Post-extubation non-invasive ventilation in the pediatric intensive care unit: a multicenter study

Juan P. Bonora, B.S.[a], Judith Frydman, B.S.[b], Alejandra Retta, B.S.[c] and Andrea Canepari, B.S.[d]

ABSTRACT

Introduction. Extubation failure is a complication that increases morbidity and mortality. Non-invasive ventilation (NIV) has demonstrated to be effective as ventilatory support therapy.

Objective. To determine the rate of post-extubation NIV success and the factors associated with procedural failure or success.

Population and methods. Design: observational, retrospective, analytical, and multicenter study. All patients who required post-extubation NIV during 2014 and 2015 were included. Rescue NIV was defined as the implementation of NIV for acute respiratory failure; elective NIV was described as its implementation for prophylaxis. NIV failure was defined as the need for orotracheal intubation within the first 48 hours. The characteristics of failure and success and the types of NIV were compared, and the equipment used was assessed.

Results. Rescue NIV was required in 112 children; elective NIV, in 143. The rates of success were 68.8% and 72.7%, respectively. Mortality was higher among patients in whom rescue NIV failed compared to those with successful NIV. A longer length of stay and more days of invasive mechanical ventilation prior to extubation were observed in the elective NIV group. The most common diagnosis was acute lower respiratory tract infection in previously healthy children.

Conclusions. The use of post-extubation NIV may be a useful tool to prevent reintubation with invasive mechanical ventilation. Immunocompromised patients and those with neurological history had a higher rate of failure. Patients with failure tolerated less hours of NIV and had a longer length of stay in the pediatric intensive care unit.

Key words: *non-invasive ventilation, pediatrics, tracheal extubation.*

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a. Hospital de Pediatría "Prof. Dr. Juan P. Garrahan."
b. Hospital Central de Pediatría de Malvinas Argentinas.
c. Hospital de Niños "Dr. Ricardo Gutiérrez."
d. Hospital Italiano de Buenos Aires. Autonomous City of Buenos Aires.

E-mail address:
Juan P. Bonora, B.S.: juampabon@yahoo.com.ar

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INTRODUCTION

Respiratory failure is one of the main reasons for admission to the pediatric intensive care unit (PICU). Children frequently require invasive mechanical ventilation (IMV) as part of a therapeutic approach, which, despite allowing to modify the prognosis, involves life-threatening complications that extend the length of stay in the hospital.[1]

Post-extubation respiratory failure is a relatively common complication that remarkably increases morbidity and mortality.[2,3] The rate of extubation failure among children ranges from 3% to 22%.[4] For this reason, strategies aimed at preventing reintubation in this population are required.

Non-invasive ventilation (NIV) has gained impetus as a ventilatory support therapy for pediatric patients.[1,5] Its implementation/administration reduces the use of accessory muscles, heart rate, and respiratory rate.[1] The main advantage of NIV is that it prevents orotracheal intubation (OTI) and, therefore, any associated risk.[2,3]

Several studies have analyzed the use and effectiveness of NIV in pediatric patients.[6-8] Some included all patients who required this type of ventilatory support, whereas other reports excluded post-extubation NIV from analysis because of the different characteristics of patients compared to those who had not previously received IMV.[9]

The bibliography on the use of post-extubation NIV in the pediatric population is scarce.[10]

OBJECTIVE

To determine the rate of post-extubation NIV success and the factors associated with procedural failure or success.

MATERIALS AND METHODS

This was an observational, retrospective, analytical, and multicenter study. The study lasted

2 years. All patients aged 1 month to 18 years old who required post-extubation NIV between January 1st, 2014 and December 31st, 2015 in four multipurpose PICUs of tertiary care facilities were included.

Patients were extubated after a spontaneous breathing trial in accordance with the criteria in place at each facility.

Rescue NIV (rNIV) was defined as the implementation of NIV for acute respiratory failure within the first 48 hours after extubation. Respiratory failure was defined as type I or type II respiratory failure and/or upper airway obstruction.[11]

Elective NIV (eNIV) was defined as the implementation of NIV immediately after extubation for prophylaxis due to a potential risk for failure. eNIV was implemented in patients with prolonged IMV,[12,13] prior extubation failures, weakness caused by intrinsic muscle disease, weakness of the inspiratory muscles evidenced by a reduced diaphragmatic mobility in the ultrasound or maximal inspiratory pressure below -20 cmH_2O, heart disease or relevant respiratory history.

