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Synchronized Nasal Intermittent Positive Pressure Ventilation versus Nasal Continuous Positive Airway Pressure for Prevention of Extubation Failure in Infants after Congenital Heart Surgery

Yi-Rong Zheng, MM, Jian-Feng Liu, MM, Yu-Qing Lei, MM, Hong-Lin Wu, MM, Hua Cao, MD,* Qiang Chen, MD*

Department of Cardiac Surgery, and Fujian Key Laboratory of Women and Children's Critical Diseases Research, Fujian Maternity and Child Health Hospital, Affiliated Hospital of Fujian Medical University, Fuzhou, China

ABSTRACT

Objective: This study aimed to evaluate the application of synchronized nasal intermittent positive pressure ventilation (SNIPPV) in the respiratory weaning of infants after congenital heart surgery.

Methods: We retrospectively analyzed the clinical data of 63 infants who were extubated from mechanical ventilation after congenital heart surgery between January 2020 and September 2020. The data, including demographics, anatomic diagnosis, radiology and laboratory test results, and perioperative variables were recorded. Results: The extubation failure rate within 48 h after extubation was significantly lower in the SNIPPV group than in the nasal continuous positive airway pressure (NCPAP) group. The PaO_2 level and PaO_2/FiO_2 ratio within 48 h after extubation were higher in the SNIPPV group than in the NCPAP group ($P < .05$). Meanwhile, the $PaCO_2$ level within 48 h was significantly lower in the SNIPPV group ($P < .05$). Compared with the NCPAP group, the median duration of postoperative noninvasive support and the duration from extubation to hospital discharge were shorter in the SNIPPV group; the total hospital cost was lower in the SNIPPV group. No significant differences were observed between the two groups concerning VAP, pneumothorax, feeding intolerance, sepsis, mortality, and other complications ($P > .05$).

Conclusion: SNIPPV was shown to be superior to NCPAP in avoiding reintubation after congenital heart surgery in infants and significantly improved oxygenation and reduced $PaCO_2$ retention after extubation. Further studies are needed to confirm the efficacy and safety of SNIPPV as a routine weaning strategy.

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**These authors contributed equally to this work.*

Correspondence: Qiang Chen, MD, Department of Cardiac Surgery, Fujian Maternity and Child Health Hospital, Affiliated Hospital of Fujian Medical University, Fuzhou, China; (e-mail: chenqiang2228@163.com).

INTRODUCTION

Extubation failure rates for mechanically ventilated patients in pediatric cardiac intensive care units (CICUs) range from 5.8% to 29% [Benneyworth 2017; Gaies 2015; Harris 2014]. Extubation failure is associated with significant morbidity and mortality and increased the length of ICU stay [Gaies 2015]. Patients with congenital heart disease (CHD) are at high risk of compromised cardiac function, especially during weaning from mechanical ventilation or under the stress of extubation. The use of noninvasive ventilation (NIV) in pediatric cardiac patients as an alternative ventilated support mode has been proved to decrease extubation failure in high-risk infants [Richter 2019]. To date, nasal continuous positive airway pressure (NCPAP) is the most widely used assisted ventilation modality for infants after extubation [Lemyre 2016]. Nasal intermittent positive pressure ventilation (NIPPV) has been described as another method of weaning infants from mechanical ventilation in different pediatric or neonatal settings [Lemyre 2016; Essouri 2005]. However, NIPPV has the limitation of not being synchronized with the patient's breathing efforts. Compared with other non-synchronized NIV modalities, synchronized nasal intermittent positive pressure ventilation (SNIPPV) has been demonstrated to reduce breathing effort, improve oxygenation, and optimize patient-ventilator interactions [Chang 2011; Bhandari 2007]. We hypothesize that the physiological advantages of SNIPPV will lead to earlier successful initial extubation. To date, no study has directly compared SNIPPV and NCPAP in terms of their ability to prevent reintubation after congenital heart surgery in infants. The purpose of this study was to investigate the efficacy and safety of SNIPPV and NCPAP in postoperative extubation in infants with CHD.

