Intensive Care Med (2009) 35:527–536
DOI 10.1007/s00134-008-1346-7

PEDIATRIC ORIGINAL

Juan Mayordomo-Colunga
Alberto Medina
Corsino Rey
Juan José Díaz
Andrés Concha
Marta Los Arcos
Sergio Menéndez

Predictive factors of non invasive ventilation failure in critically ill children: a prospective epidemiological study

Received: 20 April 2008
Accepted: 19 October 2008
Published online: 4 November 2008

J. Mayordomo-Colunga · A. Medina · C. Rey (✉) · A. Concha · M. Los Arcos · S. Menéndez
Paediatric Intensive Care Unit, Departamento de Pediatría, Hospital Universitario Central de Asturias, University of Oviedo, Celestino Villamil s/n, 33006 Oviedo, Asturias, Spain
e-mail: corsino.rey@sespa.princast.es

J. J. Díaz
Hospital San Agustín, Avilés, Asturias, Spain

Abstract *Objective:* Identification of predictive factors for non-invasive ventilation (NIV) failure and determination of NIV characteristics. *Design:* Prospective observational study. *Setting:* Paediatric Intensive Care Unit in a University Hospital. *Patients and measurements:* A total of 116 episodes were included. Clinical data collected were respiratory rate (RR), heart rate and FiO_2 before NIV began. Same data and expiratory and support pressures were collected at 1, 6, 12, 24 and 48 h. Conditions precipitating acute respiratory failure (ARF) were classified into two groups: type 1 (38 episodes) and type 2 (78 episodes). Ventilation–perfusion impairment was the main respiratory failure mechanism in type 1, and hypoventilation in type 2. Factors predicting NIV failure were determined by multivariate analysis. *Results:* Most common admission diagnoses were pneumonia (81.6%) in type 1 and bronchiolitis (39.7%) and asthma (42.3%) in type 2. Complications secondary to NIV were detected in 23 episodes (20.2%). NIV success rate was 84.5% (68.4% in type 1 and 92.3% in type 2). Type 1 patients showed a higher risk of NIV failure compared to type 2 (OR 11.108; CI 95%, 2.578–47.863). A higher PRISM score (OR 1.138; CI 95%, 1.022–1.267), and a lower RR decrease at 1 h and at 6 h (OR 0.926; CI 95%, 0.860–0.997 and OR 0.911; CI 95%, 0.837–0.991, respectively) were also independently associated with NIV failure. *Conclusions:* NIV is a useful respiratory support technique in paediatric patients. Type 1 group classification, higher PRISM score, and lower RR decrease during NIV were independent risk factors for NIV failure.

Keywords Non-invasive ventilation · Pediatrics · Respiratory monitoring

Introduction

Non invasive ventilation (NIV) is a relatively new ventilatory mode that has shown positive effects in adult patients with different types of respiratory failure [1]. Its most important effects are inspiratory muscle work reduction and gas exchange improvement [2].

Several studies in adult populations have shown that NIV is a safe and effective therapy for patients with hypercapnic acute respiratory failure (ARF) due to chronic obstructive pulmonary disease (COPD) exacerbation [3, 4] and hypoxemic ARF due to cardiogenic pulmonary oedema [5], community-acquired pneumonia [6], and immunocompromised patients with pulmonary infiltrates [7]. In hypoxemic ARF due to acute respiratory distress syndrome (ARDS)/acute lung injury (ALI) and in postextubation ARF, the role of NIV remains unclear and it should be applied in carefully selected patients [8–12].

NIV diminishes the rate of intubation when compared to conventional medical therapy [13]. NIV diminishes the

risk of ventilator-associated pneumonia and other nosocomial infections [14]. Moreover, NIV may improve survival when compared to conventional mechanical ventilation (CMV) [15].

NIV is also a well established therapy in neonates [16]. It has shown to reduce the need of CMV when applied after surfactant treatment [17], to be effective for early stabilization in very low birthweight infants [18], and in primary treatment of newborns with respiratory distress syndrome [19].

In children, most knowledge is derived from retrospective studies [20–25], little case series or case reports [26, 27] and preliminary results [28]. Most of reported results do not include a large number of patients [29, 30] or only focus on one disease [31, 32]. As a consequence, evidence is lacking in order to define indications, methods, conditions of use and complications of NIV in children.

Since respiratory pathologies seen in paediatric critical care population widely differ from pathologies seen in the adult or neonatal intensive care unit (ICU), and pathophysiology of ARF in children is different [33], extrapolation from adult or neonatal to paediatric population cannot be done.

It is very important to identify patients at risk of NIV failure. Some studies have been performed in adults to find outcome predictors [8, 9]. Predictive factors for NIV failure have been reported in paediatric patients, but they were based on retrospective data [20, 21] or they only analyzed bronchiolitis [31, 32]. There is only one prospective study which identifies some NIV outcome predictors in critically ill children [34]. Therefore, prospective information on paediatric NIV characteristics, and risk factors for NIV failure in children could be useful to improve therapeutic strategies of respiratory support. The primary objective of this study was to identify predictive factors of NIV failure in paediatric intensive care unit (PICU) patients. The secondary objective was to determine the characteristics of NIV in critically ill children.

