after extubation. Filling these knowledge gaps would both help identify important areas for future research in understanding the best practices for noninvasive respiratory support utilization and help inform quality improvement initiatives aimed at optimizing the respiratory support of infants in the cardiac ICU. Our center is a tertiary heart center in China. Many patients are referred to us from subordinate hospitals every year, and many of these patients have preoperative pneumonia or respiratory failure and are at risk of extubation failure. We designed this study to evaluate the postextubation failure rates following the use of either BPAP or nasal CPAP as respiratory support modalities in infants who underwent cardiac surgery. The primary outcome measure was the extubation failure rate within 48 h. The secondary outcome measures were the differences in postoperative duration of noninvasive respiratory support, hospital length of stay, and incidence of complications.

QUICK LOOK

Current knowledge

Infants with congenital heart disease with comorbid or preexisting conditions often require respiratory support after cardiac surgery. Noninvasive respiratory support has proven useful in pediatric patients and can effectively reduce the extubation failure rate in high-risk infants.

What this paper contributes to our knowledge

Bi-level positive airway pressure (BPAP) was not inferior to nasal CPAP as postextubation respiratory support in infants after cardiac surgery. Moreover, BPAP is shown to be superior to nasal CPAP in improving oxygenation and carbon dioxide clearance.

Methods

Subjects and Study Design

We conducted a randomized controlled study in the cardiac ICU of Fujian Maternity and Child Health Hospital, Affiliated Hospital of Fujian Medical University, Fuzhou, China, from January 2020–March 2021. A total of 186 infants who underwent cardiac surgery were randomized, postextubation, to the BPAP group ($n = 93$) or the nasal CPAP group ($n = 93$). Cardiac surgery included repair of atrial septal defects (ASDs), repair of ventricular septal defects (VSDs), and ligation operation of patent ductus arteriosus. The families of the subjects signed informed consent forms prepared by the ethics committee. The trial was approved by the Ethics Committee of Fujian Maternity and Child Health Hospital (No. 2020KY039) and adhered to the tenets of the Declaration of Helsinki (as revised in 2013). This study was registered at the Chinese Clinical Trial Registry, number ChiCTR2000041453.

The inclusion criteria were high-risk infants < 6 months of age with stable hemodynamic status after cardiac surgery. Cardiac surgery included ASD repair, VSD repair, and patent ductus arteriosus ligation. Infants at high risk for extubation failure, including factors such as pulmonary hypertension, pneumonia, preoperative or postoperative respiratory failure, oxygenation index > 8, $P_{aO_2}/F_{IO_2} < 200$ mm Hg, and ARDS, were included. Clinicians considered extubation when the following criteria were met: (1) hemodynamic stability without a large dose of vasoactive drug support; (2) $F_{IO_2} \leq 0.40$, peak inspiratory pressure ≤ 18 cm H_2O, and PEEP 2–4 cm H_2O; and (3) arterial blood gas (ABG) showing P_{aO_2} (P_{aCO_2}) < 50 mm Hg, P_{aO_2} (P_{aCO_2}) > 70 mm Hg, pH > 7.25, and lactic acid < 2.0 mmol/L. The exclusion criteria were patients who had congenital thoracic and abdominal malformations, those who received postoperative extracorporeal membrane oxygenation support or preoperative tracheotomy and intubation, those whose parents decided not to participate, those who transferred to the cardiac ICU prior to extubation, or those who died prior to extubation.

Data Collection and Definitions

The primary outcome measure was the extubation failure rate within 48 h. For secondary outcome measures, the differences in postoperative duration of noninvasive support hospital length of stay, and incidence of complications were analyzed. In addition, we analyzed the changes in ABGs (pH, P_{aO_2}, P_{aCO_2}, and P_{aO_2}/F_{IO_2}) before and after the treatment in each of the 2 groups.

The diagnostic criteria for pediatric and neonatal ARDS were proposed in 2015 and 2017.[14,15] Pulmonary hypertension was defined as a mean pulmonary arterial pressure of 25 mm Hg or higher.[16,17] The diagnosis of ventilator-associated pneumonia was based on the criteria established by the Centers for Disease Control and Prevention, with diagnosis aided by chest radiographs, positive sputum cultures, transtracheal fluid, bronchial washings, and clinical findings.[18] Extubation failure

was defined as re-intubation within 48 h after the first planned extubation. Subjects were re-intubated upon developing hypoxemia ($F_{IO_2} > 0.60$ for target S_{pO_2}), respiratory acidosis (pH < 7.20, P_{aCO_2} > 65 mm Hg), tachypnea, or elevated serum lactic acid (> 2.0 mmol/L). ABGs were taken before treatment and at 6 h, 12 h, and 24 h after treatment and were analyzed using an ABL90 FLEX system.

