Effect of High-Flow Nasal Cannula on Thoraco-Abdominal Synchrony in Pediatric Subjects After Cardiac Surgery

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BACKGROUND: We previously reported the effects of high-flow nasal cannula (HFNC) oxygen therapy on thoraco-abdominal synchrony. This study was designed to clarify the effect of HFNC on thoraco-abdominal synchrony in pediatric subjects after cardiac surgery and to investigate HFNC optimal flow in this population. METHODS: Thoraco-abdominal synchrony was evaluated with respiratory inductive plethysmography. After extubation, we delivered oxygen via face mask for 30 min to subjects with mild to moderate respiratory failure. Each subject then randomly received either 1 or 2 L/kg/min via HFNC for 30 min, followed by the other flow level via HFNC for 30 min. After HFNC, face mask delivery was resumed. Rib cage and abdominal movement were converted into volumes and 2 quantitative indexes: maximum compartmental amplitude/tidal volume (V_T) ratio and phase angle. RESULTS: Ten subjects of median (interquartile range) age 7 (6–14) months and weighing 6.5 (5.3–8.8) kg were enrolled. Compared with the first delivery via face mask, breathing frequency, maximum compartmental amplitude/V_T, phase angle, and minute volume significantly decreased at 2 L/kg/min ($P < .05$ for all) but not at 1 L/kg/min. P_{aCO_2} did not differ among oxygen therapies. None of the measured variables differed between first and second face mask periods. CONCLUSIONS: After cardiac surgery, HFNC oxygen therapy at 2 L/kg/min improved thoraco-abdominal synchrony and decreased breathing frequency in pediatric subjects. (Clinical trial registration: UMIN000023426.) *Key words: high-flow nasal cannula; neonates; thoraco-abdominal synchrony; cardiac surgery; oxygen therapy.* [Respir Care 0;0(0):1–•. © 0 Daedalus Enterprises]

Introduction

High-flow nasal cannula (HFNC) oxygen therapy is now a commonly used means of respiratory support for critically ill patients with respiratory failure.[1-5] Despite its popularity, a convincing level of evidence is lacking in children.[6-8] For subjects of all ages, a number of physiological advantages have been evaluated, including adequate humidification,[9,10] positive airway pressure,[11,12] washout of

nasopharyngeal dead space,[13,14] and stable F_{IO_2}.[10,15] The physiological effects of HFNC on children have been investigated mostly in premature infants,[16,17] and data for other pediatric subjects are lacking.[18]

Patients with respiratory failure often exhibit impaired coordinated movement of the chest and abdomen, resulting in increased work of breathing.[19,20] Previously, we studied the effect of HFNC on the movement of the chest and abdomen in adult subjects with mild to moderate respiratory failure.[21] HFNC improved thoraco-abdominal synchrony and decreased breathing frequency while P_{aCO_2} was constant. Then we discussed washout of anatomical

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dead space as a possible mechanism of the improved breathing pattern. Despite the wide use of HFNC in the management of critically ill children with respiratory insufficiency from heart failure, cardiac surgery, and neuromuscular weakness as well as obstructive airway diseases, such as bronchiolitis, almost all of the published data for its effect on the breathing pattern of pediatric subjects has been derived from preterm infants.[20,22,23] In addition, the optimal flow for pediatric subjects has yet to be determined. HFNC generates positive airway pressure and may reduce work of breathing in a flow-dependent manner.[8,11,16] However, the increase in airway pressure is unpredictable due to many factors, such as mouth opening, and may not have a linear relationship with set flow.[24,25]

The aim of this study was to determine whether HFNC improved thoraco-abdominal synchrony in pediatric subjects with mild to moderate respiratory failure after cardiac surgery. In addition, from the viewpoint of thoraco-abdominal synchrony, we examined the effect of flow level for pediatric subjects.

Methods

We conducted a prospective crossover study in a university hospital ICU. Ethical approval for this study (protocol number 1492) was provided by the ethics committee of Tokushima University Hospital. Written informed consent was obtained from parents.

Subject Enrollment

Pediatric subjects with body weight of 2–10 kg were surveyed. We included subjects with mild to moderate respiratory failure who presented with one or more of the following after extubation: $S_{pO_2} < 95\%$ without supplemental oxygen (for acyanotic heart disease); breathing frequency > 50 breaths/min; asynchronous or paradoxical breathing pattern. The exclusion criteria were: mean blood pressure < 40 mm Hg for neonates and < 50 mm Hg for infants; $P_{aO_2}/F_{IO_2} < 150$ mm Hg (for acyanotic heart disease); pH < 7.2 and $P_{aCO_2} > 60$ mm Hg; facial trauma or nasal obstruction; and inability to tolerate HFNC.