Methods

Setting and patients

A prospective observational study set in an eight-bed PICU of a university hospital was performed. All patients admitted to our unit from August 2004 to July 2008 and deemed to be candidates to receive continuous positive airway pressure (CPAP) or pressure support ventilation (PSV) were included. CPAP was considered a type of NIV [35, 36]. Criteria to initiate NIV were: ARF or acute-on-chronic respiratory failure without improvement despite medical treatment, severe dyspnea at rest (modified Wood's Clinical Asthma Score $\geq$5 in asthma [37] or bronchiolitis [38]), a respiratory rate above 2 standard deviations (SD) for child's age normal range, or a partial pressure of arterial oxygen to the fraction of inspired oxygen (PaO_2:FiO_2) ratio under 250 and above 150, or venous PCO_2 >55 mmHg or arterial PCO_2 >50 mmHg (modified from Antonelli et al [8]). Contraindications to NIV support were cardiorespiratory arrest, hemodynamic instability despite fluid load and vasoactive treatment, Glasgow coma scale score under 10, facial deformity, facial trauma or surgery, vocal cords palsy, bullous pneumopathy, pneumothorax, endotracheal intubation to manage secretions or airway protection, and upper gastrointestinal tract active bleeding.

ARF was defined as failure to sustain a threshold level of alveolar exchange to meet the metabolic demands of cellular respiration and classified in type 1 and 2 using pathophysiological and clinical criteria modified from Teague [33]. ARF with ventilation–perfusion impair, hypoxemia and parenchymal condensations on X-ray was considered as type 1. ARF with hypoventilation, hypercapnia without hypoxemia, and parenchymal condensations absence on X-ray (excluding atelectasis) was considered as type 2. Bronchiolitis was the only ARF cause classified in either type 1 or 2 group.

NIV technique

CPAP or pressure support ventilation (PSV) was delivered using a nasal mask, face mask, full-face mask or nasal prongs. The interface was chosen according to child's age and size achieving comfortability and avoiding air leaks. Initially it was applied manually onto the patient's face, and then it was held by a paediatric head cap. Colloid dressings were placed on the major pressure points to minimize skin injury. A heated humidifier (Fisher and Paykel Healthcare, Auckland, New Zealand) was used in all cases.

Ventilation strategy

Based on the protocol published by "Respiratory Group of the Spanish Society of Paediatric Intensive Care" [39], CPAP initial ventilator setting was 4–5 cmH_2O; PSV was started at 4–6 cmH_2O and expiratory positive airway pressure (EPAP) at 4 cmH_2O. PSV was increased if the attending physician considered that inspiratory volume was low according to auscultation and thoracic motion, and if hypercarbia increased or did not decrease. CPAP or EPAP were increased if no improvement of pulse-oximetry O_2 saturation or arterial PO_2 was achieved. NIV was stopped and patients were intubated when oxygen saturation was below 85% or venous PCO_2 above 65 mmHg despite maximal NIV setting, or when any of the exclusion criteria appeared.

Sedation

Midazolam intravenous boluses (0.1 mg/kg) followed by continuous perfusion (0.05–0.1 mg/kg/h) when needed were used if the child was stressed with consequent patient–ventilator asynchrony.

Feeding

A nasogastric tube was placed in all patients to avoid gastric distension or vomiting, and afterwards it was used to provide feeding when possible.

Monitoring

All patients were continuously monitored by means of electrocardiography, pulse oximeter and respiratory rate. Blood gas analysis was only performed when considered necessary by the attending physician.

NIV outcome

NIV was deemed successful when conventional mechanical ventilation (CMV) was not necessary. If CMV was needed, the episode was considered as a failure.

Data collection

Patients with multiple admissions were considered individually, since each episode requiring NIV presents new variables potentially affecting outcome. For each episode, the following variables were collected: age, sex, weight, PICU and hospital stay, ARF type, ARF cause, underlying disease, Paediatric Risk of Mortality (PRISM) score, type of interface, NIV duration, NIV outcome, CMV duration, use of sedatives, NIV complications, mortality and causes of death. Clinical data collected were respiratory rate (RR), heart rate (HR) and FiO_2 before NIV was started. The same data and CPAP, EPAP and PSV were collected at 1, 6, 12, 24 and 48 h. Complementary explorations collected were blood gas analysis and X-ray.

Statistical analysis

Descriptive analysis

Mean, median, standard deviation and range were used to describe the sample. We compared success and failure groups as well as type 1 and type 2 ARF groups. Quantitative continuous variables were compared between groups using non parametric tests (Mann Whitney's U test), and qualitative variables using Chi-square test (χ^2).

Predictive factors for NIV failure

A logistic regression analysis was performed in order to identify possible predictors of NIV failure. Multiple logistic regression analysis was performed before NIV start and after 1, 6, 12, 24 and 48 h. Variables included in the multivariate analysis were those which had a p value under 0.2 in univariate analysis between success and failure groups, and also those variables which were considered clinically important in order to control statistical confusion. Variables included in the model were age, weight, mean HR difference to initial HR, mean RR difference to initial RR, FiO_2, ARF type and PRISM score. Before NIV was started, RR and HR were also included, instead of HR or RR difference. At 24 and 48 h, EPAP was also included. Venous PCO_2 was excluded due to the lack of data. A p value < 0.05 was considered statistically significant.

This research project was approved by the Research Ethics Committee of the Hospital Universitario Central de Asturias. Written informed consent was obtained from patients' parents or guardians.

Results

Descriptive study

During the study period, there were 1,111 consecutive admissions to the PICU. There were 214 episodes of CMV and 171 of NIV with 42 patients receiving both types of respiratory support. Thirty-seven cases were excluded because of postextubation and obstructive sleep apnoea NIV indications. Also 18 episodes were excluded because an Infant Flow™ system was used. Then, 116 episodes were analyzed (Fig. 1). Type 1 ARF was indication for NIV in 38 episodes (32.8%), while type 2 ARF was indication in 78 (67.2%). Baseline characteristics of included cases are shown in Table 1.