The physical therapists working at each PICU recorded data every day using cards and collecting information from the medical records.

Interfaces included full-face masks, helmets, oronasal masks, nasal masks, and nasal cannulae. The interface choice depended on the patient's age and/or availability; full-face and oronasal masks were prioritized for acute respiratory failure patients, whereas nasal masks were reserved for chronic conditions.

Microprocessor-controlled ventilators with NIV-dedicated software, intermediate ventilators, and continuous flow bi-level ventilators were used.[14] The ventilator was selected depending on its availability at each PICU.

Ventilation modes included pressure support ventilation, pressure-assist/control ventilation, bi-level pressure support delivered in the spontaneous or spontaneous/timed mode, and continuous positive airway pressure. The ventilation mode was chosen based on the patient's condition in an attempt to achieve the best patient-ventilator synchrony. The prevailing mode during NIV requirement was taken into consideration.

The ventilation strategy consisted in using positive end-expiratory pressure (PEEP) and fraction of inspired oxygen (FiO_2) levels necessary to achieve an oxygen saturation above 92% and the assistance pressure necessary to reach a tidal volume between 8 and 10 mL/kg. Once the therapeutic target is achieved, ventilatory parameters were progressively reduced, with rotation of the interface or periodic equipment disconnection, depending on the patient's stability in terms of clinical, blood gases, and radiological parameters, until ventilatory support was removed completely.

The following outcome measures were considered: age, weight, sex, severity score (pediatric index of mortality 2, PIM2), length of stay in the PICU (days), reason for admission to the PICU (cardiac, respiratory, neurological, postoperative period after non-cardiovascular surgery, septic shock, external injury, other), diagnosis (trauma, acute lower respiratory tract infection [ALRTI], ALRTI in a patient with sequelae [from prior comorbidities], postoperative period of a general surgery, neurosurgery, neuromuscular condition, immunocompromise, acute neurological event, non-respiratory infection, heart failure, other), reason for implementation of NIV (respiratory distress, hypoventilation, upper airway obstruction, risk for extubation failure), history (sequelae of lung disease, heart disease, neurological injury, immunocompromise, airway, digestive or liver malformations, more than one factor corresponding to the history).

The different comorbidities present in the patients were classified based on the history outcome measure, considering the classification mentioned by Feudtner et al.,[15] which coded patients based on the type of chronic disease.

The following parameters were monitored: partial pressure of oxygen (PO_2), saturation and partial pressure of carbon dioxide (PCO_2) prior to NIV, and delta of pressure, PEEP, FiO_2 or liters of oxygen (O_2) at NIV initiation.

To measure technique effectiveness, the following outcome measures were recorded: NIV type (rescue, elective), NIV result (success, failure), hours of NIV, days of IMV prior to extubation, and mortality. NIV failure was defined as the need for endotracheal intubation within the first 48 hours in accordance with the criteria in place at each PICU. Depending on the time of failure, initial failure was defined as the need for reintubation within the first hour; early failure, as the need for reintubation from 1 to 12 hours; and late failure (> 12 hours), as the need for reintubation in any other occasion.[5] The reasons for failure included

progression of respiratory distress, hypoxemia, impaired sensorium, upper airway obstruction, hemodynamic alterations, and inability to protect the airway.

Statistical analysis

The sample was described using the median as a measure of central tendency and the 25-75 interquartile range as a measure of dispersion for numerical outcome measures; whereas, absolute count and percentage were used for categorical outcome measures. Numerical outcome measures were compared using the Mann-Whitney test and categorical outcome measures, using the χ^2 test. A p value < 0.05 was considered statistically significant. Data were analyzed using the IBM SPSS Macintosh software, version 20.0 (IBM Corp., Armonk, NY, USA).

RESULTS

A total of 255 patients who received post-extubation NIV were included. *Figure 1* shows the flow chart of included patients.

The clinical and demographic characteristics of patients are described in *Table 1*.

The success of eNIV reached 72.7%. A comparison of relevant clinical outcome measures between patients who experienced eNIV failure or success is shown in *Table 2*.

The success of rNIV reached 68.8%. *Table 3* describes the differences between patients who experienced rNIV failure or success.

