Non-invasive ventilation in bronchiolitis: Analysis according to a chronologic classification

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Abstract.

OBJECTIVE: To study patients diagnosed with bronchiolitis receiving ventilatory support with non-invasive ventilation (NIV) according to a chronologic classification: initial support (i-NIV), rescue post-extubation (r-NIV) and elective post-extubation (e-NIV); and to identify predictive factors of failure for each group. Prospective observational study (January 2004–December 2009), including all the patients with bronchiolitis admitted to pediatric intensive care unit and receiving ventilatory support with NIV. Clinical data collected at 0 (pre-NIV), 1, 2, 8, 12, 24 h of treatment were analyzed. Need for intubation was considered as NIV failure. NIV was successful in 65.8% of 152 cases included. Success rates were as follows: i-NIV (52.2%); r-NIV (72.2%); and e-NIV (90.9%) (Anova $P < 0.000$). Bi-level modes had higher efficacy (73%) than continuous positive airway pressure (61.5%) (Fisher's-test $P = 0.049$). Predictive factors of success in i-NIV group were inspired fraction of oxygen (FiO_2) at 2 h, $P = 0.003$, higher pulse oximeter saturation (SpO_2)/ FiO_2 values at 2 h ($P = 0.009$), and SpO_2 / FiO_2 - 12 h ($P = 0.05$), lower heart rate (HR) at 12 h ($P = 0.01$), lower partial pressure of carbon dioxide (PCO_2) previous to NIV ($P = 0.009$) and HR decrease-12 h ($P = 0.008$). In e-NIV: respiratory rate (RR)-1 h ($P = 0.02$), RR decrease-1 h ($P = 0.006$) and higher SpO_2 / FiO_2 - 24 h ($P = 0.01$); in r-NIV: SpO_2 / FiO_2 - 12 h ($P = 0.04$), lower HR-2 h ($P = 0.03$) and HR-8 h ($P = 0.01$). Multivariate analysis identified the groups as an independent variable ($P = 0.04$) but didn't show any significant value in any of the analyzed groups. Separate evaluation is advisable for i-NIV, r-NIV and e-NIV.

Keywords: Non-invasive ventilation, interface, bronchiolitis, failure predictive factors, extubation, children

1. Introduction

Although bronchiolitis generally evolves mildly, 1–5% of pediatric patients require hospital admission, and 5–16% develop respiratory failure and ultimately need respiratory support in a pediatric intensive care unit

(PICU) [1]. Non-invasive ventilation (NIV) has become a universally accepted treatment for respiratory failure in pediatric patients [2]. Its multiple advantages over conventional mechanical ventilation (e.g. lower rate of nosocomial infections) have been described in various studies in adult patients [1–3]. However, there are only a few reports on the utility of NIV for supporting patients with bronchiolitis [1–7]. To date, studies evaluating NIV for bronchiolitis have focused on using it as initial support NIV (i-NIV) option to support patients with acute respiratory failure (ARF) [7–12]. We aimed

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to assess differences in NIV efficacy based on treatment type (i-NIV, rescue post-extubation [r-NIV] and elective post-extubation [e-NIV]); and to identify predictive factors of failure for each group.

2. Materials and methods

A prospective study was conducted in a tertiary hospital PICU (14 critical care beds) that receives patients from birth to 18-year-old. Consecutive sampling was conducted on patients diagnosed with bronchiolitis (Mcconochie criteria) [13] that admitted and received ventilatory support with NIV, were prospectively from January 2004 to December 2009. Continuous positive airway pressure (CPAP) was considered as a type of NIV [14,15]. We divided our patients into i-NIV, e-NIV and r-NIV groups, based on the moment when NIV was used during their admission. The efficacy of NIV was assessed in all three groups.

Bronchiolitis patients that presented with clinical signs of ARF (those described in the inclusion criteria) following extubation were treated with r-NIV. Intubated bronchiolitis patients that had previously experienced a failed extubation were given elective CPAP. Those who did not meet standard clinical criteria for extubation (peak inspiratory pressure: 10 cmH₂O; positive end expiratory pressure: 5 cmH₂O; FiO₂: <40%), were given elective bilevel NIV; this strategy started in 2006.