MATERIALS AND METHODS

Patient Characteristics

We performed a retrospective cohort study of all CHD infants aged less than three months admitted to our center between January 2020 and November 2020 who received cardiac surgery (with or without cardiopulmonary bypass). SNIPPV became available in our CICU in June 2020. We

identified patients from the SNIPPV era (June 2020 to November 2020) and compared them to historical controls when only NCPAP was available (January 2020 to May 2020) to decrease selection bias. Choice of postextubation NIV ventilation method was made prior to extubation, based on physician's preference. The inclusion criteria included those postoperative patients with satisfactory anatomical correction and stable hemodynamics. The exclusion criteria included postoperative extracorporeal cardiopulmonary support, tracheostomy tube cannulation before surgery, parents' decision not to participate, discharged from the CICU before extubation, or death before extubation. If patients achieved the following criteria, we would consider extubation: hemodynamic stability; the fraction of inspired oxygen (FiO_2) ≤40%; peak inspiratory pressure (PIP) ≤18 cmH_2O; positive end-expiratory pressure (PEEP) 2~4 cmH_2O; and the arterial blood gases (ABGs) indicating that: partial pressure of carbon dioxide in arterial blood ($PaCO_2$) <50 mmHg, partial pressure of oxygen in arterial blood (PaO_2) >70 mmHg, pH >7.30, and lactic acid <2.0 mmol/L. The local ethics committee approved this study and a summary of the data collection methods. All procedures performed in studies involving human participants followed the institutional and national research committee's ethical standards and the Declaration of Helsinki and its later amendments, or comparable ethical standards.

Respiratory Modalities and Equipment

After extubation, either SNIPPV or NCPAP would be connected to infants using silicone nasal prongs. SNIPPV was delivered through a time-cycled, pressure-limited, and continuous-flow ventilator (Sophie, Fritz Stephan, Gackenbach, Germany), which detected the inspiratory effort of the infants utilizing the Graseby abdominal capsule-triggering device (Fritz Stephan, Gackenbach, Germany). The ventilator's initial parameters were as follows: FiO_2 regulated from 0.21 to 0.60, PIP regulated from 15 to 20 cmH_2O, RR regulated from 20 to 30 times/min, and PEEP regulated from 2 to 6 cmH_2O. Infants assigned to NCPAP were initiated using a PEEP of 3 cm H2O (subsequent regulation range, 3-6 cm H_2O) with a nasal CPAP-system (Infant Flow System, EME, UK), with FiO_2 regulated from 0.21 to 0.60. Extubation failure was defined as reintubation within 48 h after the first planned extubation. Indications for reintubation were based on the following criteria: upper airway obstruction, respiratory dysfunction (severe hypoxemia or hypercapnia), hemodynamic instability, loss of consciousness, weak or stopped breathing, and thoracic active hemorrhage [Lu 2010]. For infants with failed extubation, we would adopt synchronized intermittent mandatory ventilation (SIMV) mode for respiratory support. To avoid gastric/intestinal dilatation, an oral gastrointestinal catheter was used in both groups during the intervention and evacuated regularly. ABGs were monitored every 6 h, and all infants had continuous pulse oximetry monitoring. Dexamethasone was administered intravenously at 0.5 mg/kg per dose every 12 h for four doses, 24 h before extubation for every infant in each group to prevent laryngeal edema and stridor.

Data Collection and Definitions

We conducted a detailed retrospective review of all medical records. The data collection included demographics, anatomic diagnosis, radiology and laboratory test results, and perioperative variables. The primary outcomes included the reintubation rate within 48 h of extubation, and the reasons for the failure (hypoxemia, hypercapnia, and heart failure) were analyzed. Besides, we analyzed the changes in ABGs (pH value, PaO_2, $PaCO_2$, and PaO_2/FiO_2 ratio) before and after the treatment in the two groups. For secondary outcomes, the differences in postoperative NIV support time, duration from extubation to hospital discharge, time to full gastrointestinal feeding, postoperative length of stay (LOS), total hospital costs, and total hospital LOS were analyzed. After treatment, complications and short-term outcomes, such as ventilator-associated pneumonia (VAP), sepsis, mortality, pneumothorax, diaphragm and vocal cord paresis, feeding intolerance, and gastroesophageal reflux, were also evaluated in the two groups of children. Pulmonary hypertension was defined as a mean pulmonary artery pressure of 25 mmHg or higher [Badesch 2009]. Inotropes and vasopressors were used to maintain hemodynamic stability. The vasoactive-inotropic score (VIS) was calculated as: VIS = dopamine dose (g/kg/min) + dobutamine dose (ug/kg/min) + 100 × epinephrine dose (ug/kg/min) + 10 × milrinone dose (ug/kg/min) + 10,000 × vasopressin dose (units/kg/min) + 100 × norepinephrine dose (ug/kg/min) [Gaies 2010].