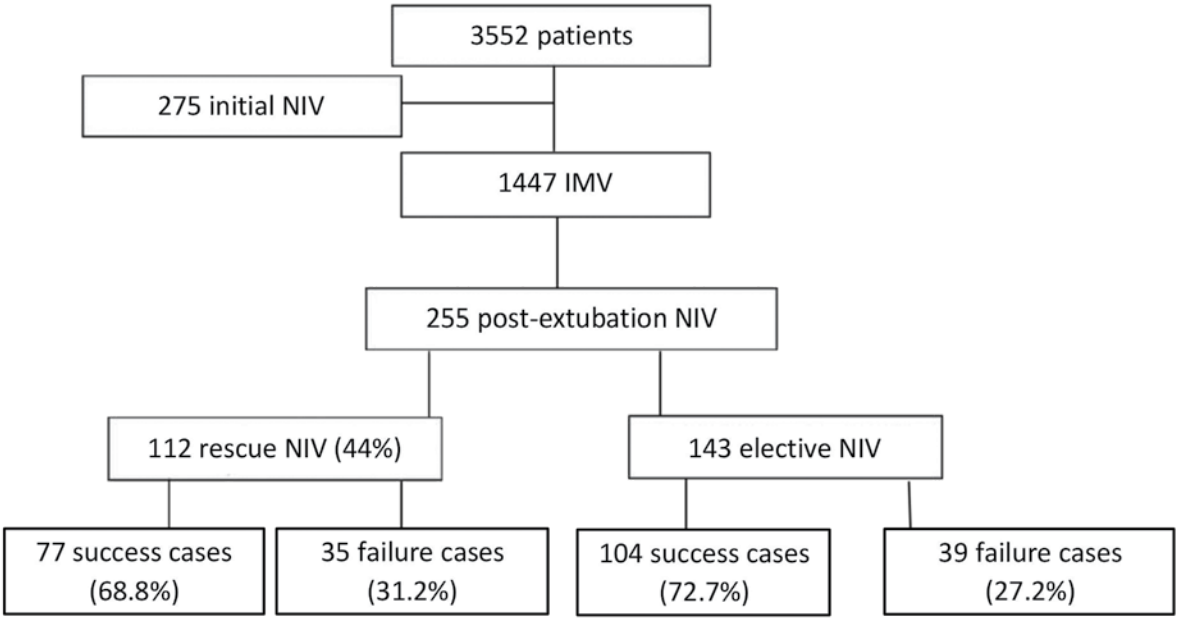
The full-face mask was the most commonly used interface (106 patients, 41.6%), followed by the oronasal mask (28.6%), nasal cannula (16%), nasal mask (8.6%), nasal pillow mask (4.3%), and helmet (0.8%).

Also, 69% of ventilators were microprocessor-controlled ventilators for intensive care with software to account for leakages; 29% were intermediate ventilators, and only 2% were continuous flow bi-level ventilators.

Ventilation modes included pressure support (70.5%), pressure assist-control (26.1%), bi-level pressure support delivered in the spontaneous/timed mode (1.7%), and continuous positive airway pressure (1.7%).

The total analysis of failures revealed that 60% corresponded to late failure; 20%, to early failure; and 20%, to initial failure. The causes of failure in the eNIV and rNIV groups were progression of respiratory distress (38.5% and 19.7%), upper airway obstruction (15.4% and 36.3%), inability to protect the airway (15.4% and 13.3%), impaired sensorium (11.5% and 13.3%), hypoxemia (11.5% and 6.7%), and hemodynamic alterations (7.7% and 10.7%, respectively). Patients with neurological history and immunocompromised

FIGURE 1. *Flow chart of patients*



NIV: non-invasive ventilation; IMV: invasive mechanical ventilation.

patients had a higher rate of failure (n = 19; 41.3% and n= 13; 39.4%, respectively) compared to those with other comorbidities, for whom the rate of failure was similar to that of the population without prior sequelae (n= 19; 21.7%) (p= 0.007).

The overall mortality of patients with post-extubation NIV was 4.4% (11 patients). Eight deaths (5.6%) were recorded in the eNIV group; of these, 4 corresponded to those with successful eNIV, 1 with initial failure, and 3 with late failure.

Only 3 patients died in the rNIV group: 1 case of initial failure, 1 case of early failure, and 1case of late failure.