Study Protocol

Thoraco-abdominal movements were measured with respiratory inductive plethysmography (Inductotrace, Ambulatory Monitoring, Ardsley, New York) via 2 elastic transducers (Inductobands, Ambulatory Monitoring) placed around the thorax and abdomen to record changes in cross-sectional area.

After extubation, we observed the subjects under ambient conditions for 5 min. Each subject that met the inclusion criteria was enrolled into the study, and conventional

QUICK LOOK

Current knowledge

High-flow nasal cannula (HFNC) oxygen therapy improves thoraco-abdominal synchrony and reduces breathing frequency in adult patients with moderate hypoxemic respiratory failure. The impact of HFNC and flow level on breathing pattern has not been described in pediatric subjects.

What this paper contributes to our knowledge

In pediatric subjects with mild to moderate respiratory failure after cardiac surgery, HFNC oxygen therapy at 2 L/kg/min flow improved thoraco-abdominal synchrony by improving the phase angle and the ratio of maximum compartmental amplitude to tidal volume and decreasing breathing frequency.

oxygen therapy was applied to deliver oxygen via a loosely attached standard face mask (OX-130, Atom Medical, Saitama, Japan), at 0–3 L/min. Flow was titrated to keep S_{pO_2} at $\geq 95\%$. After 30 min, we measured thoraco-abdominal movement, heart rate, blood pressure, breathing frequency, and S_{pO_2} and drew an arterial blood sample for blood gas analysis. We then applied the HFNC through a system composed of an air-oxygen blender (San-You Technology, Saitama, Japan), a heated humidifier (MR850, Fisher & Paykel Healthcare, Auckland, New Zealand), a breathing circuit (RT330, Fisher & Paykel Healthcare), and a nasal cannula (OPT312/314/316, Fisher & Paykel Healthcare). The breathing circuit included a heating wire and a pressure-relief valve to keep circuit pressure at < 45 cm H_2O. Nasal cannula size was chosen to enable leakage at the nose by occluding approximately half the nares.

We evaluated the effect of HFNC at 2 flow levels within the maximum flow that the manufacturer claimed for each nasal cannula. HFNC flow of 1 and 2 L/kg/min were consecutively applied in digitally randomized order (ie, initial gas flow was 1 L/kg/min for 30 min, followed by 2 L/kg/min for 30 min in some subjects, and vice versa for the others). At the end of each 30-min protocol, we measured thoraco-abdominal movement, heart rate, blood pressure, breathing frequency, and S_{pO_2} and drew arterial blood for blood gas analysis. After the HFNC protocols, conventional oxygen therapy was resumed, and the same measurements were taken after 30 min. The study was stopped and routine management resumed if subjects revealed intolerance for HFNC, severe upper-airway obstruction, or acidosis pH < 7.3 with $P_{aCO_2} > 50$ mm Hg.
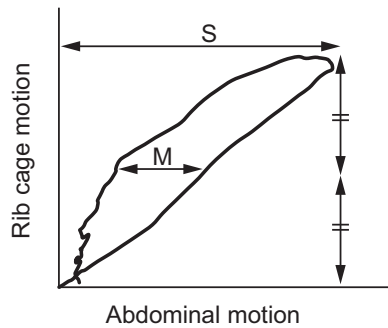
Fig. 1. Konno-Mead diagram of abdominal motion versus rib cage motion. The phase angle (θ) is calculated according to the formula, $\theta = \sin^{-1}(M/S)$, where M is the horizontal distance on the Konno–Mead diagram at the midpoint between the maximal and minimal rib cage excursions, and S is the maximal abdominal excursion. Asynchrony produces a wide open loop. Synchronous rib cage/abdominal motion has a θ of 0°, and paradoxical motion has a θ of 180°.