Statistical Analysis

SPSS software version 22.0 was used for the statistical analysis. Independent continuous variables were presented as the mean ± standard deviation (SD) and analyzed by t tests. Counts and percentages described enumeration data. For testing differences between categorical variables, Pearson chi-square test or Fisher exact analysis was used. The Mann–Whitney U test was applied for non-normally distributed data. A *P* value of less than .05 was regarded as statistically significant.

RESULTS

Patient Characteristics

During the study period, 63 infants who underwent congenital heart surgery met the inclusion criteria for analysis, including 36 males and 27 females. We recruited 38 infants with ventricular septal defect, 9 infants with patent ductus arteriosus, 8 infants with pulmonary stenosis, 3 infants with coarctation of aorta, 3 infants with total anomalous pulmonary venous connection and 2 infants with interrupted aortic arch. In these infants, 33 were supported with SNIPPV, and 30 were supported with NCPAP after extubation. There were no significant differences between the two groups in terms of age, sex, weight at surgery, preoperative pneumonia, preoperative respiratory failure, pulmonary hypertension, inhaled nitric oxide treatment at extubation, sedation at extubation, VIS at extubation and cardiopulmonary bypass (CPB) time (Table 1). The clinical characteristics at the time of extubation

Table 1. Baseline Characteristics

	SNIPPV (n = 33)	NCPAP (n = 30)	*P*
Sex (M/F)	18/15	16/14	1.000
Gestation age at birth, weeks, mean ± SD	38.4 ± 1.8	38.0 ± 1.7	.402
Age at surgery, days, mean ± SD	43.0 ± 11.1	46.2 ± 11.9	.280
Weight at surgery, kg, mean ± SD	4.5 ± 0.7	4.6 ± 0.8	.500
Preoperative pneumonia, n (%)	8 (24)	6 (20)	.767
Preoperative respiratory failure, n (%)	5 (15)	3 (10)	.710
Pulmonary hypertension, n (%)	17 (52)	19 (63)	.446
Disease			
Ventricular septal defect	20	18	.943
Patent ductus arteriosus	4	5	
>Pulmonary stenosis	5	3	
Coarctation of aorta	2	1	
Total anomalous pulmonary venous connection	1	2	
Interrupted aortic arch	1	1	
Surgery with cardiopulmonary bypass, n (%)	28 (85)	26 (87)	1.000
CPB time, min, mean ± SD	135 ± 49	137 ± 30	.855
Sedation (midazolam dose), μg/kg/min, mean ± SD	3.6 ± 2.1	3.7 ± 2.5	.772
Inhaled NO at extubation, n (%)	5 (15)	6 (20)	.744
Vasoactive-Inotropic Score at extubation, median (IQR)	7.5 (5–7.5)	7.0 (5–8.5)	.840

Data reported as number and percentage, mean ± standard deviation, or median and interquartile range. CPB indicates cardiopulmonary bypass; IQR, interquartile range.

