High-Flow Nasal Prong Oxygen Therapy or Nasopharyngeal Continuous Positive Airway Pressure for Children With Moderate-to-Severe Respiratory Distress?*

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Objectives: The aim of this study was to compare the use of high-flow nasal prong oxygen therapy to nasopharyngeal continuous positive airway pressure in a PICU at a tertiary hospital; to understand the safety and effectiveness of high-flow nasal prong therapy; in particular, what proportion of children require escalation of therapy, whether any bedside monitoring data predict stability or need for escalation, and complications of the therapies.

Methods: This was a prospective observational study of the first 6 months after the introduction of high-flow nasal prong oxygen therapy at the Royal Children's Hospital in Melbourne. Data were collected on all children who were managed with either high-flow nasal prong oxygen therapy or nasopharyngeal continuous positive airway pressure. The mode of respiratory support was determined by the treating medical staff. Data were collected on each patient before the use of high-flow nasal prong or nasopharyngeal continuous positive airway pressure, at 2 hours after starting the therapy, and the children were monitored and data collected until discharge from the ICU. Therapy was considered to be escalated if children on high-flow nasal prong required a more invasive form or higher level of respiratory support, including nasopharyngeal continuous positive airway pressure or mask bilevel positive airway pressure or endotracheal intubation and mechanical ventilation. Therapy was considered to be escalated if children on nasopharyngeal continuous positive airway pressure required bilevel positive airway pressure or intubation and mechanical ventilation.

Measurements and Main Results: As the first mode of respiratory support, 72 children received high-flow nasal prong therapy and 37 received nasopharyngeal continuous positive airway pressure. Forty-four patients (61%) who received high-flow nasal prong first were weaned to low-flow oxygen or to room air and 21 (29%) required escalation of respiratory support, compared with children on nasopharyngeal continuous positive airway pressure: 21 (57%) weaned successfully and 9 (24%) required escalation. Repeated treatment and crossover were common in this cohort. Throughout the study duration, escalation to a higher level of respiratory support was needed in 26 of 100 high-flow nasal prong treatment episodes (26%) and in 10 of 55 continuous positive airway pressure episodes (18%; $p = 0.27$). The need for escalation could be predicted by two of failure of normalization of heart rate and respiratory rate, and if the F_{IO_2} did not fall to lower than 0.5, 2 hours after starting high-flow nasal prong therapy. Nasopharyngeal continuous positive airway pressure was required for significantly longer periods than high-flow nasal prong (median 48 and 18 hours, respectively; $p \leq 0.001$).

Conclusions: High-flow nasal prong therapy is a safe form of respiratory support for children with moderate-to-severe respiratory distress, across a large range of diagnoses, whose increased work of breathing or hypoxemia is not relieved by standard oxygen therapy. About one quarter of all children will require escalation to another form of respiratory support. This can be predicted by simple bedside observations. (*Pediatr Crit Care Med* 2013; 14:e326–e331)

Key Words: continuous positive airway pressure; high-flow nasal prong oxygen therapy; oxygen therapy; respiratory support

***See also p. 730.**

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Supported, in part, by University Medical Centre Rotterdam for Ms. ten Brink's role in the study. Ms. ten Brink was supported by University Medical Centre Rotterdam. The remaining authors have not disclosed any potential conflicts of interest.

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DOI: 10.1097/PCC.0b013e31828a894d

Humidified high-flow nasal prong (HFNP) oxygen therapy is a method for providing oxygen and continuous positive airway pressure (CPAP) to children with respiratory distress. It has been used for similar indications as the traditional method of CPAP using a nasopharyngeal tube. The largest experience of HFNP therapy is among premature infants with respiratory distress (1). HFNP therapy may also be useful in older infants and children with bronchiolitis and pneumonia (2–4). We also considered if HFNP therapy may be useful in heterogenous pediatric intensive care populations,

including children with congestive heart failure, as respiratory support following extubation from mechanical ventilation, weaning therapy from other forms of noninvasive respiratory support such as mask CPAP or bilevel positive airway pressure (BiPAP), respiratory support to children with neuromuscular disease, and in the management of apnea of prematurity. However, there is currently limited evidence to support its safety and efficacy, and wide variation in indications, the flow rates, and weaning strategies (5, 6).