Inclusion criteria were as follows; children with ARF due to bronchiolitis that met at least one of the following conditions: (a) Apneas; (b) Dyspnea at rest, despite having a FiO₂ > 30% for a SpO₂ > 95%. Dyspnea is defined as the presence of at least subcostal and intercostal or suprasternal retractions; with paradoxical breathing being the maximum expression of dyspnea; (c) Respiratory rate (RR) greater than the sum of the average age-appropriate value plus two standard deviations [16].

Exclusion criteria were (a) Oxygen requirements <30% for an SpO₂ > 95%; (b) Any contraindication for NIV: these include cardiopulmonary arrest; hemodynamic instability requiring vasoactive treatment; severe arrhythmia; Glasgow coma index score less than 10; facial trauma, surgery or deformity; vocal chord paralysis; bullous pneumonia; undrained pneumothorax; endotracheal intubation required for managing secretions or protecting the airway; or active bleeding of the upper gastrointestinal tract; (c) Tracheostomized patients.

Approval by our institutional review board was obtained. NIV comprised either CPAP or other modes at

bilevel positive airway pressure (BLPAP). The selection was made according to the patient's needs, based on the attending physician's criteria, who considered: Mainly CPAP use for patients with apnea or mild respiratory distress; BLPAP mode was used for patients with persisting, significant respiratory workload in spite of CPAP or low inspiratory volume according to auscultation and thoracic motion, or blood gases criteria (increasing hypercapnia).

The following interfaces were used: ProfileLite (Respironics) and Comfortclassic® nasal used as oral-nasal, Small Child ProfileLite Nasal Mask (Respironics) nasal, Helmet Castar (Starmed)® and endotracheal tubes as nasopharyngeal tubes (NT). Hydrocolloid dressings (Comfeel®; Coloplast) and hyperoxygenated fatty acid solution (Mepentol®; Bama-Geve) were applied to prevent lesions. A heated humidifier (Fisher Paykel® Healthcare, Auckland, New Zealand) was used since 2007.

Devices and ventilators were used following these general but not restrictive criteria: Patients who required CPAP: Benveniste device; bubble CPAP Fisher Paykel® or Helmet(Starmed)®.

Patients who required BLPAP: Giulia® Ginevri (younger than 1 mo), Servo-i (1–3 mo) Maquet, BiPAP Vision® Respironics and Carina® Dräger (older than 3 mo).

2.1. Ventilation strategy

Ventilation was administered according to the protocol by the Grupo Respiratorio de la Sociedad Española de Cuidados Intensivos Pediátricos [17]. For CPAP, the startup parameters were 4–5 cmH₂O, and for BLPAP modes an inspiratory positive airway pressure (IPAP) or peak inspiratory pressure of 6–8 cmH₂O and an expiratory positive airway pressure or positive end expiratory pressure of 4 cmH₂O were used. In those patients treated initially with CPAP, whose respiratory workload did not improve or apnea was still present, CPAP was increased up to 8 cmH₂O. In those patients treated with BLPAP, the IPAP was increased step-wise by 2 cm of water up to 22 cmH₂O if the clinician observed that the inspiratory volume was inadequate, when respiratory workload did not improve or if hypercapnia did not decrease. When any of the following signs of treatment failure were observed, NIV was withdrawn and the patient was intubated: SpO₂ < 85%; venous PCO₂ > 65 mmHg, despite maximum NIV settings; or progressively worsening clinical signs of work of breathing (e.g. frequent apneas, paradoxical

breathing not responding to NIV), or appearance of any of the exclusion criteria. Weaning from NIV is performed progressively, reducing IPAP value step-wise by 2 cmH₂O, when decrease of RR and respiratory workload is observed and oxygen needs are under 40%.

2.2. Sedation

Sedation is usually required for the initial stages of adaptation in the acute intensive care patient. Infants showing discomfort were treated with levomepromazine oral (1 mg/kg/d) as a first step approach. Those patients suffering from severe agitation or major patient-ventilator asynchrony were treated intravenously with midazolam (0.1 mg/kg bolus followed by 0.05 to 0.1 mg/kg/h continuous infusion). In post-extubation patients, fentanyl was sometimes maintained (0.5 to 1 µg/kg/h continuous infusion).