DISCUSSION

In the studied population, it was possible to avoid reimplementation of IMV in 71% of patients. Patients' median age, weight, and mortality score were 15 months, 15 kg, and 4.8, respectively. Besides, 48.3% of patients were girls; the most common diagnosis was respiratory infection in previously healthy children. No significant differences were observed between failure and success cases in terms of any of these outcome measures.

eNIV accounted for 56% of studied children. Gupta et al. allocated patients to receive eNIV if

TABLE 1. *Demographic outcome measures*

Outcome measure	**Post-extubation NIV n = 255**	**Rescue NIV n = 112**	**Elective NIV n = 143**
Age (months old), median (Q_2-Q_3)	15 (4-72)	21 (4-81)	12 (4-66)
Weight (kg), median (Q_2-Q_3)	15 (7-26)	15 (7.5-25)	12,5 (6,75-30)
Sex, n (%)	122 (48,4%) fem.	59 (52,3%) fem.	65 (45,4%) fem.
PIM2, median (Q_2-Q_3)	4,8 (1,52-10,6)	4,65 (1,5-10)	5,6 (1,54-10.8)
Diagnosis, n (%):			
Trauma	9 (3.5%)	7 (6.3%)	2 (1.4%)
ALRTI in previously healthy child	70 (27.5%)	27 (24.1%)	43 (30.1%)
ALRTI in a patient with sequelae	47 (18.4%)	14 (12.5%)	33 (23.1%)
Post-operative period of a general surgery	41 (16.1%)	19 (17%)	22 (15.4%)
Neurosurgery	9 (3.5%)	8 (7.1%)	1 (0.7%)
Neuromuscular condition	9 (3.5%)	2 (1.8%)	7 (4.9%)
Immunocompromise	13 (5.1%)	6 (5.4%)	7 (4.9%)
Acute neurological event	11 (4.3%)	5 (4.5%)	6 (4.2%)
Non-respiratory infection	24 (9.4%)	13 (11.6%)	11 (7.7%)
Heart failure	3 (1.2%)	-	3 (2.1%)
Other	19 (7.5%)	11 (9.8%)	8 (5.6%)
Reason for admission to the PICU, n (%):			
Cardiac	10 (3.9%)	3 (2.7%)	7 (4.9%)
Respiratory	114 (44.7%)	40 (35.7%)	74 (51.7%)
Neurological	14 (5.5%)	8 (7.1%)	6 (4.2%)
Post-operative period after non-cardiovascular surgery	52 (20.4%)	28 (25%)	24 (16.8%)
Septic shock	39 (15.3%)	17 (15.2%)	22 (15.4%)
External injury	12 (4.7%)	10 (8.9%)	2 (1.4%)
Other	14 (5.5%)	6 (5.4%)	8 (5.6%)
History, n (%):			
Heart disease	17 (6.7%)	4 (3.6%)	13 (9.2%)
Sequelae of lung disease	25 (9.9%)	12 (10.9%)	13 (9.2%)
Neurological injury	46 (18.3%)	21 (19.1%)	25 (17.6%)
Immunocompromise	33 (13.1%)	14 (12.7%)	19 (13.4%)
Airway, liver, digestive malformation	29 (11.5%)	15 (13.6%)	14 (9.9%)
More than one factor corresponding to history	16 (5.2%)	5 (4.5%)	8 (5.6%)
No history	89 (35.3%)	41 (37.3%)	51 (35.9%)
Reason for implementation of NIV, n (%):			
Respiratory distress	75 (28.2%)	72 (64.3%)	-
Hypoventilation	19 (7.5%)	16 (14.3%)	-
Upper airway obstruction	24 (9.4%)	24 (21.4%)	-
Risk for extubation failure	143 (54.9%)	-	143 (100%)

Q_2-Q_3: 25%-75% quartile; fem.: female; ALRTI: acute lower respiratory tract infection; PICU: pediatric intensive care unit; PIM2: severity score.

they were at a high risk for extubation failure and if they were weaning from IMV, and achieved a success rate of 74%.[16] In addition, James et al. reached a 90% success rate with eNIV in children who were in the immediate postoperative period.[17] In our study, the success of eNIV was 72.7%, which was similar to that observed in comparable studies.[9,18] A direct association was observed between the hours of NIV and therapeutic success, and a reverse association was noted between the length of stay in the PICU and NIV success. This evidences that patients with successful NIV remained more hours in NIV, but had a shorter stay in the PICU. Although we believe that, in our study, some children in this group would have possibly avoided OTI without eNIV, the potential side effects of this therapy appear to be minimal.