Measurement of Thoraco-Abdominal Movement

We calibrated respiratory inductive plethysmography using the qualitative diagnostic calibration technique described by Sackner et al[26] The motions of the rib cage and abdomen were evaluated from changes in the inductance of the transducers during respiratory support via oronasal mask and HFNC. Signals were recorded, and the data were later analyzed with a software application (WINDAQ, DATAQ Instruments, Akron, Ohio). The arithmetic sums of the maximal peak-to-trough amplitudes of rib cage and abdomen excursions represent the maximum compartmental amplitudes. The algebraic sum of rib cage and abdomen excursions represents the tidal volume (V_T). We then calculated the ratio of maximum compartmental amplitude to V_T. Plotting abdominal motion against rib cage motion, we also created Konno–Mead diagrams. Phase angle (θ) was calculated using the formula $\theta = \sin^{-1}(M/S)$, where M is the horizontal distance on the Konno–Mead diagram at the midpoint between the maximal and minimal rib cage excursions, and S is the maximal abdomen excursion (Fig. 1). Near the end of each protocol, data for 3 consecutive stable breaths were selected, and the mean was used as a single value for final analysis.

Statistical Analysis

The data, collected for 4 protocols (conventional oxygen therapy, HFNC 1 L/kg/min, HFNC 2 L/kg/min, and conventional oxygen therapy) were analyzed among all subjects by repeated measures of analysis of variance with multiple comparisons for effect over time. Statistical calculations were carried out with statistics software (SPSS 11.0.1, SPSS, Chicago, Illinois). Data are expressed as

Table 1. Subject Characteristics

Characteristics	Values
Age, median (IQR) months	7 (6–14)
Male/female, n	3/7
Body weight, median (IQR) g	6,527 (5,288–8,788)
Height, median (IQR) cm	63 (59–74)
Surgery, n	
VSD closure	4
Glenn shunt	2
Pulmonary artery banding	1
Pulmonary artery debanding	1
Coronary artery reconstruction	1
ASD closure	1
Length of mechanical ventilation, median (IQR) d	7 (3–10)
pH before extubation, median (IQR)	7.46 (7.43–7.50)
P_{aCO_2} before extubation, median (IQR) mm Hg	32.1 (31.2–37.7)
F_{IO_2} before extubation, median (IQR)	0.23 (0.21–0.25)
Inclusion criteria, n	
Hypoxia ($S_{pO_2} < 95\%$)	1
Tachypnea (>50 breaths/min)	2
Abnormal breathing pattern	7

$N = 10$. Data are expressed as median (interquartile range) unless otherwise indicated.
IQR = interquartile range
VSD = ventricular septal defect
ASD = atrial septal defect

mean (95% CI) unless otherwise indicated. $P < .05$ was considered statistically significant.

Results

A total of 12 subjects who met inclusion criteria were enrolled in the study. Two subjects were subsequently excluded because they were overly restless, preventing respiratory inductive plethysmography measurements, reducing the study population to 10. Two excluded subjects were observed under conventional oxygen therapy and never experienced further respiratory management. None of the remaining subjects experienced severe upper-airway obstruction or acidosis. We did not observe any apparent harm associated with treatment. Details of each subject are summarized in Table 1. The median (interquartile range) age was 7 (6–14) months. Body weight was 6,527 (5,288–8,788) g, and 7 subjects (70%) were female. The most common inclusion criterion was asynchronous or paradoxical breathing pattern (70%).

Table 2 shows variables measured during conventional and HFNC oxygen therapy for all subjects; changes in values over time are shown in Figures 2 and 3. Compared with the first period of conventional delivery, statistically significant decreases in HFNC at 2 L/kg/min, but not in HFNC at 1 L/kg/min, were detected in breathing frequency (mean [95% CI], 33 [28–33] vs 37 [33–41] breaths/min,

Table 2.   Measurement Variables During Conventional Oxygen Therapy and Different Levels of High-Flow Nasal Cannula Delivery

Variables	Control 1	HFNC 1 L/kg/min	HFNC 2 L/kg/min	Control 2
Heart rate, beats/min	134 (124–143)	137 (121–153)	138 (123–153)	136 (120–152)
Breathing frequency, breaths/min	37 (33–41)	35 (31–39)	33 (28–33)*	36 (31–42)†
V_T (vs control 1), %	100	96 (63–129)	101 (75–127)	104 (72–135)
Minute volume, mL/kg	303 (223–383)	245 (185–306)	242 (191–293)*	261 (214–309)
Phase angle, degrees	32 (20–45)	21 (14–29)	19 (10–28)*	22 (14–30)
MCA/V_T	1.07 (1.02–1.12)	1.03 (1.01–1.06)	1.03 (1.01–1.05)*	1.04 (1.01–1.07)
P_{aCO_2}, mm Hg	36 (33–39)	35 (32–38)	34 (31–38)	35 (32–37)