At the Royal Children's Hospital (RCH) Melbourne, for more than 20 years, CPAP has been delivered by a nasopharyngeal tube (a cut-down polyvinylchloride endotracheal tube) and a mechanical ventilator. Infants on NP-CPAP are often uncomfortable and receive sedation with chloral hydrate and other drugs (7). We wondered if HFNP therapy may be better tolerated than NP-CPAP and reduce sedation requirements.

We developed a model for the introduction and evaluation of HFNP therapy. The model for introduction included a detailed guideline for its use and training for staff.

The aims of this prospective observational study were to evaluate the safety and efficacy of HFNP and NP-CPAP, in particular, what proportions of children require escalation of therapy, whether simple bedside monitoring can predict stability or the need for escalation, the complications of the therapies, whether children receiving HFNP required less sedation than those on NP-CPAP, and whether there was compliance with the guideline.

METHODS

Setting

This study was conducted in the PICU in the RCH in Melbourne. This is the largest PICU in Australia. It is a 19-bed mixed surgical/cardiac/medical unit with approximately 1,400 admissions per year. Patient care is provided by the intensive care team that consists of the medical consultant, intensive care registrars, nurses, and technologists. It has high acuity, with over 70% of admissions requiring intubation and mechanical ventilation. RCH PICU provides pediatric intensive care for the state of Victoria, southern New South Wales, and northern Tasmania, a population of over 5 million. The study was conducted between July and November, which encompasses the second half of the respiratory virus infection season, which typically peaks in Victoria during the winter months (June–August).

Design and Patients

This was an observational prospective study. Data were gathered on all children in whom either HFNP or NP-CPAP was commenced in PICU. As this was only an observational study of practice, and all treatment decisions including which type of respiratory support was provided were made by the treating consultant intensive care physician, written consent from parents or guardians was not required. Parents were given an information sheet and the study was explained to them. The study was approved by the RCH Ethics Committee: Human Research Ethics Committee 31157 A.

Indications for HFNP or NP-CPAP and Method of Delivering HFNP

HFNP or NP-CPAP was used if there was hypoxemia (Sao_2 < 90%) and signs of moderate-to-severe respiratory distress despite standard flow oxygen, the method chosen was based on physician preference. High flow was defined as 2 L/kg/min, using appropriate nasal prongs, a humidifier, and oxygen blender. We used the Fisher and Paykel oxygen delivery system RT329 for patients less than 10 kg body weight, RT203 for patient greater than 10 kg, and the MR850 humidifier. The RCH guideline for HFNP therapy is available at: http://www.wch.org.au/picu/index.cfm?doc_id=15591.

Data Collection

Data collected included age, weight, diagnosis, sex, initial respiratory support, and Pediatric Index of Mortality (PIM) 2 risk of death (8). The response to HFNP or NP-CPAP in the first 2 hours was recorded. This included respiratory rate (RR), heart rate (HR), and oxygen saturation at baseline and 2 hours later. Some vital signs, such as HR and RR are highly variable, so these were recorded when they had reached a steady state over 1 minute of observation. We designed a respiratory distress score, the scale of which estimates four parameters each with a 1 (mild) to 3 (severe) score: oxygen saturation, chest wall retraction, respiratory sounds, and difficulties in feeding (**Table 1**).

We recorded the need to escalate to other forms of respiratory support, including from HFNP to NP-CPAP or from either therapy to intubation and mechanical ventilation. We also recorded data on sedation drugs used: how many sedative drugs were used, and given that more than 90% of sedation used was chloral hydrate, we calculated the dose of this drug administered in mg/kg/hour of respiratory support. We also recorded how the children were fed while on the respiratory support. We recorded the duration of the HFNP or NP-CPAP therapy and complications that occurred including abdominal distention, nasal mucosal injury, pneumothorax, or blocked tubes by secretions.

Diagnoses were classified according to the Australian and New Zealand Pediatric Intensive Care (ANZPIC) registry coding criteria (9). We classified patients into eight broad categories: bronchiolitis; pneumonia; respiratory, other; cardiac conditions, preoperative; cardiac conditions, postoperative; neurological and neuromuscular conditions; immunodeficiency; and other.

We prospectively tested therapeutic goals that could be used as criteria for stability after commencing respiratory support. We recorded whether children receiving HFNP or NP-CPAP achieved these and whether achievement of these therapeutic goals predicted outcome. These therapeutic goals were: RR reduction by 20% or to within normal range, HR reduction by 20% or to within normal range, and inspired oxygen fraction reduced to less than 0.5. Our hypothesis was that if a child achieved any two or more of these criteria, they would be less likely to require escalation of therapy, and that such criteria could be used to ensure the safety of the model and its implementation. For respiratory and HRs for age, we used the reference ranges reviewed by Fleming et al (10).