2.3. Monitoring

All patients were continuously monitored by electrocardiography and pulse oximetry and for heart rate (HR) and RR. Blood gases were only measured when deemed necessary by the physician.

2.4. NIV results

Non-invasive ventilation was considered successful if intubation was not required and the patient remained with spontaneous respiration for that episode. For those patients treated with CPAP, failure was also considered if BLPAP was used as a rescue option previous to intubation.

2.5. Data collected

The following variables were collected: patient demographics (age, sex and underlying disease) and, for each patient, the length of stay (PICU and hospital); duration of NIV (h); the PCO₂ and pH pre-NIV when available; the interface, ventilator and ventilation mode used; NIV complications; and the sedatives employed. Physiological variables RR, HR, SpO₂ and SpO₂/FiO₂ (SF) ratio were collected before NIV was started and at 1, 2, 8, 12 and 24 h of treatment; ventilator variables (FiO₂, IPAP, EPAP) were collected at 1, 2, 8, 12 and

24 h of treatment. The SF ratio values were correlated to respiratory conditions according to equivalence values published by Khemani et al. [18]. The pre-NIV FiO₂ was estimated based on the following values for oxygen delivery system: nasal prongs (1 lpm: 24%; 2 lpm: 28%; 3 lpm: 32%; and 4 lpm: 36%); [19,20].

2.6. Statistical analysis

Statistical analysis was performed using the SPSS program version 17.0 (Chicago, IL, USA). Categorical variables were expressed as percentages and were compared using the Chi-squared test. Qualitative variables were expressed in percentage and compared using the Chi-squared test. Continuous variables were described with the mean ± standard deviation or the median and interquartile range, and compared with Student's *t*-test, or Mann-Whitney *U* test, where appropriate. Clinical data and several variables such as age, sex, FiO₂, SpO₂, RR, HR, SF ratio and PCO₂ were compared using different statistical tests (Mann-Whitney *U*, and Wilcoxon tests, asymptotic and exact significance between the successful NIV and failed NIV groups).

2.7. Predictive factors for NIV failure

The Cox regression hazard ratio was used with forward stepwise analysis to identify possible predictors of NIV failure. The variables included in the multivariate analysis comprised those, which had a *P* value of less than 0.2 in the univariate analysis and those considered clinically important for controlling statistical error: age, sex, HR, RR, FiO₂, SpO₂, PCO₂ and SF ratio. A *P* value of <0.05 was considered statistically significant. 95% confidence intervals were calculated. Multivariate analysis was also performed separately in all three groups (initial, rescue and elective NIV).

3. Results

3.1. Descriptive study

A total of 640 cases of NIV treatment were recorded in the PICU during the study period (January 2004 to December 2009). Of the valid cases, 152 pertaining to bronchiolitis were studied separately. There were 90 cases (52.9%) in which NIV was received during

the initial period (i-NIV) of ARF; 18 (11.8%) in which NIV was employed as rescue treatment (r-NIV) after extubation (eight had received NIV previous to intubation); and 44 (28.9%) in which NIV was used as elective treatment after mechanical intubation (e-NIV) (18 had received NIV previous to intubation) (Fig. 1). The patients' (pre-NIV) values for principal clinical parameters, broken down by NIV treatment group, are summarized in Table 1. In the whole sample, there were some underlying diseases (two cardiopathies, 12 ex-premature, three bronchopulmonary dysplasia, two Down's syndrome and some six others), without

significant differences among any of the groups. Significant differences in RR and in HR were found among the three groups: RR between pre-NIV and r-NIV ($P = 0.017$), SpO_2 throughout the duration of the treatment between i-NIV and e-NIV; and PCO_2 between i-NIV and r-NIV ($P = 0.004$).