Data are mean (95% CI).
* $P < .05$ versus control 1.
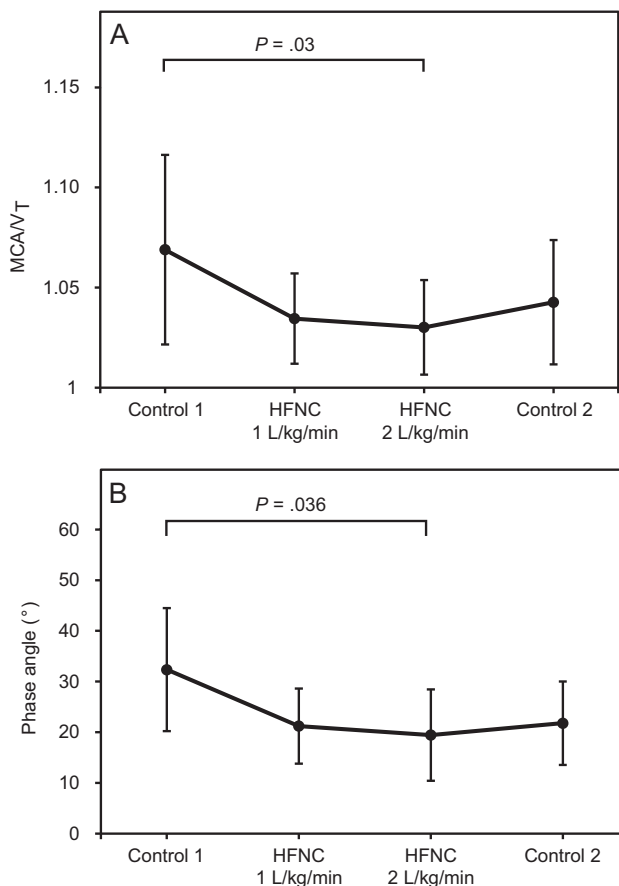† $P < .05$ versus 2 L/kg/min.
HFNC = high-flow nasal cannula
V_T = tidal volume
MCA/V_T = ratio of maximum compartmental amplitude to tidal volume

Fig. 2. Changes in variables related to thoraco-abdominal synchrony for conventional oxygen therapy and different levels of high-flow nasal cannula (HFNC) delivery. A: Ratio of maximum compartmental amplitude to tidal volume (MCA/V_T). B: Phase angle. Both parameters did not differ between controls. Data are expressed as means and 95% CI.

$P = .01$), maximum compartmental amplitude/V_T (1.03 [1.01–1.05] vs 1.07 [1.02–1.12], $P = .03$), phase angle (19° [10–28°] vs 32° [20–45°], $P = .036$), and minute volume (242 [191–293] vs 303 [223–383] mL/kg, $P = .037$). No statistically significant difference in any variable was found after comparing data for HFNC at 1 and 2 L/kg/min. During the second period of conventional delivery, breathing frequency was statistically significantly higher than during 2 L/kg/min (36 [31–42] vs 33 [28–33] breaths/min, $P = .03$). Maximum compartmental amplitude/V_T, phase angle, and minute volume, however, did not change after final discontinuation of HFNC. P_{aCO_2} was similar during each protocol. No statistically significant difference in any variable was found after comparing data for the first and second periods of conventional delivery.

Discussion

The major finding of our study is that, for pediatric subjects after cardiac surgery, HFNC oxygen therapy at flow 2 L/kg/min improved thoraco-abdominal synchrony and reduced breathing frequency. To our knowledge, this is the first crossover study to investigate the effect of different HFNC flows on thoraco-abdominal synchrony.