Interfaces and ventilators

Face masks were used in 89 episodes and nasal masks in 27 cases. Face mask was chosen in 71.1% of ARF type 1 cases and in 79.5 % of ARF type 2. No statistical relation was found between type of interface and age, weight or NIV indication.

We employed in all episodes specific ventilators for NIV: in one case a Vivo™ (Breas, Mölnlycke, Sweden), in

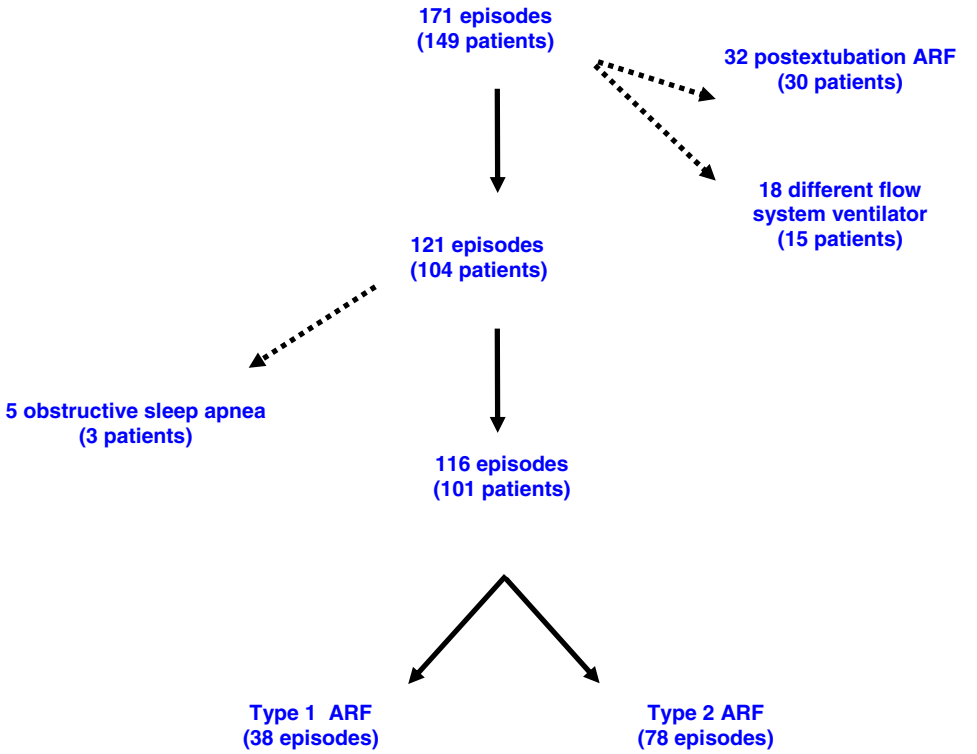

Fig. 1 Flow chart of patients and episodes included in the study and its classification in type 1 or type 2 acute respiratory failure groups. *ARF* acute respiratory failure

two cases BiPAP® Harmony® (Respironics, Pittsburgh, PA) and in the rest of them BiPAP® Vision® (Respironics, Pittsburgh, PA). In only three cases CPAP was used.

NIV duration

NIV median duration was 41.0 h (range: 0.5–375); 45.0 h (range 11–375) in successful cases, and 13.0 h (range: 0.5–77) in failure episodes.

Pressures applied

Mean maximum EPAP was significantly higher in type 1 ARF group (8.2 ± 1.7 vs. 6.7 ± 1.2 cmH_2O; $p < 0.001$). No significant differences were observed in PSV between ARF groups.

Evolution of clinical parameters

A progressive decrease of FiO_2, HR and RR was seen during NIV therapy. Evolution of RR is shown in Fig. 2. HR decreased from 158.1 ± 30.0 before NIV to 127.0 ± 27.3 at 6 h in type 1 ARF, and from 165.0 ± 28.5 to 138.5 ± 21.0 in type 2 ARF. FiO_2 decreased from 0.51 ± 0.30 before NIV to 0.41 ± 0.14 at 6 h in type 1 ARF, and from 0.39 ± 0.19 to 0.37 ± 0.14 in type 2 ARF.

Sedatives

Midazolam boluses were administered in 12.2% of the cases and continuous perfusion of midazolam was needed in 52.2%. Median age of patients who received midazolam boluses or perfusion was 8.5 months (range 0.6–163.8), significantly lower than children's who were not given any sedative (34.2 months, range 0.8–169.7; $p = 0.001$). There were no secondary effects due to sedatives and no failure could be attributed to this medication.

NIV complications

Complications were detected in 23 cases (20.2%). A non-deep skin lesion, without producing skin necrosis, was found in 18 cases, three developed a pneumothorax, one had an upper airway bleeding, and another one had a gastric distension. Skin injuries were directly related with NIV duration (92.5 h, range 16–248, vs. 39.0 h, range 0.5–375; $p < 0.001$). None of the children with a skin lesion needed analgesics and no failures could be attributed to this cause.