3.2. Ventilation modes, ventilators, and interfaces

Among all patients, the most widely-used ventilation mode was CPAP (51.3%), followed by assisted/pressure control (A/C-P) (24.3%), Spontaneous/timed (S/T) (17.1%), and pressure support (PS) (7.2%); the most frequently-used device was Benveniste (a home made device) (36.2%), followed by Servo-i® (35.5%), and BiPAP Vision® (13.8%); and the most widely-employed interface was the nasopharyngeal tube (NT) (79.6%), followed by nasal used as oral-nasal (11.2%). In the e-NIV group, the most widely used ventilation mode was (A/C-P) (45.5%) compared to i-NIV (18%) and r-NIV (5.5%); and in the r-NIV group, the most frequently used device was the Benveniste (61%).

3.3. Duration of NIV and length of stay in the PICU

The average duration of NIV was 56.1 h (range: 0 to 216 h). Patients for whom NIV was successful had a significantly longer average duration than those for

*640 patients were admitted to PICU and treated with NIV during the study period.

**43 NIV failure.

Fig. 1. Whole sample distribution.

Table 1
Pre-treatment clinical parameter values for whole sample and each treatment group

Respiratory assistance	i-NIV* (mean $\pm$ SD)	r-NIV** (mean $\pm$ SD)	e-NIV*** (mean $\pm$ SD)	<i>P</i> value
Age (mo)	2.5 $\pm$ 3	1.8 $\pm$ 2	1.7 $\pm$ 17	0.061
Pre NIV SpO_2 ****	95.7 $\pm$ 6	96 $\pm$ 3	97 $\pm$ 3	0.363
Pre NIV respiratory rate*****	53 $\pm$ 23	46 $\pm$ 15	34 $\pm$ 9	0.001
Pre NIV heart rate*****	161 $\pm$ 25	149 $\pm$ 27	145 $\pm$ 23	0.340
Pre NIV pCO_2	50 $\pm$ 12.51	39 $\pm$ 6	42 $\pm$ 8	0.029
Pre NIV pH	7.34 $\pm$ 0.07	7.43 $\pm$ 0.03	7.42 $\pm$ 0.04	0.07
Pre NIV SpO_2/FiO_2 ratio*****	261 $\pm$ 100	284 $\pm$ 61	320 $\pm$ 64	0.270
Pre NIV FiO_2 *****	43.62 $\pm$ 23	36 $\pm$ 9.5	32 $\pm$ 7	0.141

NIV = Non invasive ventilation.

*Initial support.

**Rescue post-extubation.

***Elective post-extubation.

****Pulse oximetric saturation previous to NIV.

*****Respiratory rate previous to NIV.

*****Heart rate previous to NIV.

*****Pulse oximetric saturation/inspired fraction of oxygen previous to NIV.

*****Inspired fraction of oxygen previous to NIV.

whom it failed (successful: 71.7 h [range: 4 to 216 h]; failed: 24.83 h [0 to 143 h]; $P = 0.000$). The average length of stay in the PICU was 10.8 days (range: 1 to 38 days). Patients for whom NIV was successful had a significantly shorter length of stay than those for whom it failed (successful: 9 days [range: 1 to 35 days]; failed: 13.7 days [1 to 38 days]; $P = 0.001$).

3.4. Complications

Complications with NIV treatment were detected in three (1.9%) cases: two with rashes in the interface area and one with skin sores. However, none of these complications caused NIV to fail.

3.5. Efficacy analysis

Non-invasive ventilation was successful in 100 cases (65.8%). In terms of the three treatment groups, the success rates were 52.2% for i-NIV; 72.2% for r-NIV; and 90.9% for e-NIV. Although the same trends were observed among all three treatment groups, there was a statistically significant difference in efficacy according to the ventilation mode used: the combined success rate for all bi-level modes (PS, S/T and A/C P; 72.9%) was higher than that for CPAP (55%), with Chi-squared test $P < 0.009$. The success rate according to the ventilator or interface used did not differ significantly. Servo-i® reached 75.9% of success, BiPAP Vision® 66.7%, Carina® 50%, Giulia® 50%, bubble CPAP® 50% and Benveniste 46%. Regarding interfaces, helmet had a 100% rate of success, while the other interfaces had less success: oral-nasal 80%, NT 66.1%, nasal prongs 60% and nasal as oral-nasal interface reached 58.8% of success. It should be noted that the average age of the patients who used NT (1.5 mo) was significantly lower ($P < 0.000$) than that of the patients who used a nasal (5.7 mo) or oral-nasal (8.8 mo) interface. We did not observe significant differences in efficacy between CPAP and BLPAP modes in any group. However, it should be noted that the success rates of BLPAP doubled those of CPAP in r-NIV group.