Ventilation Strategies

All subjects were extubated in the cardiac ICU. After extubation, either BPAP or nasal CPAP was immediately applied to each infant through silicone binasal prongs. BPAP or nasal CPAP was delivered through a time-cycled, pressure-limited, and continuous-flow ventilator (Infant Flow SiPAP System, CareFusion, Yorba Linda, California), which detected the inspiratory effort of the infants by means of the Graseby abdominal capsule-triggering device. The initial lower and higher respiratory parameters in the BPAP group were set at 3–6 cm H_2O and 8–10 cm H_2O, respectively; the F_{IO_2} was 0.21–0.60, and the pressure exchange rate was 20–30 exchanges/min. Respiratory settings were adjusted to maintain blood gas analysis within normal ranges. The respiratory parameter settings in the nasal CPAP group were set at a pressure of 3–6 cm H_2O; the oxygen flow was 6–8 L/min, and the F_{IO_2} was 0.21–0.60. Respiratory settings were adjusted to maintain blood gas analysis within normal ranges. S_{pO_2} was maintained at 90–95% during ventilation. After extubation, all infants were intravenously injected with methylprednisolone sodium succinate 1 mg/kg for the prevention of laryngeal edema. Subjects with excessive secretions were given an intravenous infusion of ambroxol hydrochloride to facilitate mucociliary clearance and chest physical therapy.

Allocation and Blinding

Randomization was performed using random numbers generated by a computer. Sequentially numbered and sealed opaque envelopes were used to hold group assignments. When the infants were admitted to the cardiac ICU and had satisfied the inclusion criteria, envelopes were opened by the cardiac ICU physician, who was not directly involved in the study or the analysis of results. The allocated BPAP or nasal CPAP treatment was started immediately. The BPAP device produces audible noise that cannot be masked. Accordingly, clinicians involved in patient care were not blinded to the study treatments. The researchers who collected and analyzed the data were blinded to the study.

Statistical Analysis

Sample size estimation was calculated with PASS software (version 15; NCSS, Kaysville, Utah). A reasonable hypothesis was that BPAP would not be inferior to nasal CPAP in preventing re-intubation. According to our pre-experiment studies, we found that the incidence of extubation failure in the BPAP group was 18% and that the incidence of extubation failure in the nasal CPAP group was 11%. With 80% power and a 2-sided significance level of 0.05, at least 93 infants would need to be recruited in each group. We defined BPAP as not inferior to nasal CPAP if the lower boundary of the bilateral 95% CI for the difference (BPAP minus nasal CPAP) was $< -5\%$.

An intention-to-treat analysis was performed. The data of this study were analyzed by SPSS 25.0 (IBM, Armonk, New York). The results were expressed as the means with 95% CI or SD for continuous variables and as frequencies for categorical variables. To demonstrate normal data distribution, a Kolmogorov-Smirnov test was performed before each analysis. If the results were normally distributed, a *t* test analysis was performed; otherwise, the Mann-Whitney test was applied. To further characterize the blood gas analysis data, we used repeated-measure analysis of variance (2-way ANOVA) and displayed the interaction between and within the study group. The least significant difference method was used for pairwise comparisons between different times. A chi-square test was used to compare the qualitative data between the 2 groups. A *P* value of $< .05$ was defined as the level of statistical significance.

Results

A total of 236 infants were screened between January 2020–March 2021, of which 23 did not meet the inclusion criteria; 20 underwent preoperative tracheotomy and intubation, and the parents of 7 declined to participate. Ultimately, 186 infants were enrolled and finished the trial (93 in each group) (Fig. 1).

The baseline characteristics of the 2 groups were similar (Table 1). There was no significant difference in extubation failure rates between groups within 48 h (15.05% in the BPAP group vs 11.82% in the nasal CPAP group; $P = .52$, Table 2) . Before treatment, there was no significant difference in pH, P_{aO_2}, P_{aCO_2}, or P_{aO_2}/F_{IO_2} between the 2 groups (Table 3). For both groups, compared with the values before treatment, the P_{aCO_2} gradually decreased; and the pH, P_{aO_2}, and P_{aO_2}/F_{IO_2} gradually increased after treatment. However, the P_{aCO_2} of the BPAP group was significantly lower than that of the nasal CPAP group at 12 h and 24 h after treatment. Additionally, the P_{aO_2}/F_{IO_2} in the BPAP group was significantly > that in the nasal CPAP group at 6 h, 12 h, and 24 h after treatment. At all other time points during the experiment, the pH, P_{aO_2}, P_{aCO_2}, and P_{aO_2}/F_{IO_2} were similar between the 2 groups (Table 3). There was no significant difference between the 2 groups in the duration of noninvasive respiratory support or hospital length of stay. Furthermore, there was no statistically significant difference in terms of complications (Table 2). Complications included