Table 1 Base-line characteristics of the non-invasive ventilation episodes and ARF causes

	Whole sample ($N = 116$)	Type 1 ARF ($N = 38$)	Type 2 ARF ($N = 78$)	P value
Variable				
Age (months)	10.3 (0.6–169.7)	22.1 (1–169.1)	8.0 (0.6–169.7)	0.007
Males	64.7%	60.5%	66.7%	0.516
Weight (kg)	9.0 (2.8–58.0)	11.0 (4.0–55.0)	8.0 (2.8–58.0)	0.030
PRISM score	8.1 ± 5.2	9.1 ± 6.4	7.6 ± 4.5	0.197
HR (beats/min)	162.8 ± 29.0	158.1 ± 30.0	165.0 ± 28.5	0.236
RR (breaths/min)	52.5 ± 17.7	53.6 ± 16.0	52.0 ± 18.6	0.666
FiO_2 (%)	43.3 ± 23.8	51.0 ± 29.9	39.4 ± 18.9	0.035
Venous PCO_2 (mmHg)	49.6 ± 15.0	44.6 ± 13.3	51.7 ± 15.3	0.043
ARF causes, no (%)				
Bronchiolitis		2 (5.2)	31 (39.7)	
Pneumonia		31 (81.6)	0 (0)	
Asthma		0 (0)	33 (42.3)	
Upper airways respiratory infection		0 (0)	6 (7.7)	
Laryngitis		0 (0)	2 (2.6)	
Central apnoeas		0 (0)	5 (6.4)	
ARDS		3 (7.9)	0 (0)	
Others		2 (5.3)	1 (1.3)	
Underlying disease				
None		19 (50.0)	52 (66.7)	
Neuromuscular disease		2 (5.3)	8 (10.3)	
Immunodeficiency		7 (18.4)	0 (0)	
Restrictive pulmonary dis.		1 (2.6)	1 (1.3)	
Sepsis		4 (10.5)	1 (1.3)	
Congenital cardiopathy		2 (5.3)	3 (3.8)	
BPD		0 (0)	2 (2.6)	
Others		3 (7.9)	11 (14.0)	

Age and weight are expressed in median and range, sex in %, and the rest of variables are expressed in mean ± standard deviation. P value refers to the comparison between type 1 and type 2 ARF groups

PRISM paediatric risk of mortality, *HR* heart rate, *RR* respiratory rate, *ARDS* acute respiratory distress syndrome, *BPD* bronchopulmonary dysplasia

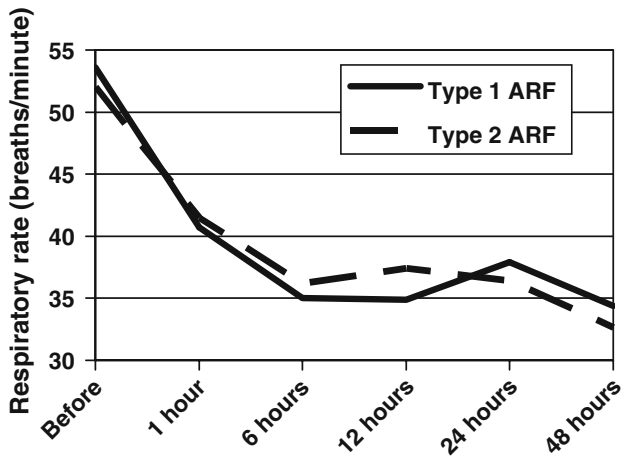

Fig. 2 Evolution of respiratory rate at the hours studied in type 1 and 2 acute respiratory failure groups. *ARF* acute respiratory failure

Outcome

Ninety-eight episodes succeeded (84.5%). Success was more frequent in type 2 than in type 1 group [92.3% (CI 95%: 98.2–86.4) vs. 68.4% (CI 95%: 83.1–53.7); $p = 0.001$]. Baseline characteristics of successful and failed episodes are shown in Table 2. NIV failure before 6 h was significantly more frequent in ARF type 2 group: three out of six episodes, while only two out of 12 cases in ARF type 1 group ($p = 0.024$). Causes of NIV failure were hemodynamic instability, apneas and hypoxemia (five episodes for each cause), hypercapnia in two episodes, and pneumothorax in one.

PICU stay

Median PICU length of stay was 7 days (range 2–157). In failure episodes it was 14.5 days (range 3–134), while it was 7 days (range 2–157) in successful cases ($p = 0.003$).

Mortality

Five patients died. None of the deaths were related to the use of NIV. Nevertheless NIV had failed in four out of five of these patients. In the case in which NIV had not failed, death was due to a massive intestinal necrosis in a patient with leukemia (47 days after NIV). In three

Table 2 Base-line characteristics of non-invasive ventilation episodes in success and failure groups

	Success group ($N = 98$)	Failure group ($N = 18$)	P value
Variable			
Age (months)	11.6 (0.6–169.7)	6.1 (0.8–115.9)	0.028
Males	62.2%	77.8%	0.205
Weight (kg)	9.6 (2.8–58.0)	6.3 (2.8–39.0)	0.016
PRISM score	7.4 ± 4.4	11.7 ± 7.6	0.026
HR (beats/min)	162.4 ± 30.2	165.1 ± 22.4	0.972
RR (breaths/min)	53.5 ± 18.2	47.5 ± 14.5	0.231
FiO_2 (%)	43.6 ± 23.5	40.8 ± 24.9	0.293
Venous PCO_2 (mmHg)	48.6 ± 14.9	57.8 ± 14.3	0.062

Age and weight are in median and range, sex in %, and the rest of variables are expressed in mean ± standard deviation
PRISM paediatric risk of mortality, *HR* heart rate, *RR* respiratory rate

episodes, death cause was a septic shock, and in the last one it was a malignant arrhythmia. None of the last four deaths happened in the first 45 h after intubation (median 48.0 h, range 45–312).