rNIV accounted for 44% of cases. As in the study by Gupta et al.,[16] our results show an association between a reduced mortality and ventilatory support success. In addition, Mayordomo-Colunga et al. observed a 50% success rate in their pilot study.[9] In this group, the rate of success was 68.8%, which seems logical considering that conditions are different from the eNIV group that used the therapy as prophylaxis, whereas in the rNIV group patients had signs of respiratory failure. The bibliography on the use of rNIV in the pediatric population is scarce. Studies in the adult population have not been conclusive in relation to its use. Esteban et al. demonstrated,

TABLE 2. *Elective non-invasive ventilation*

Outcome measure	Successful (n = 104)	Failed (n = 39)	p value
Age (months old), median (Q_2-Q_3)	12 (5-60)	15 (4-85)	0.85
Weight (kg), median (Q_2-Q_3)	12 (7-27.5)	17 (5.75-36)	0.29
PIM2, median (Q_2-Q_3)	4.5 (0.95-10.8)	7.4 (2.4-11.8)	0.14
Length of stay in the PICU (days), median (Q_2-Q_3)	21 (15-28)	28 (17-45.5)	0.019
O_2 saturation (%), median (Q_2-Q_3)	99 (97-100)	98 (97-100)	0.16
PaO_2 (mmHg), median (Q_2-Q_3)	148 (120-183)	138 (104-167.2)	0.61
ΔP (cmH_2O), median (Q_2-Q_3)	9 (7-10)	10 (7.5-11)	0.18
PCO_2 (mmHg), median (Q_2-Q_3)	37 (31.2-42.3)	38.5 (33-46.5)	0.56
PEEP (cmH_2O), median (Q_2-Q_3)	5 (5-6)	6 (5-7)	0.12
FiO_2, median (Q_2-Q_3)	0.5 (0.4-0.6)	0.5 (0.4-0.6)	0.33
Days of prior IMV, median (Q_2-Q_3)	10 (5-15)	10 (5.5-22)	0.47
Hours of NIV, median (Q_2-Q_3)	72 (35.2-120)	24 (20-66)	< 0.001
Mortality, n (%)	4 (3.9%)	4 (11%)	0.1
History, n (%)	62 (60.2%)	30 (76.9%)	0.062

Q_2-Q_3: 25%-75% quartile; PaO_2: partial pressure of oxygen in arterial blood; PCO_2: partial pressure of carbon dioxide; PEEP: positive end expiratory pressure; ΔP: Delta of pressure; FiO_2: fraction of inspired oxygen; PICU: pediatric intensive care unit; NIV: non-invasive ventilation; O_2: oxygen; PIM2: severity score.

TABLE 3. *Rescue non-invasive ventilation*

Outcome measure	Successful (n = 77)	Failed (n = 35)	p value
Age (months old), median (Q_2-Q_3)	30 (4-84)	10 (3-60)	0.6
Weight (kg), median (Q_2-Q_3)	15 (7.2-24.7)	14 (6.5-26)	0.59
PIM_2, median (Q_2-Q_3)	4.5 (1.8-10)	4.8 (1-9.7)	0.49
Length of stay in the PICU (days), median (Q_2-Q_3)	15.5 (11-24.25)	22 (15-37)	0.005
O_2 saturation (%), median (Q_2-Q_3)	99 (97-100)	99 (95-100)	0.6
PaO_2 (mmHg), median (Q_2-Q_3)	122.7 (132.5-165.5)	101.5 (81.1-232.7)	0.2
PCO_2 (mmHg), median (Q_2-Q_3)	39.5 (33.7-44.1)	31.5 (29.2-37.5)	0.08
ΔP (cmH_2O), median (Q_2-Q_3)	10 (7-10)	10 (8-11)	0.2
PEEP (cmH_2O), median (Q_2-Q_3)	5 (5-6)	6 (5-7)	0.15
FiO_2, median (Q_2-Q_3)	0.5 (0.4-0.6)	0.6 (0.5-0.6)	0.2
Days of prior IMV, median (Q_2-Q_3)	5 (2.5-10)	6 (3-9)	0.33
Hours of NIV, median (Q_2-Q_3)	66 (24-120)	24 (2-45)	< 0.001
Mortality, n (%)	-	3 (8.6%)	0.01
History, n (%)	48 (62.3%)	23 (69.7%)	0.46