Table 1. Demographic Data of Subjects Included in the 2 Ventilation Mode Groups

Variable	BPAP ($n = 93$)	CPAP ($n = 93$)	*P*
Male/female	43/50	39/54	.56
Age, months	1.8 ± 1.0	1.7 ± 0.8	.55
Weight, kg	4.4 ± 1.7	4.6 ± 1.5	.69
Operation duration, h	3.8 ± 1.2	4.0 ± 1.1	.38
Operation type			
Repair of ASD	43 (46.2)	37 (39.8)	.54
Repair of VSD	28 (30.1)	35 (37.6)	
Ligation of patent ductus arteriosus	22 (22.6)	21 (22.6)	
Cardiopulmonary bypass duration, h	1.4 ± 0.3	1.5 ± 0.3	.69
Respiratory failure	28 (30.1)	32(34.4)	.53
Pneumonia	57 (61.3)	50 (53.8)	.30
Pulmonary hypertension	68 (73.1)	64 (68.8)	.52

Data are expressed as *n* (%) or mean (± SD).
BPAP = bi-level positive airway pressure
ASD = atrial septal defect
VSD = ventricular septal defect

Table 2. Primary Outcomes and Complications of the 2 Ventilation Mode Groups

Variable	BPAP ($n = 93$)	Nasal CPAP ($n = 93$)	*P*
Duration of support, h	49.57 ± 8.49	48.46 ± 7.71	.54
Extubation failure	14 (15.05)	11 (11.82)	.52
Total enteral feeding time, d	6.74 ± 0.88	6.84 ± 0.88	.59
Complications, *n*	17 (18.3)	16 (17.2)	.85
Pneumothorax	3	2	
Abdominal distention	4	3	
Ventilator-associated pneumonia	3	3	
Iatrogenic infection	2	1	
Nasal injury	5	7	

Data are expressed as *n* (%) or mean (± SD).
BPAP = bi-level positive airway pressure

pneumothorax, abdominal distention, ventilation-related pneumonia, iatrogenic infection, and nasal injury.

Discussion

Persistent hypoxemia may occur after extubation in patients who undergo cardiac surgery; it affects the prognosis of patients and increases the cost of hospitalization. Hypoxemia may be due to blood contact with foreign matter and organ hypoperfusion during the process of cardiopulmonary bypass, which leads to an increase in systemic inflammatory mediators and results in lung injury.[19-21] During pulmonary ischemia-reperfusion, infiltration by inflammatory cells occurs, pulmonary interstitial exudation increases, and the abundance of microvilli on the surface of type II alveolar epithelial cells decreases. Therefore, patients are more likely to experience complications such as alveolar collapse, atelectasis, acute respiratory failure, and pulmonary infection.[22,23] At the same time, during invasive mechanical ventilation, alveolar mechanical ectasia and partial alveolar structure destruction cause lung injury and airway remodeling.[24-26] Thus, for this patient population, noninvasive respiratory support is usually required after extubation.

In this study, we found that a total of 33 subjects were reintubated within 48 h, which represents an incidence of 17.7%. There was no significant difference in the extubation failure rate between the BPAP and nasal CPAP groups. Fernández Lafever et al[27] noted that noninvasive respiratory support is increasingly being used in the postoperative period of heart surgery with a high success rate and is associated with a lower need for invasive mechanical ventilation. CPAP was the most common modality. Many studies have shown that as a well-tolerated therapy noninvasive respiratory support can be safely and successfully applied in critically ill children with cardiac disease to prevent extubation failure.[28,29] The independent predictors of noninvasive support success include a good left ventricular ejection fraction, lower Risk Adjustment for Congenital Heart Surgery 1 (RACHS-1) score (1–3), normal heart rate and oxygen saturations demonstrated within 24 h after initiation of support and minimal organ dysfunction.[30] All subjects included in this study were high-risk infants who were only a few months of age but their RACHS-1 scores were low, and they did not have organ dysfunction, which may be the reason for the high success rate (82.3%) of extubation in this study.

Our study showed that in the 2 groups the P_{aO_2} and P_{aO_2}/F_{IO_2} gradually increased, and the P_{aCO_2} gradually decreased after treatment. The continuous air flow of nasal CPAP can reduce upper airway resistance, limit thoracic deformation, support the natural work of breathing, maintain alveolar functional residual capacity, prevent alveolar collapse, and reduce the consumption of autologous alveolar surfactant, thus improving alveolar ventilation and reducing the use of exogenous pulmonary surfactant and the need for invasive ventilation.[31,32] At present, nasal CPAP is still widely used as the initial mode of respiratory support in the clinic. BPAP not only retains the characteristics of nasal CPAP but also combines the advantages of the pressure support/pressure control of mechanical ventilation. BPAP provides 2 different levels of pressure support during the respiratory cycle, and patients can breathe spontaneously and completely under high pressure and low pressure, avoiding the problem of patient-ventilator asynchrony.[33,34] After 24 h of treatment, P_{aO_2}/F_{IO_2} in the BPAP group was higher than in the nasal CPAP group, whereas P_{aCO_2} in the BPAP group was lower than that in the nasal CPAP group. The reason may be that compared with nasal CPAP BPAP can intermittently give higher pressure