3.6. Predictive factors for NIV failure

The clinical parameters for which significant differences were observed between patients for whom NIV succeeded and those for whom it failed are listed in Table 2. Significant differences were observed in

HR, RR, and SF ratio at 12 h NIV. Moreover, a non-significant difference in RR was observed at 24 h NIV. Cox regression analyses were performed for the parameters whose values exhibited significant differences between patients for whom NIV was successful, which included all the values with a p value less than 0.2 and the parameter of age (in mo), the only significant variable was the group of treatment (i-NIV, r-NIV, e-NIV).

4. Discussion

The efficacy of NIV for treatment other than i-NIV as we had hypothesized, has been demonstrated as significantly different.

4.1. NIV efficacy/success analysis

The overall success rate for NIV in our study, 64.8%, is lower than those reported by Campion et al. [11] (82.6%), Larrar et al. [10] (75.5%) or Mayordomo-Colunga et al. [8] (83%). If we compare the NIV success rate in our PICU during our study we observe that this success rate has increased from 38.5% (2004–2006 period) to 68.9% (2007–2009). This is due to the following factors: (1) Increased availability of NIV ventilators, second and third BiPAP Vision ventilators (2007), and later on, Servo-i ventilator with NIV option since 2007; (2) Using nasal interfaces as oral-nasal interfaces for infants younger than 1-year-old; (3) Providing nurses with annual NIV training courses since 2005; (4) Increasing number of e-NIV with higher efficacy has biased our overall results. These factors support the link between treatment success and the availability and quality of equipment, on one hand, and the experience, preparation and motivation of the nursing and medical staff [21,22], on the other. Earlier NIV therapy in bronchiolitis patients, as recently published Chabernaude et al. [6], could explain the differences of efficacy between units with different patient-care demands. Our PICU, often saturated during the peak of the bronchiolitis epidemic, probably admits patients with clinical criteria closer to intubation than to starting NIV. That is in our opinion, the most reasonable explanation for our lower success rate. A higher success rate for the e-NIV group is observed. The fact that one out of ten cases of e-NIV failed, indicates that some patients were really at risk of reintubation; however, the data for the e-NIV group should be taken with caution: some of these children may not have required any type of respiratory

Table 2
Principal characteristics of the patients for whom NIV was successful, and of those for those who failed, according to treatment group

Variable	Successful NIV (mean $\pm$ SD)	Failed NIV (mean $\pm$ SD)	<i>P</i> value
i-NIV group*	(n = 47)	(n = 43)	
Pediatric intensive care stay (days)	5 $\pm$ 2.6	13 $\pm$ 8	0.000
Hospital stay (days)	10 $\pm$ 4	22 $\pm$ 19	0.000
NIV duration (days)	3.4 $\pm$ 2.2	0.75 $\pm$ 1	0.000
NIV duration (h)	83 $\pm$ 50	23 $\pm$ 29	0.000
FiO ₂ at 2 h**	42 $\pm$ 13.5	44 $\pm$ 12	0.003
Respiratory rate at 12 h***	40 $\pm$ 12	47 $\pm$ 15	0.048
Heart rate at 12 h****	146 $\pm$ 26	161 $\pm$ 19	0.014
SF ratio at 2 h*****	268 $\pm$ 71	230 $\pm$ 51	0.009
SF ratio at 12 h	266 $\pm$ 67	232 $\pm$ 46	0.050
Heart rate decrease at 12 h	20 $\pm$ 29	0.6 $\pm$ 14	0.008
PCO ₂ 1 h	41.7 $\pm$ 7	49.2 $\pm$ 5.0	0.009
pH 1 h	7.36 $\pm$ 0.07	7.32 $\pm$ 0.07	0.006
Bicarbonate at 12 h	26.4 $\pm$ 2	24.6 $\pm$ 1.2	0.045
r-NIV group*****	(n = 13)	(n = 5)	
Pediatric intensive care stay (days)	16 $\pm$ 8	10 $\pm$ 3.7	0.019
NIV duration (days)	3.3 $\pm$ 2.2	2 $\pm$ 1.7	0.048
SpO ₂ at 12 h	99 $\pm$ 1	96.5 $\pm$ 0.7	0.049
Heart rate at 2 h	131 $\pm$ 19	162 $\pm$ 20	0.033
Heart rate at 8 h	146 $\pm$ 15	175 $\pm$ 3	0.014
SpO ₂ /FiO ₂ ratio at 12 h	299 $\pm$ 73	183 $\pm$ 33	0.046
e-NIV group*****	(n = 40)	(n = 4)	
FiO ₂ at 24 h	34 $\pm$ 8	45 $\pm$ 7	0.048
Respiratory rate 1 h	34 $\pm$ 11	43 $\pm$ 10	0.026
SpO ₂ /FiO ₂ ratio at 24 h	305 $\pm$ 72	221 $\pm$ 31	0.010
Respiratory rate increase, 1 h	0.35 $\pm$ 11	13 $\pm$ 10	0.006