Table 2. Clinical Characteristics at the Time of Extubation

	SNIPPV (n = 33)	NCPAP (n = 30)	*P*
Duration of mechanical ventilation, days	1.5 (1.1, 2.3)	1.8 (1.3, 2.6)	.285
PIP, cmH_2O	15 (14, 17)	16 (13, 17)	.180
PEEP, cmH_2O	3 (2–5)	3 (2–4)	.673
MAP, cmH_2O	6 (6.0, 7.5)	7 (6.5, 8.0)	.853
OI	6.5 (5.2, 7.6)	6.2 (4.5, 7.2)	.677
FiO_2, %	0.30 (0.25, 0.38)	0.29 (0.25, 0.36)	.849
PaO_2, mmHg	71.5 (65.6, 76.3)	69.7 (63.5, 76.9)	.183
$PaCO_2$, mmHg	42.1 (39.6, 47.3)	43.8 (38.5, 48.2)	.090

Data reported as number and percentage, mean ± standard deviation, or median and interquartile range. PIP indicates peak inspiratory pressure; PEEP, positive end-expiratory pressure; MAP, mean airway pressure; OI, oxygen index,

were similar between the two groups, which are shown in Table 2.

Primary Outcomes

The rate of extubation failure within 48 h after extubation was significantly lower in the SNIPPV group than in the NCPAP group (extubation failure: 2:32 vs 8:32, respectively; $P < .001$). The main reasons for extubation failure in the two groups were hypercapnia (n = 5), hypoxemia (n = 4), and heart failure (n = 1). Moreover, ABGs indexes, including PaO_2 and the PaO_2/FiO_2 ratio, were higher in the SNIPPV group than in the NCPAP group within 48 h after extubation ($P < .05$)

(Table 3). Nevertheless, the $PaCO_2$ levels within 48 h were significantly lower in the SNIPPV group than in the NCPAP group ($P < .05$) (Table 3). There was no significant difference in PH between the two groups ($P > .05$).

Secondary Outcomes

The median SNIPPV duration was 2.3 days (range 1.3-4.5 days), which was shorter than that for NCPAP (4.0 days; range 2.8-6.4 days) ($P = .013$). Moreover, the postoperative LOS and the duration from extubation to hospital discharge were found to be significantly shorter in the SNIPPV group than in the NCPAP group: 12.5 days (range 9.0-16.7 days) vs 15.7 days (range 13.0-21.7 days) and 8.2 days (range 5.1-11.2 days) vs 11.3 days (range 7.5-16.8 days), respectively ($P < .05$) (Table 4). The total hospitalization expense of infants in the SNIPPV group was \$9790 ± \$3530, which was significantly lower than that of the NCPAP group (\$12133 ± \$4582) ($P = .031$). We did not find significant differences between the two groups for other secondary outcomes, including the incidence of VAP, sepsis, perioperative mortality, pneumothorax, diaphragm paresis, vocal cord paresis, feeding intolerance, gastroesophageal reflux and time to full gastrointestinal feeding after surgery (Table 4).

DISCUSSION

With the development of noninvasive ventilation technology, new noninvasive respiratory support modes, such as NIPPV, bilevel positive airway pressure (BiPAP), SNIPPV, nasal high-frequency ventilation (NHFV), and nasal neurally adjusted ventilatory assist (NNAVA), have been gradually applied in clinical practice. Related studies confirmed that a significant aspect of these new noninvasive ventilation methods is that they could provide better-assisted ventilation effects, improve alveolar ventilation, reduce respiratory function, and increase gas exchange efficiency compared with the traditional NCPAP mode [Chen 2019; Fedor 2017; Parashar 2019].

In this study, we found that SNIPPV was more effective than NCPAP in reducing the rate of reintubation, and the duration of respiratory support was shorter in the SNIPPV group. Moreover, compared with NCPAP, we found that the application of SNIPPV after extubation had apparent effects on improving oxygenation and reducing the retention of PaCO2. Therefore, SNIPPV could effectively improve respiratory function, which was beneficial to those patients who underwent cardiac surgery. This result was consistent with the conclusions reported in other studies [Tao 2016; Sai 2009; Zhou 2015; Lemyre 2017].