Predictive factors for NIV failure

Failure group showed lower age, weight and RR decrease from initial RR at hours 1 and 24. In other hand, they had higher PRISM score, HR and RR at 24 h, EPAP at 24 and 48 h, FiO_2 at 1, 6, 24 and 48 h, and PCO_2 at 6 and 24 h when compared to success group (Table 3).

Multiple regression analysis performed including age, weight, HR, RR, FiO_2, ARF type and PRISM score (and EPAP at hours 6, 12, 24 and 48), identified type 1 ARF and higher PRISM score as independently associated variables with NIV failure. Moreover, it identified lower RR decrease (at 1 h and at 6 h) also independently associated with NIV failure (Table 4).

Discussion

To our knowledge, this is the largest prospective study of NIV in paediatric ARF which tries to identify NIV outcome predictors in paediatric population. As it occurs in the vast majority of paediatric studies, the lack of a control group obligates us to evaluate carefully the conclusions obtained. However, this work is based on daily clinical practice even though a NIV protocol has been used.

Our study included a typical, heterogeneous critically ill paediatric population similar to that of the majority of European multidisciplinary PICUs. All patients

Table 3 Parameters with significant differences between success and failure groups expressed in mean ± standard deviation (except for age and weight, expressed in median and range)

	Success group ($N = 98$)	Failure group ($N = 18$)	P value
Age (months)	11.6 (0.6–169.7) ($N = 98$)	6.1 (0.8–115.9) ($N = 18$)	0.028
Weight (kg)	9.6 (2.8–58.0) ($N = 98$)	6.3 (2.8–39.0) ($N = 18$)	0.016
PRISM score	7.4 ± 4.4 ($N = 98$)	11.7 ± 7.6 ($N = 18$)	0.026
HR at 24 h (beats/min)	129.7 ± 22.2 ($N = 83$)	149.6 ± 20.9 ($N = 8$)	0.033
RR at 24 h (breaths/min)	35.7 ± 8.3 ($N = 83$)	48.9 ± 11.6 ($N = 8$)	0.001
EPAP at 24 h (cmH_2O)	6.4 ± 1.3 ($N = 83$)	7.9 ± 1.0 ($N = 8$)	0.001
EPAP at 48 h (cmH_2O)	6.5 ± 1.5 ($N = 52$)	9 ± 2.6 ($N = 4$)	0.040
RR decrease in the first hour (breaths/min)	12.2 ± 12.9 ($N = 98$)	4.9 ± 11.9 ($N = 18$)	0.032
RR decrease at 24 h (breaths/min)	17.8 ± 16.4 ($N = 83$)	3.1 ± 18.2 ($N = 8$)	0.015
FiO_2 at 1 h (%)	43.3 ± 18.9 ($N = 98$)	50.5 ± 19.0 ($N = 18$)	0.040
FiO_2 at 6 h (%)	37.9 ± 14.6 ($N = 98$)	46.5 ± 14.7 ($N = 13$)	0.025
FiO_2 at 24 h (%)	32.8 ± 9.4 ($N = 83$)	45.0 ± 14.9 ($N = 8$)	0.015
FiO_2 at 48 h (%)	31.6 ± 8.9 ($N = 52$)	50.0 ± 14.1 ($N = 4$)	0.006
Venous PCO_2 at 6 h (mmHg)	46.5 ± 9.9 ($N = 19$)	65.9 ± 10.7 ($N = 3$)	0.021
Venous PCO_2 at 24 h (mmHg)	46.5 ± 7.6 ($N = 19$)	78.1 ± 36.8 ($N = 3$)	0.030

Number of episodes analyzed in each item is specified beside
HR heart rate, *RR* respiratory rate, *EPAP* expiratory pressure, *PRISM* paediatric risk of mortality

Table 4 Multivariate analysis before non-invasive ventilation initiation, and after 1, 6, 12, 24 and 48 h

	P value	Odds ratio	95% CI for OR	
			Lower	Upper
Before NIV initiation				
Age (months)	0.183	0.958	0.899	1.021
Weight (kg)	0.646	1.049	0.856	1.284
HR	0.928	0.999	0.969	1.029
RR	0.091	0.955	0.905	1.007
FiO_2	0.944	1.099	0.077	15.778
PRISM score	0.019	1.138	1.022	1.267
Type 1 ARF (vs. type 2 ARF)	0.001	11.108	2.578	47.863
At 1 h				
Age (months)	0.141	0.956	0.900	1.015
Weight (kg)	0.784	1.030	0.833	1.274
Mean HR decrease	0.278	0.979	0.941	1.018
Mean RR decrease	0.042	0.926	0.860	0.997
FiO_2	0.068	26.449	0.784	892.026
PRISM score	0.029	1.134	1.013	1.270
Type 1 ARF (vs. type 2 ARF)	0.001	18.215	3.456	95.999
At 6 h				
Age (months)	0.080	0.914	0.827	1.011
Weight (kg)	0.223	1.195	0.897	1.591
Mean HR decrease	0.911	0.998	0.963	1.034
Mean RR decrease	0.030	0.911	0.837	0.991
FiO_2	0.375	7.014	0.095	519.982
EPAP (cmH_2O)	0.239	1.679	0.709	3.974
PRISM score	0.109	1.124	0.974	1.298
Type 1 ARF (vs. type 2 ARF)	0.001	20.317	3.212	128.504
At 12 h				
Age (months)	0.156	0.917	0.813	1.034
Weight (kg)	0.300	1.209	0.844	1.731
Mean HR decrease	0.168	0.964	0.914	1.016
Mean RR decrease	0.551	0.971	0.881	1.070
FiO_2	0.083	145.307	0.525	40,229.185
EPAP (cmH_2O)	0.538	1.394	0.484	4.017
PRISM score	0.102	1.166	0.970	1.402
Type 1 ARF (vs. type 2 ARF)	0.006	69.092	3.284	1,453.792
At 24 h				
Age (months)	0.549	0.328	0.009	12.545
Weight (kg)	0.581	6.319	0.009	4,411.423
Mean HR decrease	0.763	1.032	0.841	1.266
Mean RR decrease	0.395	0.798	0.474	1.342
FiO_2	0.256	7E + 008	0.000	1E + 024
EPAP (cmH_2O)	0.341	6.799	0.132	350.203
PRISM score	0.441	1.183	0.771	1.816
Type 1 ARF (vs. type 2 ARF)	0.214	1,798.983	0.013	2E + 008
At 48 h				
Age (months)	1.000	1.201	0.000	–
Weight (kg)	1.000	0.117	0.000	–
Mean HR decrease	0.999	2.198	0.000	–
Mean RR decrease	0.999	0.306	0.000	–
FiO_2	0.995	5.3E + 136	0.000	–
EPAP (cmH_2O)	1.000	1.056	0.000	–
PRISM score	0.993	0.000	0.000	–
Type 1 ARF (vs. type 2 ARF)	0.999	5.3E + 039	0.000	–