Effect of HFNC on Thoraco-Abdominal Synchrony

Despite an open system, HFNC generates positive airway pressure in a flow-dependent manner.[8,11,16] Moreover, unidirectional high gas flow toward the lung during the inspiratory phase offloads the diaphragm and reduces work of breathing.[16,19,27,28] Both positive airway pressure and better matching of the patient's inspiratory flow are supposed to eliminate the rib cage lag after the abdominal motion, which is often seen in patients with respiratory failure.[20] Reduced nasopharyngeal dead space may be another possible reason for the improvement of thoraco-ab-
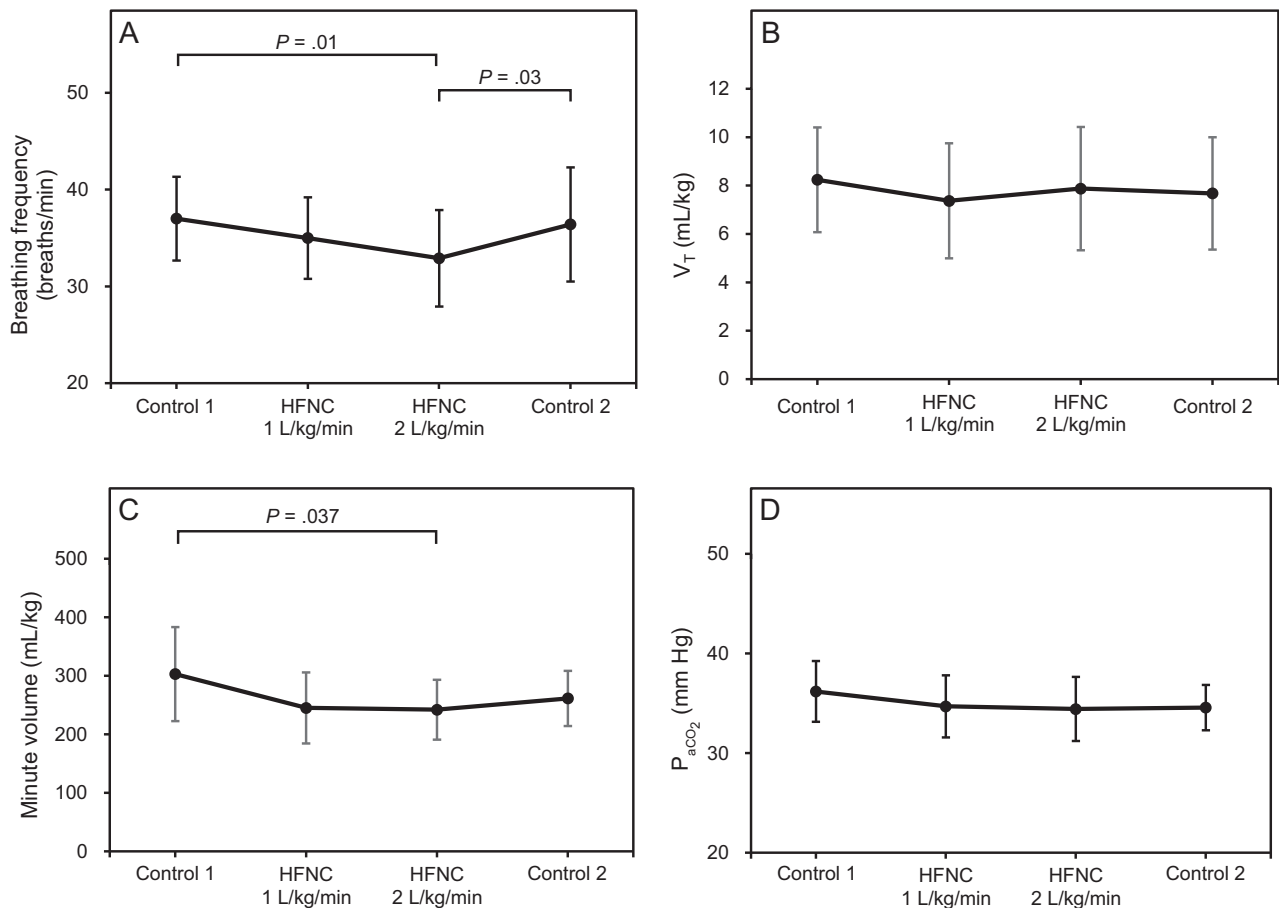
Fig. 3. Changes in ventilation variables among conventional oxygen therapy and different levels of high-flow nasal cannula (HFNC) delivery. A: Breathing frequency. B: Tidal volume (V_T). C: Minute volume. D: P_{aCO_2}. All parameters did not differ between controls. Data are expressed as means and 95% CI.

dominal synchrony. As seen in our adult study,[21] we observed decreased minute volume and breathing frequency, without alteration of P_{aCO_2} during HFNC. It is possible that HFNC improved breathing pattern through washout of airway dead space.

Our finding is also consistent with other studies reporting the favorable effects of HFNC on the breathing pattern of preterm infants. Studying preterm infants requiring supplemental oxygen but not mechanical ventilation, Locke et al[22] found a significant flow-dependent decrease in phase angle from 80 to 53° when oxygen was administered through a large-bore nasal cannula at 0.5–2 L/min. In a study of neonates, including some who had undergone mechanical ventilation, de Jongh et al[20] observed a small decrease in phase angle from 115 to 87° when HFNC flow increased from 3 to 5 L/min. Compared with studies in preterm infants, we observed a lower phase angle, possibly because we studied older subjects with better lung mechanics and chest wall stability.[29] Rather than the small airway obstruction seen in premature infants,[30] our population had decreased lung and chest wall compliance in-

duced by edema after cardiac surgery responsive to greater positive airway pressure. Pham et al[16] found that HFNC reduced work of breathing both in infants with bronchiolitis and in infants with cardiac problems, although the effects were less prominent in the latter. We can conclude that there are some differences in the mechanisms involved in the improvement of thoraco-abdominal synchrony in preterm infants and in our population.