Extubation failure after congenital heart surgery is associated with prolonged hospital stay and mortality [Richter 2019]. The entire extubation failure rate was 15.6% in this study, which was related to younger age, more severe preoperative lung infections, and cardiac surgeries of the enrolled infants. After weaning from mechanical ventilation in infants following cardiovascular surgery, NCPAP assisted ventilation was usually adopted for the transition. NCPAP could increase functional residual capacity and prevent alveolar collapse, thereby improving pulmonary oxygenation and reducing intrapulmonary shunts [Polin 2002]. However, 25%-34% of children supported with NCPAP still needed reintubation due to low oxygen pressure, tachypnea, or severe CO2 retention, which might increase attendant risks and expense [Tao 2016; Sai 2009]. Lemyre and his team evaluated three randomized trials and compared NIPPV (synchronous or asynchronous mode) with NCPAP in premature infants after extubation [Lemyre 2017]. They showed that NIPPV was more effective than NCPAP in reducing the need for reintubation within one week. Bhandari et al also found that NIPPV was more conducive to extubation than NCPAP [Bhandari 2010]. Compared with NCPAP, SNIPPV could reduce the forced inhalation of infants with respiratory distress, and due to the intermittently higher positive pressure in the nasopharynx, it could promote the expansion of the upper airway. Moreover, the additional peak pressure provided by SNIPPV could reduce the work of the respiratory muscles, increase mean airway pressure and tidal volume, improve lung capacity, and increase gas exchange [Barrington 2001]. We also found that SNIPPV significantly reduced the rate of reintubation and improved ABG parameters after extubation. This result might be associated with the fact that SNIPPV increased intermittent positive pressure at a particular frequency based on NCPAP to increase average airway pressure and tidal volume [Chang 2011]. Also, the synchronized delivery of NIPPV according to the infant's breathing efforts could cause changes in ventilator pressure following the infants' physiological status. In theory, this synchronous mode could synchronize the pressure exerted by the ventilator with the patient's spontaneous inhalation during assisted ventilation so that the gas could enter the lower respiratory tract to the lungs more effectively, which could effectively prevent alveolar collapse, expand the small airways, and decrease work of breathing [Zhou 2015; Bhandari 2010; Aghai 2010].

This study showed that the length of hospital stay was shorter in the SNIPPV group, which might be associated with a lower extubation failure rate. The prevalence of VAP and mortality in the SNIPPV group were lower than those in the NCPAP group, but the difference was not statistically significant. This result might be related to the small number of subjects in the study. Due to the increased transpulmonary pressure, SNIPPV and NCPAP might lead to excessive lung expansion, so one should be aware of the possibility of pneumothorax. The present study showed no significant difference in the incidence of pneumothorax between the two groups. SNIPPV was a synchronized mode of NIPPV, which was closer to the infants' physiological state and theoretically could reduce the incidence of lung air leakage or pneumothorax. Jasani et al and Kahramaner et al indicated that the incidence of pulmonary air leakage in the NIPPV group was lower than that in the NCPAP group [Jasani 2015; Kahramaner 2014]. The possible digestive complications of noninvasive ventilation, such as gastrointestinal dilatation, feeding difficulties, and the risk of gastrointestinal perforation, had always been scholars' concern. Studies had shown that there was no significant difference in the feeding intolerance rate and incidence of gastrointestinal perforation between the NIPPV group and the NCPAP group during assisted

Table 3. Primary Outcomes after Extubation

		SNIPPV (n = 33)	NCPAP (n = 30)	*P*
Extubation failure	Hypoxemia, n	1	3	.038
	Hypercapnia, n	1	4	
	Heart failure, n	0	1	
After 1 hour of non-invasive ventilation	PH	7.34 ± 0.04	7.32 ± 0.05	.085
	PaO_2, mmHg	72.58 ± 4.83	66.06 ± 5.30	<.001
	$PaCO_2$, mmHg	45.48 ± 4.85	49.09 ± 4.43	.003
	PaO_2/FiO_2	228.75 ± 38.60	203.68 ± 45.30	.010
After 12 hours of non-invasive ventilation	PH	7.31 ± 0.04	7.29 ± 0.05	.146
	PaO_2, mmHg	74.94 ± 8.54	63.65 ± 6.99	<.001
	$PaCO_2$, mmHg	47.97 ± 7.53	52.68 ± 8.41	.019
	PaO_2/FiO_2	220.56 ± 57.91	190.95 ± 41.66	.020
After 24 hours of non-invasive ventilation	PH	7.32 ± 0.05	7.30 ± 0.04	.108
	PaO_2, mmHg	78.97 ± 7.49	69.68 ± 5.66	.010
	$PaCO_2$, mmHg	37.65 ± 7.12	42.74 ± 8.05	.010
	PaO_2/FiO_2	251.68 ± 51.39	226.92 ± 48.94	.035
After 48 hours of non-invasive ventilation	PH	7.35 ± 0.06	7.33 ± 0.08	.122
	PaO_2, mmHg	83.50 ± 7.55	74.51 ± 5.12	<.001
	$PaCO_2$, mmHg	38.21 ± 8.49	44.26 ± 9.51	.010
	PaO_2/FiO_2	248.03 ± 53.86	245.78 ± 67.73	.400