NIV non invasive ventilation, *RR* respiratory rate, *ARF* acute respiratory failure, *CI* confidence interval, *OR* odds ratio, *PRISM* paediatric risk of mortality, *EPAP* expiratory pressure, *HR* heart rate

considered to be candidates to receive NIV according to our inclusion criteria entered the study, without any exception. The posterior exclusion of obstructive sleep apnoea patients was done because it is not an ARF, and its treatment with nocturnal CPAP is well established. We also excluded postextubation cases, as their characteristics are proved to be very different to those of children who had not received CMV. Postextubation ARF in adults has been studied separately from other NIV indications [11, 12].

Previous studies have shown success rates for the use of NIV in paediatric patients to be between 57 and 92%

[20–22, 29–31, 34]. Our results are comparable to those reporting a high success rate (over 84%). The improved results of Fortenberry et al [22] and Padman et al [30] in comparison to ours could be related to a higher patients' age. Our sample had a low median age: 10.3(0.6–169.7), compared to other series which included older children [20–22, 29, 30, 34]. Median age in Campion et al [32] and Larrar et al [31] studies was lower than ours because they only included infants with bronchiolitis.

Neuromuscular disease was the most frequent underlying disease. Because of their lack of strength these children usually achieve a good patient–ventilator synchrony, with a good outcome [29]. Immunodeficiency was also a usual underlying disease, and our good outcome (five successful NIV episodes out of seven) goes in accordance with literature [7].

Status asthmaticus was the most frequent diagnosis, and it is noteworthy that only one of these patients required CMV, in accordance with the case series reported by Akingbola [27] and Carroll [24]. Pneumonia was also quite frequent, with a 22.6% failure rate, higher than 13% reported by Essouri et al [20]. NIV failed in only five out of 33 bronchiolitis, a better outcome than the one reported by Campion and Larrar [34, 35].

Interfaces mostly used were the face masks, as little infants do not cooperate and air leaks through the mouth could occur. This would result in ventilator–child asynchrony and could be a cause of NIV failure. Due to the lack of cooperation, sedative use was quite frequent (64% of the episodes, similar to 56–76% reported by Essouri and Campion) [20, 32].

NIV was a safe therapy, and the most frequent damage (skin-lesion) usually has a good outcome. The five deaths during our study were not related to NIV use.

The main objective of our study was to identify predictive factors of NIV failure in PICU patients. Three independent risk factors of NIV failure were type 1 ARF, PRISM score and lower RR decrease during NIV initial period. Type 1 ARF patients are potentially more likely to suffer a NIV failure. This finding agrees with most of previous studies, in which higher NIV failure risk was found in hypoxemic cases (similar to type 1 ARF). ARDS diagnosis was independently associated with failure in Essouri's study [20] and a primary pulmonary parenchymal disease was a risk factor for NIV failure in Joshi's report [21]. Therefore, we consider extremely important to classify all ARF patients in one of these groups before NIV therapy is started. PRISM score has already been identified as a predictive factor for NIV outcome [31, 32]. Pediatric Logistic Organ Dysfunction, another prognostic severity score was reported in Essouri's study [20]. However, Bernet et al [34] did not find differences in Paediatric Index of Mortality score between responders and non-responders. The other risk factor was related to RR emphasizing the importance of close RR monitoring when performing NIV. Once NIV is started, lower RR decrease at 1–6 h was associated with NIV failure. A similar finding was made by Essouri, who found a significantly higher RR decrease at 2 h in the success group [20]. In summary, patients with type 1 ARF and high PRISM score are candidates to CMV, as well as children who do not reduce RR in the first 6 h of NIV therapy.

In univariate analysis, we found that smaller children are in higher risk of failure. An age under or equal to 6-year-old was associated with NIV failure in Joshi's study [21]. Our result could be related to the difficulties in achieving a good ventilator–child synchrony due to gas leakage, the lack of adequate mask sizes [25] and not sensitive enough triggers. A higher EPAP was found at 24 and 48 h in failure group. This result has not been reported in any paediatric study, but Antonelli found that a higher level of EPAP was independently associated with NIV failure in adult patients with ARDS [9].