TABLE 1. Respiratory Distress Score Estimating Oxygen Saturation, Chest Wall Retraction, Respiratory Sounds, and Difficulties in Feeding

Clinical Feature and Score	1	2	3
Oxygen saturation[a]	Mild hypoxemia, Sao_2 90–93% during crying only	Mild hypoxemia, Sao_2 90–93% at rest	Hypoxemia, $Sao_2 < 90\%$
Chest wall retraction	None or minimal	Moderate chest wall retraction	Marked chest wall retractions, tracheal tug
Respiratory sounds	None or minimal	Intermittent soft grunting and/or nasal flaring	Grunting with every breath and nasal flaring
Feeding	Normally	Difficulty with feeding or reduced feeding because of respiratory distress	Unable to feed because of respiratory distress or lethargy

Mild = 4–6 points, moderate = 7–9 points, severe = 10–12 points.
[a]For cyanotic congenital heart disease: 1 = 70–80%, 2 = 60–69%, 3 = <60%.

To evaluate compliance with the HFNP guideline, we recorded the flow rates used and compliance with humidification recommendations in the guideline. Because several children received more than one episode of respiratory support, we present the primary outcome—the need for escalation of respiratory therapy—for the first episode of respiratory support with HFNP or NP-CPAP, and for each episode of either support.

Data Analysis

Chi-square or Fisher exact tests were used for categorical variables and variables presented as percentages as appropriate. The Wilcoxon rank-sum test was used for continuous variables because many had nonnormal distributions. These data are presented with medians and their interquartile range (IQR). Logistic regression analysis was used to determine whether clinical data predicted treatment failure and treatment success of HFNP therapy. Results from the logistic models are expressed as adjusted odds ratio with 95% CIs. All data were analyzed with STATA (version 12.0; StataCorp, College Station, TX).

RESULTS

Between July and November 2011, 72 children received HFNP therapy and 37 received NP-CPAP as the first form of respiratory support greater than standard oxygen therapy. Because of repeated treatment and crossover in this cohort of 109 patients, for the entire duration of the study, there were 100 episodes of HFNP and 55 episodes of CPAP therapy.

Patient Population

Table 2 shows the baseline patient characteristics. Among the 72 children who received HFNP as the first form of respiratory support, 28 children were older than 1 year and eight children were 5 years of age or older. The baseline PIM2 score was lower in the HFNP group compared with the CPAP group, and a respiratory distress score of 3 was observed in 13% of the HFNP group compared with 8% of the NP-CPAP group; however, no differences were significant.

Table 3 presents the cases by disease categories. There were 121 diagnoses in the HFNP group and 66 diagnoses in the CPAP group. There were a higher proportion of children with

TABLE 2. Baseline Patient Characteristics and the Baseline Vital Signs

Characteristic: Median (Interquartile Range) or %	High-Flow Nasal Prong ($n = 72$)	Continuous Positive Airway Pressure ($n = 37$)	p
Age in months	6 (1.4–29.5)	5 (1.25–14)	0.69
Weight in kg	6 (4.0–11.8)	5.3 (3.5–8.1)	0.25
Sex, no. (%), male	41 (56.9)	19 (51.4)	0.58
Respiratory rate in breaths/min	45.5 (31.5–62.5)	41 (32–50)	0.41
Heart rate in beats/min	148 (130–164)	150 (132–164)	0.75
Arterial oxygen saturation (Sao_2)	94 (89–99)	96 (90–99)	0.34
Pediatric Index of Mortality 2	−4.45 (−4.88 to −3.22)	−3.51 (−4.78 to −2.84)	0.12
Respiratory distress score (mild to moderate to severe)	Moderate	Moderate	0.46
Respiratory distress score = severe	8 (12.7%)	3 (9.4%)	0.63

TABLE 3. Diagnostic Categories of the Children Receiving High-Flow Nasal Prong or Nasopharyngeal Continuous Positive Airway Pressure

	HFNP (%)	NP-CPAP (%)
Total number	72	37
Bronchiolitis	17 (23.6)	11 (29.7)
Pneumonia[a]	14 (19.4)	1 (2.7)
Respiratory, other	30 (41.7)	17 (45.9)
Cardiac, preoperative	4 (5.6)	2 (5.4)
Cardiac, postoperative	32 (44.4)	16 (43.2)
Neurological/neuromuscular	8 (11.1)	4 (10.8)
Immunodeficiency	3 (4.2)	2 (5.4)
Other	13 (18.1)	13 (35.1)
Total diagnoses	121	66

HFNP = high-flow nasal prong; NP-CPAP = nasopharyngeal continuous positive airway pressure.