Optimal Flow During HFNC

HFNC up to 2 L/kg/min could be safely applied, and at this flow, thoraco-abdominal synchrony was statistically significantly better than with conventional oxygen therapy. Testing HFNC flows of 0.3, 0.6, and 1.3 L/kg/min, Locke et al[22] observed linear phase angle improvement but were unable to detect a value at which improvement ceased. Meanwhile, testing HFNC flows of 2.0 and 3.3 L/kg/min, de Jongh et al[20] discerned only a slight decrease in phase angle. We refrained from testing flow at more than the recommended level of 2 L/kg/min, although an observa-

tional study on pediatric HFNC noted flows up to 3 L/kg/min.[31] Within safe limits, higher flows that de Jongh et al applied[20] should be tested to provide additional evidence.

In a lung-injured animal model, Frizzola et al[14] found that the effect of increasing HFNC flow on CO_2 removal was independent of mouth opening and tracheal pressure. P_{aCO_2} plateaued, however, once flow reached a certain level, which may be the point at which all dead space is flushed out. Airway pressure also rises flow-dependently during HFNC in adults,[11,32,33] children,[12,34] and preterm infants.[14,34,35] In a recent adult study, Mauri et al[36] found that although pressure-related effects, such as oxygenation, end-expiratory lung volume, and lung mechanics, improved linearly, increasing HFNC flow exponentially decreased the work of breathing and minute ventilation, and most of the effects were already obtained at a minimum flow of 30 L/min. The improvement of thoraco-abdominal synchrony over time may possibly be linked to those linear effects, which are related to increasing airway pressure. Even so, we must remain aware that the effects, as well as other factors, can be largely influenced by cannula size,[29,35] mouth leakage,[11,29] and, as Mauri et al[36] observed, significant individual variability of flow, which accounted for the largest physiological improvements.

Strengths and Limitations of This Study

We designed the study so as to both determine and compare the effects of 2 levels of HFNC flow on thoraco-abdominal synchrony for each subject. This made it possible to conduct within-subject comparisons, rather than intergroup comparisons, which would have necessitated a much larger sample size. Using a crossover study design also allowed us to minimize the sequence effect of the 2 different HFNC flows. In theory, flow per se could have contributed to the improvement of breathing pattern.

There are several limitations to this study. First, even in a crossover study, results from a sample of only 10 subjects with mild to moderate respiratory failure is inadequate for broad extrapolation. Studies using larger sample sizes are necessary to determine the optimal level of HFNC and its clinical importance. Second, our population, age 0–28 months, was also age-limited. Because the airway anatomy and respiratory mechanics of babies differ substantially from those of older infants and pre-teen children, extrapolation may not be prudent. Even so, there is no evident relationship between baseline phase angle and age. Third, during each protocol, we collected data from only 3 consecutive breaths, and there is no guarantee that all of these samples were typical; on the other hand, when the samples were collected, 30 min into each protocol, parameters had mostly stabilized.

Clinical Implications

In this study, HFNC at 2 L/kg/min flow improved breathing pattern in pediatric cardiac subjects. Additionally, we observed a significant decrease in breathing frequency with HFNC. Indeed, reduced breathing frequency has been the most salient beneficial clinical effect of HFNC in previous studies for both adults[21,37-40] and pediatric subjects.[18,41] In an adult clinical study, Sztrymf et al[37] concluded that absence of a decrease in respiratory frequency and persistent paradoxical breathing pattern as well as lower oxygenation after HFNC initiation were key and often early observable signs of impending respiratory failure. Our findings indicate that careful physical examination may also be valuable in children as a surrogate as HFNC flow levels are adjusted and used to recognize success or failure of this therapy.

Conclusions

In pediatric subjects after cardiac surgery, HFNC oxygen therapy at 2 L/kg/min flow improved thoraco-abdominal synchrony and decreased breathing frequency. Further studies are required to ascertain optimal flow levels and to predict which types of patients will derive the most benefit from HFNC.

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