This study has several limitations. First, an observational study does not allow us to make any conclusion about gasometric determinations as predictive factors of NIV outcome. In the protocol we followed, blood gas sampling was not mandatory. We tried to use clinical data, performing blood gas analysis only in case of doubts about patient clinical evolution. If child's comfortability with good patient–ventilator synchrony, adequate thorax motion and auscultation, and decreasing heart and respiratory rate are achieved, there is no point on blood gas sampling. We think that in paediatric patients on NIV, blood sampling could produce patient/ventilator asynchrony. In the opposite side, when clinical parameters did not improve, we performed blood gas determinations. Second, the study was conducted in only one PICU. This limits the generalization of the results, although our PICU is likely comparable to most European multidisciplinary PICUs.

This study has several strengths. First, it is a prospective study, following the protocol published by "Spanish Respiratory Group of the Spanish Society of Paediatric Intensive Care" [39] conducted in all consecutive patients admitted in PICU. Second, it is the only paediatric prospective cohort done in a 4-year period, which allowed the findings to be representative and accounted for possible seasonal variation. Third, it is the biggest study focusing on predictive factors of NIV success in critically ill children. Finally, our study provides recent descriptive NIV data, not available in the current PICU literature.

Conclusions

Paediatric NIV is a new respiratory support technique that in our experience is useful in more than 84% of the cases. Type 1 ARF group classification, PRISM score and lower

RR decrease were independent risk factors for NIV failure which suggest that focus should be given to the correct classification of patients, PRISM score, and close RR monitoring.

Acknowledgments The authors gratefully acknowledge the assistance of the medical and nursing staff of the Hospital Universitario Central de Asturias PICU. We would also like to thank Martí Pons, Antonio Rodríguez and Vicente Modesto for helpful comments on this manuscript.

References

1. Meduri GU (1996) Noninvasive positive-pressure ventilation in patients with acute respiratory failure. Clin Chest Med 17:513–553
2. Mehta S, Hill NS (2001) Noninvasive ventilation. Am J Respir Crit Care Med 163:540–577
3. Celikel T, Sungur M, Ceyhan B, Karakurt S (1998) Comparison of noninvasive positive pressure ventilation with standard medical therapy in hypercapnic acute respiratory failure. Chest 114:1636–1642
4. Thys F, Roeseler J, Reynaert M, Liistro G, Rodenstein DO (2002) Noninvasive ventilation for acute respiratory failure: a prospective randomised placebo-controlled trial. Eur Respir J 20:545–555
5. Chadda K, Annane D, Hart N, Gajdos P, Raphael JC, Lofaso F (2002) Cardiac and respiratory effects of continuous positive airway pressure and noninvasive ventilation in acute cardiac pulmonary edema. Crit Care Med 30:2457–2461
6. Confalonieri M, Potena A, Carbone G, Porta RD, Tolley EA, Umberto MG (1999) Acute respiratory failure in patients with severe community-acquired pneumonia. A prospective randomized evaluation of noninvasive ventilation. Am J Respir Crit Care Med 160:1585–1591
7. Hilbert G, Gruson D, Vargas F, Valentino R, Gbikpi-Benissan G, Dupon M, Reiffers J, Cardinaud JP (2001) Noninvasive ventilation in immunosuppressed patients with pulmonary infiltrates, fever, and acute respiratory failure. N Engl J Med 344:481–487
8. Antonelli M, Conti G, Moro ML, Esquinas A, Gonzalez-Diaz G, Confalonieri M, Pelaia P, Principi T, Gregoretti C, Beltrame F, Pennisi MA, Arcangeli A, Proietti R, Passariello M, Meduri GU (2001) Predictors of failure of noninvasive positive pressure ventilation in patients with acute hypoxemic respiratory failure: a multi-center study. Intensive Care Med 27:1718–1728
9. Antonelli M, Conti G, Esquinas A, Montini L, Maggiore SM, Bello G, Rocco M, Maviglia R, Pennisi MA, Gonzalez-Diaz G, Meduri GU (2007) A multiple-center survey on the use in clinical practice of noninvasive ventilation as a first-line intervention for acute respiratory distress syndrome. Crit Care Med 35:18–25
10. Delclaux C, L'Her E, Alberti C, Mancebo J, Abroug F, Conti G, Guerin C, Schortgen F, Lefort Y, Antonelli M, Lepage E, Lemaire F, Brochard L (2000) Treatment of acute hypoxemic nonhypercapnic respiratory insufficiency with continuous positive airway pressure delivered by a face mask: A randomized controlled trial. JAMA 284:2352–2360
11. Keenan SP, Powers C, McCormack DG, Block G (2002) Noninvasive positive-pressure ventilation for postextubation respiratory distress: a randomized controlled trial. JAMA 287:3238–3244
12. Esteban A, Frutos-Vivar F, Ferguson ND, Arabi Y, Apezteguia C, Gonzalez M, Epstein SK, Hill NS, Nava S, Soares MA, D'Empaire G, Alia I, Anzueto A (2004) Noninvasive positive-pressure ventilation for respiratory failure after extubation. N Engl J Med 350:2452–2460
13. Martin TJ, Hovis JD, Costantino JP, Bierman MI, Donahoe MP, Rogers RM, Kreit JW, Sciurba FC, Stiller RA, Sanders MH (2000) A randomized, prospective evaluation of noninvasive ventilation for acute respiratory failure. Am J Respir Crit Care Med 161:807–813
14. Nourdine K, Combes P, Carton MJ, Beuret P, Cannamela A, Ducreux JC (1999) Does noninvasive ventilation reduce the ICU nosocomial infection risk? A prospective clinical survey. Intensive Care Med 25:567–573
15. Carlucci A, Richard JC, Wysocki M, Lepage E, Brochard L (2001) Noninvasive versus conventional mechanical ventilation. An epidemiologic survey. Am J Respir Crit Care Med 163:874–880
16. Courtney SE, Barrington KJ (2007) Continuous positive airway pressure and noninvasive ventilation. Clin Perinatol 34:73–92 vi
17. Dani C, Bertini G, Pezzati M, Cecchi A, Caviglioli C, Rubaltelli FF (2004) Early extubation and nasal continuous positive airway pressure after surfactant treatment for respiratory distress syndrome among preterm infants <30 weeks' gestation. Pediatrics 113:e560–e563
18. López M, Pallás CR, Muñoz MC, Barrio MC, Medina C, de la Cruz J (2006) The use of the continuous positive airway pressure for early stabilization in very low birthweight infants. An Pediatr (Barc) 64:422–427
19. Verder H (2007) Nasal CPAP has become an indispensable part of the primary treatment of newborns with respiratory distress syndrome. Acta Paediatr 96:482–484
20. Essouri S, Chevret L, Durand P, Haas V, Fauroux B, Devictor D (2006) Noninvasive positive pressure ventilation: five years of experience in a pediatric intensive care unit. Pediatr Crit Care Med 7:329–334
21. Joshi G, Tobias JD (2007) A five-year experience with the use of BiPAP in a pediatric intensive care unit population. J Intensive Care Med 22:38–43
22. Fortenberry JD, Del TJ, Jefferson LS, Evey L, Haase D (1995) Management of pediatric acute hypoxemic respiratory insufficiency with bilevel positive pressure (BiPAP) nasal mask ventilation. Chest 108:1059–1064
23. Padman R, Lawless S, Von NS (1994) Use of BiPAP by nasal mask in the treatment of respiratory insufficiency in pediatric patients: preliminary investigation. Pediatr Pulmonol 17:119–123
24. Carroll CL, Schramm CM (2006) Noninvasive positive pressure ventilation for the treatment of status asthmaticus in children. Ann Allergy Asthma Immunol 96:454–459
25. Medina A, Prieto S, Los Arcos M, Rey C, Concha A, Menendez S (2005) Noninvasive ventilation in a pediatric intensive care unit. An Pediatr (Barc) 62:13–19