[a]There were differences in the case-mix among the children receiving HFNP therapy and NP-CPAP, with more children with pneumonia receiving HFNP ($p = 0.02$).

pneumonia in the HFNP group. Almost half the use of either HFNP or NP-CPAP was in children at some stage after cardiac surgery, reflecting the population of children in our PICU.

Outcome

The outcome for the first treatment episode of either HFNP or CPAP is described in **Table 4**. Sixty-one percent of patients who received HFNP first were weaned to low-flow oxygen or to room air compared with 57% of those who received CPAP first. There was no difference in the proportion of children who were able to be successfully weaned to low-flow oxygen or room air in the two groups ($p = 0.67$) or in the proportion of children requiring escalation in respiratory support ($p = 0.59$). The median duration of the CPAP episodes was 48 hours and for HFNP, it was 18 hours ($p < 0.001$).

For the cohort of patients during the entire study period, among the 100 episodes of HFNP, 26% required an escalation of respiratory support, and among the 55 episodes of NP-CPAP, 18% required an escalation of respiratory support ($p = 0.27$).

Physiological Stability and Safety

In the first 2 hours after commencing children on either HFNP therapy or NP-CPAP, there were significant improvements in HR, Sao_2, and respiratory distress score, and nonsignificant reductions in RR.

Table 5 shows changes in vital signs in the 155 episodes of HFNP or NP-CPAP. In 88% of occasions, the HFNP group achieved two or more of the predetermined criteria for stability compared with 73% of occasions in the NP-CPAP group ($p = 0.02$). In 42 episodes of HFNP, the RR was reduced by 20% or to within normal range compared with 25 episodes of CPAP. In 30% of patients in the HFNP group, the HR was reduced by 20% or to within normal range compared with 11% of patients in the CPAP group. In 70% and 72% of episodes of HFNP and NP-CPAP, respectively, the FIO_2 was reduced to less than 0.5.

Among the children on HFNP therapy, those with a respiratory distress score of 3 at baseline had an odds ratio for treatment failure requiring escalation 3.15 (95% CIs, 0.83–12.05; $p = 0.09$).

TABLE 4. The Respiratory Outcomes When the First Episode of Respiratory Support Was Either High-Flow Nasal Prong or Nasopharyngeal Continuous Positive Airway Pressure

Outcomes of First Episode of Respiratory Support	HFNP ($n = 72$) (%)	CPAP ($n = 37$) (%)
1. Successfully weaned to standard flow oxygen or room air	44 (61)	21 (57)
2. Weaned to HFNP		4 (11)
3. Transfer to neonatal ICU (still on HFNP)	1 (1)	
4. Unable to wean CPAP, remained on		3 (8)
5. Escalation to NP-CPAP	13 (18)	
6. Escalation to mask bilevel positive airway pressure	5 (7)	5 (13)
7. Intubation and mechanical ventilation (nonelective, emergency escalation of respiratory support)	3 (4)	4 (11)
8. Intubation and mechanical ventilation (elective anesthetic for surgery or diagnostic procedures)	7 (9)	
9. Escalation in respiratory support[a]	21 (29)	9 (24)

HFNP = high-flow nasal prong; NP-CPAP = nasopharyngeal continuous positive airway pressure.

[a]Escalation in respiratory support: HFNP: 5 + 6 + 7; CPAP: 6 + 7. Intubation for elective procedures was not considered to be escalation of the need for respiratory support.

TABLE 5. Change in Physiological Variables 2 Hours After Commencing High-Flow Nasal Prong or Nasopharyngeal Continuous Positive Airway Pressure

Physiological Change	HFNP (%)	CPAP (%)	*p*
Respiratory rate reduced by 20%	42 (43.3) ($n = 97$)	25 (37.3) ($n = 52$)	0.53
Heart rate reduced by 20%	28 (29.5) ($n = 95$)	6 (11.1) ($n = 54$)	0.77
Fio_2 reduced to < 0.5	67 (69.8) ($n = 96$)	38 (71.7) ($n = 53$)	0.81
≥2 standard criteria	83 (88.3) ($n = 94$)	37 (72.6) ($n = 51$)	0.02

HFNP = high-flow nasal prong; NP-CPAP = nasopharyngeal continuous positive airway pressure.
n = number of criteria recorded, out of 100 episodes of HFNP and 55 episodes of NP-CPAP.