Q_2-Q_3: 25%-75% quartile; PaO_2: partial pressure of oxygen in arterial blood; PCO_2: partial pressure of carbon dioxide; PEEP: positive end expiratory pressure; ΔP: Delta of pressure; FiO_2: fraction of inspired oxygen; PICU: pediatric intensive care unit; NIV: non-invasive ventilation; O_2: oxygen; PIM_2: severity score.

in a multicenter study, a higher mortality among patients who required rNIV compared to conventional therapy, and attributed such effect to a delay in reintubation times.[19] Keenan et al. did not find differences between both groups in terms of the reintubation rate and mortality.[20] Girault et al. observed that rNIV was beneficial for patients with hypercapnic ventilatory failure after extubation.[21] Dean Hess recommended caution in the use of rNIV and to prevent reintubation delays if no satisfactory response is observed in the first hour of implementation.[22]

In our study, 15% of patients who were admitted to the critical care unit required post-extubation NIV. This is comparable to what has been described by Wolfler et al. in a study with 13 Italian intensive care units where the percentage was similar.[23]

The presence of a complex chronic disease seems to have an impact on the outcomes of NIV implementation.[15] In the studied population, 35% of patients had some type of prior comorbidity. Immunocompromised patients and those with neurological sequelae showed a higher percentage of failures. Mayordomo-Colunga et al. described a higher rate of failure among patients with neurological history and attributed it to pharyngeal hypotonia and inability to protect the airway adequately.[9]

The analysis of failures revealed that most patients had a late failure. It has been described that a delay in reintubation increases mortality, so a late failure may increase it.[19,20] However, the low mortality level observed in the studied population prevented us from establishing an association with the types of failure.

Interfaces and harnesses play a key role in NIV use. Since the introduction of the full-face mask for pediatric patients in Argentina, in 2013, there has been an increase in its demand, and, at present, it has become the preferred interface. The mask adjusts on the front, cheeks, and chin of the face, all areas where there is much subcutaneous tissue, and this has helped to reduce pressure ulcers and improve patients' comfort, especially, younger ones. Chacur et al. found that the full-face mask was more comfortable than the oronasal mask for adult patients, allowing them to use it for more time, but the authors did not find differences in the success-failure rates.[24] Lemyze et al. managed to prevent intubation in adult patients with hypercapnic ventilatory failure who were receiving NIV for a prolonged time or who had facial injuries when changing from an oronasal mask to the full-face mask.[25]

Microprocessor-controlled ventilators are the most commonly used ones for NIV at the PICUs, which now include software to account for leakages. Faroux et al. compared, in a lab setting, the performance of 17 ventilators for NIV in pediatrics mimicking different clinical situations and patient weights. They concluded that no ventilator responded correctly to all simulation settings and had trouble working in younger children.[26] The reduced respiratory effort, the high respiratory rate, and leakages in pediatric patients are a major technological challenge that needs to be resolved by advances in ventilators.

The retrospective nature of this study makes it more susceptible to biases and errors. Besides, since this is a multicenter study, there is no information on the management of each patient's underlying condition at each participating PICU. Other limitation of this study is that it did not have a randomized, controlled design and lacked a control group with patients who did not receive NIV to prevent reintubation. In this regard, patients who received eNIV may have not required any type of positive pressure, and this may have affected the end results. Lastly, there is a semantic limitation because the authors worked in four different hospitals, so each may have used different terms typical of each PICU to record NIV events.

CONCLUSIONS

The use of post-extubation NIV may be useful to prevent the reimplementation of IMV. The most common diagnosis was ALRTI in previously healthy children. Immunocompromised patients and those with neurological history had a higher rate of failure compared to those with other comorbidities, for whom the rate of failure was similar to that of the population without prior sequelae. Patients with failure tolerated less hours of NIV and had a longer length of stay in the PICU. Further studies are required to confirm the effectiveness of post-extubation NIV in the pediatric population, as well as the influence of the different interfaces and ventilators on its performance. ■

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