26. Piastra M, Antonelli M, Chiaretti A, Polidori G, Polidori L, Conti G (2004) Treatment of acute respiratory failure by helmet-delivered non-invasive pressure support ventilation in children with acute leukemia: a pilot study. Intensive Care Med 30:472–476
27. Akingbola OA, Simakajornboon N, Hadley EF Jr, Hopkins RL (2002) Noninvasive positive-pressure ventilation in pediatric status asthmaticus. Pediatr Crit Care Med 3:181–184
28. Mayordomo J, Fernández-Barrio B, Medina A, Rey C, Prieto S, Concha A (2007) Evaluation of noninvasive ventilation success or failure. Pediatr Crit Care Med 8(3 Suppl):A266
29. Piastra M, Antonelli M, Caresta E, Chiaretti A, Polidori G, Conti G (2006) Noninvasive ventilation in childhood acute neuromuscular respiratory failure: a pilot study. Respiration 73:791–798
30. Padman R, Lawless ST, Kettrick RG (1998) Noninvasive ventilation via bilevel positive airway pressure support in pediatric practice. Crit Care Med 26:169–173
31. Larrar S, Essouri S, Durand P, Chevret L, Haas V, Chabernaud JL, Leyronnas D, Devictor D (2006) Effects of nasal continuous positive airway pressure ventilation in infants with severe acute bronchiolitis. Arch Pediatr 13:1397–1403
32. Campion A, Huvenne H, Leteurtre S, Noizet O, Binoche A, Diependaele JF, Cremer R, Fourier C, Sadik A, Leclerc F (2006) Non-invasive ventilation in infants with severe infection presumably due to respiratory syncytial virus: feasibility and failure criteria. Arch Pediatr 13:1404–1409
33. Teague WG (2003) Noninvasive ventilation in the pediatric intensive care unit for children with acute respiratory failure. Pediatr Pulmonol 35:418–426
34. Bernet V, Hug MI, Frey B (2005) Predictive factors for the success of noninvasive mask ventilation in infants and children with acute respiratory failure. Pediatr Crit Care Med 6:660–664
35. L'Her E, Deye N, Lellouche F, Taille S, Demoule A, Fraticelli A, Mancebo J, Brochard L (2005) Physiologic effects of noninvasive ventilation during acute lung injury. Am J Respir Crit Care Med 172:1112–1118
36. Peñuelas O, Frutos-Vivar F, Esteban A (2007) Noninvasive positive-pressure ventilation in acute respiratory failure. CMAJ 177:1211–1218
37. Ream RS, Loftis LL, Albers GM, Becker BA, Lynch RE, Mink RB (2001) Efficacy of IV theophylline in children with severe status asthmaticus. Chest 119:1480–1488
38. Martinon-Torres F, Rodriguez-Nunez A, Martinon-Sanchez JM (2002) Heliox therapy in infants with acute bronchiolitis. Pediatrics 109:68–73
39. Pons M, Cambra A (2003) Noninvasive ventilation. An Pediatr (Barc) 59:165–172