If children on HFNP therapy had improvement in any two or more of the criteria for stability, the odds ratio for not requiring escalation of therapy was 3.35 (95% CIs, 0.87–12.97; $p = 0.08$).

Two patients on HFNP had abdominal distention, one had mucosal injury. In the CPAP group, six patients had mucosal injury during treatment, two pneumothorax, and two with blocked tubes because of secretions. Mucosal injury usually consisted of nasal bleeding of a mild degree or ulceration.

Table 6 presents sedation use for all episodes of HFNP and CPAP. In 38% of episodes of HFNP, sedation was given compared with 60% in the CPAP group. Chloral hydrate was, by far, the commonly used sedative drug. Five percent of the HFNP group patients received more than one sedative drug compared with almost 11% in the CPAP group ($p = 0.17$). The median dose of chloral hydrate in milligram per kilogram per hour respiratory support was 0.79 in the HFNP group and 0.81 in the CPAP group.

There were no significant differences in feeding and fluid management of infants on HFNP therapy or NP-CPAP. During 60% of HFNP episodes, children were fed by a nasogastric tube compared with 71% on CPAP. Oral feeding was successful in 13% of episodes of HFNP compared with 9% of episodes of NP-CPAP. On HFNP, 23% had IV fluids only and 18% among those treated with NP-CPAP.

Compliance With the HFNP Guideline

The guideline specified a flow rate of 2 L/kg/min. At commencement of HFNP and 2 hours later, the median flow rate (IQR) was 1.95 L/kg/min (1.8–2.0) and 1.90 L/kg/min (1.8–2.0), respectively. The guideline specified a humidifier temperature above 36°C. At commencement of HFNP therapy and 2 hours later, in 22% and 12% of times, respectively, the humidifier temperature was lower than this.

DISCUSSION

In this prospective evaluation, we describe the use of HFNP and NP-CPAP in a heterogeneous population of children in intensive care. This study gives further evidence to support the safety and effectiveness of HFNP, and a better understanding of how to recognize children for whom it is sufficient and for those who require more advanced respiratory support. This builds on the work of Schibler et al (4) and McKiernan et al (3) who showed that HFNP reduced intubation rates for bronchiolitis after the introduction of HFNP oxygen delivery. We used flow rates of 2 L/kg/min. Previous research has shown that these flows deliver a distending pressure of 4–8 cm H_2O (6). This improves functional residual capacity, thereby reducing work of breathing. Because flows are high, heated water humidification is necessary to avoid drying of respiratory secretions, minimize atelectasis, decrease heat loss, and maintain nasal cilia function (11). Our study showed that HFNP also has utility in the management of children with a wide variety of other conditions impairing oxygenation or the mechanics of breathing, including pneumonia, after cardiac surgery, and neuromuscular weakness. Although the majority of our experience with HFNP therapy was with infants who have traditionally been treated with NP-CPAP, 28 children (39%) were older, and HFNP was well-tolerated and effective also for children 5 years of age or older ($n = 8$).

The study has limitations. It was not randomized, and the treatment reflected current practice. There were no significant differences between the two groups in the baseline severity criteria measured. However, more children with a diagnosis of pneumonia received HFNP therapy (Table 3). NP-CPAP was given for a much longer time than HFNP, possibly partly reflecting differences in case-mix or differences in severity that are not apparent from the baseline variables measured. We are

TABLE 6. Sedation Use in All Episodes of High-Flow Nasal Prong or Nasopharyngeal Continuous Positive Airway Pressure: Median (Interquartile Range) or Percent

Measurement of Sedation Use	HFNP	CPAP	*p*
Percentage who received sedation during respiratory support	38.0 (38/100)	60.0 (33/55)	0.09
Percentage who received >1 sedation drug during respiratory support	5.0 (5/100)	10.9 (6/55)	0.17
Dose of chloral hydrate (mg/kg/hr respiratory support)	0.79 (0.57–1.62) ($n = 37$)	0.81 (0.39–1.51) ($n = 32$)	0.60

CPAP = continuous positive airway pressure; HFNP = high-flow nasal prong.

not concluding from this study that HFNP is as effective as NP-CPAP in all children, but that HFNP provides sufficient support for a majority of children with a wide variety of conditions who would otherwise receive NP-CPAP. The proportion of children requiring escalation to other forms of respiratory support (29%) is comparable with the study of Schibler et al (4), where 30% of children overall treated with HFNP therapy required escalation to either other noninvasive ventilation or invasive ventilation.