Data reported as number and percentage, mean ± standard deviation, or median and interquartile range.

Table 4. Secondary Outcomes and Complications after Extubation

	SNIPPV (n = 33)	NCPAP (n = 30)	*P*
VAP, n (%)	5 (15)	6 (20)	.744
Sepsis, n (%)	8 (24)	6 (20)	.767
Mortality, n (%)	1 (3)	2 (7)	.601
Pneumothorax, n (%)	3 (9)	5 (2)	.462
Diaphragm paresis, n (%)	0	1 (3)	.476
Vocal cord paresis, n (%)	1 (3)	2 (7)	.601
Feeding intolerance, n (%)	5 (15)	8 (27)	.353
Gastroesophageal reflux, n (%)	4 (12)	7 (22)	.325
Time to full gastrointestinal feeding after surgery, days (median, IQR)	6.5 (3.2–13.6)	7.6 (4.5–16.2)	.172
Duration of postoperative noninvasive support, days (median, IQR)	2.3 (1.3–4.5)	4.0 (2.8–6.6)	.013
Extubation to hospital discharge, days (median, IQR)	8.2 (5.1–11.2)	11.3(7.5–16.8)	.007
Postoperative hospital LOS, days (median, IQR)	12.5 (9.0–16.7)	15.7 (13.0–21.7)	.002
Total hospital LOS, days (median, IQR)	18.5 (15.4 - 23.8)	22.2 (18.7 - 30.1)	.003
Total hospital costs in $ (median ± SD)	9790 ± 3530	12133 ± 4582	.031

Data reported as number and percentage, mean ± standard deviation, or median and interquartile range. VAP indicates ventilator associated pneumonia; LOS, length of stay; IQR, interquartile range.

ventilation [Jasani 2015; Khalaf 2001]. We also found no statistically significant difference in the incidence of feeding intolerances, gastrointestinal perforation, and gastroesophageal reflux between the two groups, which suggested that the side effects of SNIPPV on the digestive system were similar to those of NCPAP. Besides, our study showed that the postoperative length of hospital stay and the duration from extubation to hospital discharge were significantly shorter in the SNIPPV group than in the NCPAP group, leading to a significant difference in hospital costs between the two groups.

This study was the first study comparing post-extubation respiratory support with SNIPPV and NCPAP after congenital heart surgery in infants. The present study has several limitations. First, this was a retrospective and observational study that only intended to evaluate the post-extubation respiratory support modality's efficiency in infants who underwent cardiac surgeries requiring CPB. It could not generalize the effectiveness of SNIPPV versus NCPAP to other pediatric patients in critical condition. Due to the small sample size of this study, further stratification analysis was not conducted according to the severity of pulmonary disease. Furthermore, for all of the infants, the clinical data were recorded until they were discharged from the hospital, and there was a lack of comparison of the results of long-term lung function, neurodevelopmental outcome, and other prognostic data. Finally, as a relatively new non-invasive ventilation technology, few relevant clinical studies were found in infants with CHD. This mode's safety and efficiency still need to be confirmed by prospective, multicenter, and large-sample studies in the future.

CONCLUSION

Compared with NCPAP, the application of SNIPPV is a safer and more effective mode for post-extubation respiratory support after congenital heart surgery in infants. SNIPPV could improve invasive mechanical ventilation extubation success in infants with CHD, significantly improve oxygenation, and reduce PaCO2 retention after extubation. At the same time, it does not increase the risk of ventilator-related complications. Future studies are needed to confirm the efficacy and safety of SNIPPV as a routine weaning strategy after congenital heart surgery.

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