Table 3. Secondary Outcomes in the 2 Groups

Parameter	Group	Before treatment	P^*	After treatment			$P^\#$
				6 h	12 h	24 h	
pH	BPAP	7.28 ± 0.12	.78	7.32 ± 0.11	7.34 ± 0.12	7.37 ± 0.13	.43
	Nasal CPAP	7.30 ± 0.12		7.34 ± 0.12	7.38 ± 0.16	7.42 ± 0.13	
P_{aCO_2}, mm Hg	BPAP	44.75 ± 5.67	.69	49.18 ± 8.86	43.08 ± 8.36	36.69 ± 10.60	.001
	Nasal CPAP	41.83 ± 7.73		53.96 ± 8.85	47.57 ± 10.29	43.22 ± 7.19	
P_{aO_2}, mm Hg	BPAP	65.49 ± 8.80	.71	67.56 ± 5.82	77.52 ± 7.97	90.11 ± 8.91	.32
	Nasal CPAP	68.12 ± 9.39		66.65 ± 5.54	74.73 ± 7.59	84.35 ± 9.41	
P_{aO_2}/F_{IO_2}	BPAP	167.57 ± 10.13	.58	221.33 ± 56.53	233.47 ± 62.07	388.78 ± 60.38	.001
	Nasal CPAP	170.29 ± 9.30		194.85 ± 48.91	237.77 ± 58.69	329.31 ± 51.25	

Data are expressed as mean (± SD).
*Comparison between the 2 groups before intervention.
#Comparation of the changes over time after the intervention between the 2 groups.
BPAP = bi-level positive airway pressure

support based on PEEP, which is conducive to improving oxygenation and removing carbon dioxide. Therefore, BPAP provides better respiratory support by both improving oxygenation and promoting CO_2 clearance.[35,36]

We found that there were no statistically significant differences between BPAP and nasal CPAP in terms of duration of noninvasive respiratory support, hospital length of stay, and ventilator-related complications. Zoremba et al[37] noted that short-term use of BPAP improved lung function within 24 h. Compared with endotracheal intubation, BPAP is more comfortable, has lower rates of mortality and iatrogenic infection, and helps to avoid ventilator-related complications such as ventilator-associated pneumonia and the need for deep sedation.[38-40] Other advantages include the improvement in oxygenation and the reduction in respiratory work, resulting in a lower myocardial oxygen demand. Diaphragmatic paralysis or dysfunction is common in patients who undergo cardiac surgery, and it can also be used as an indication for the application of BPAP.[41] Tobias' study showed a decrease in the breathing frequency and P_{aCO_2} in postoperative subjects.[42] These subjects were in a state of impending respiratory failure, and BPAP improved oxygenation, lowered carbon dioxide levels, and enabled patients to avoid re-intubation.

Our study has several limitations. First, subjects in this study were limited to infants with RACHS 1–2. It may very well be that the outcomes differ substantially for infants with other congenital cardiac disorders and with higher RACHS scores. Second, there was no control group to whom, following extubation, noninvasive respiratory support was not offered. These data would have allowed us to determine whether there is a group of patients who do not require re-intubation even without noninvasive support postextubation. However, our goal was to assess the frequency of success for noninvasive respiratory support rather than for all cases after cardiac surgery. At the same time, the subjects included in our study all had high risk factors for extubation failure. Third, the medical staff could not be blinded to the randomized mode of support. Although we used objective failure criteria and management protocols, the possibility of a bias might exist. Fourth, although the short-term effects of noninvasive respiratory support on ventilation were considered, the relationship between noninvasive respiratory support and long-term clinical outcomes was not shown. Fifth, this study is a single-center study that involved a small sample size. We look forward to a larger, multi-center study in the future to further determine whether our conclusions are correct and feasible.

Conclusions

In summary, the introduction of BPAP for postextubation respiratory support did not reduce extubation failure rates compared with the rates of nasal CPAP. However, BPAP was shown to be superior to nasal CPAP in improving oxygenation levels and carbon dioxide clearance. Before the routine clinical application of this ventilation mode, more research is needed to confirm its effectiveness and safety.

ACKNOWLEDGMENTS

We highly acknowledge the contribution of the participating researchers Qi-Liang Zhang, Wang-Sheng Dai, Ze-Wei Lin, Li-Wen Wang, Jing Wang, and Ling-Shan Yu.

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