HFNP was associated with a trend toward less use of sedation and fewer complications than NP-CPAP, and HFNP was well-tolerated. The use of sedation can prolong length of stay in ICU, and this may be a factor in the longer duration of respiratory support in infants on NP-CPAP. Another explanation for the shorter duration of support required by children on HFNP therapy may be the ease of weaning to standard flow oxygen, which requires merely a reduction in the flow rate and increase the delivered oxygen concentration to 100%. With NP-CPAP, the patient interface needs to change, and the risk of failing and needing to reinsert an NP tube may discourage or delay trials of weaning.

The simple criteria we used for assessing patients can be measured at the bedside and were valid measures of stability and, if used in a guideline, can identify children who may need escalation of respiratory support in a timely manner. If children in the first 2 hours of HFNP did not achieve a reduction in two or more of RR and HR by 20% or to within the normal range, or the F_{IO_2} could not be weaned to less than 0.5, there was an increased risk of escalation to other forms of respiratory support.

We conclude that HFNP therapy is an effective treatment for moderate-to-severe respiratory distress from a variety of causes in children younger than 5 years. In older children, the therapy is also promising, but given the small sample size, further research is warranted. HFNP may require less sedation than CPAP delivered using a nasopharyngeal tube and the effectiveness of HFNP can be monitored clinically by simple bedside observations. HFNP therapy adds to treatments that can make intensive care for seriously ill children simpler, less invasive, and less distressing. Implementation requires standardized equipment, guidelines, training for staff, and ongoing monitoring for guideline compliance, and complications. HFNP therapy has the potential to be used in general wards and in regional hospitals if comprehensive implementation approaches are adopted. This might reduce the need for referral of infants and children with moderate respiratory distress, and free up intensive care beds, but this approach requires more experience with HFNP therapy in different clinical settings and carefully conducted implementation research to ensure its safety.

REFERENCES

1. Lampland AL, Plumm B, Meyers PA, et al: Observational study of humidified high-flow nasal cannula compared with nasal continuous positive airway pressure. *J Pediatr* 2009; 154:177–182
2. Spentzas T, Minarik M, Patters AB, et al: Children with respiratory distress treated with high-flow nasal cannula. *J Intensive Care Med* 2009; 24:323–328
3. McKiernan C, Chua LC, Visintainer PF, et al: High flow nasal cannulae therapy in infants with bronchiolitis. *J Pediatr* 2010; 156:634–638
4. Schibler A, Pham TM, Dunster KR, et al: Reduced intubation rates for infants after introduction of high-flow nasal prong oxygen delivery. *Intensive Care Med* 2011; 37:847–852
5. Hough JL, Shearman AD, Jardine LA, et al: Humidified high flow nasal cannulae: Current practice in Australasian nurseries, a survey. *J Paediatr Child Health* 2012; 48:106–113
6. Dysart K, Miller TL, Wolfson MR, et al: Research in high flow therapy: Mechanisms of action. *Respir Med* 2009; 103:1400–1405
7. Devlin JW, Nava S, Fong JJ, et al: Survey of sedation practices during noninvasive positive-pressure ventilation to treat acute respiratory failure. *Crit Care Med* 2007; 35:2298–2302
8. Slater A, Shann F, Pearson G; Paediatric Index of Mortality (PIM) Study Group: PIM2: A revised version of the Paediatric Index of Mortality. *Intensive Care Med* 2003; 29:278–285
9. Slater A, Shann F, McEniery J; ANICS Study Group: The ANZPIC registry diagnostic codes: A system for coding reasons for admitting children to intensive care. *Intensive Care Med* 2003; 29:271–277
10. Fleming S, Thompson M, Stevens R, et al: Normal ranges of heart rate and respiratory rate in children from birth to 18 years of age: A systematic review of observational studies. *Lancet* 2011; 377:1011–1018
11. Waugh JB, Granger WM: An evaluation of 2 new devices for nasal high-flow gas therapy. *Respir Care* 2004; 49:902–906