NIV = Non invasive ventilation.

*Initial support.

**Inspired fraction of oxygen at 2 h of treatment.

***Respiratory rate at 2 h of treatment.

****Heart rate at 12 h of treatment.

*****Hemoglobin oxygen saturation oxygen/inspired fraction of oxygen at 2 h of treatment.

*****Rescue post-extubation.

*****Elective post-extubation.

support at all, and therefore, the efficacy rate for this group could be inflated.

4.2. NIV failure analysis

The overall failure rate for NIV in our study was 34.2%. As mentioned above, studies published to date have only analyzed i-NIV [6–12]. Thus, among our results, the only findings we can compare to an external reference are those for the i-NIV group. Unlike other researchers [6], we did not confirm as we had expected that a younger age correlated to a higher risk of NIV failure. NTs are the most commonly used interface for the youngest patients in our hospital,

despite being less effective than a nasal interface used as oral-nasal, the results that we have obtained with them especially in the e-NIV group are testament to their utility. The encouraging results obtained by Larrar et al. [10] (75.5% efficacy rate) for delivering CPAP via nasal prongs suggest that these could be the interface of choice for small patients [10]. In terms of the ventilator used, the highest success was achieved with the Servo-i® (73.1%). Although BiPAP Vision® and Carina® reached a success rate of 66.7% and 60% respectively; our PICU rarely uses these ventilators, given that the low sensitivity of its inspiratory trigger causes asynchrony, a fact described in the literature [8]. Some authors have previously reported that

BLPAP modes offer greater efficacy than CPAP [6,8], an observation that contrasts with the results of the two prospective studies published to date, by the groups of Campion et al. [11] and Larrar et al. [10]. These authors reported similar overall NIV efficacy rates, despite using both CPAP and BLPAP modes (Campion et al. [11], 83%) or only CPAP (Larrar et al. [10] 75.5%). Our lower efficacy of CPAP could certainly be attributed to inadequate leak compensation of our homemade Benveniste device. To improve synchronization, our patients were often sedated. Our rates of sedation are similar to reported values [8].

4.3. Predictive factors for NIV success or failure

Cox regression analysis indicates that the only significant variable was the treatment group (i-NIV, r-NIV, e-NIV).

4.3.1. i-NIV group

We did not observe the pre-NIV RR being a predictive factor of i-NIV success or failure, but we did observe a decrease in RR at 12 h in patients for whom NIV succeeded ($P=0.051$), a trend described by Mayordomo-Colunga et al. [8] and Essouri et al. [2]. We could not confirm the conclusions of Mayordomo-Colunga et al. [8], who observed a decrease of 11 beats per minute in HR at 12 h NIV as a cut off value. Nevertheless, we reiterate the importance of monitoring the RR and HR during the first few hours of i-NIV in order to detect failure early on.

4.3.2. e-NIV group

Among patients for whom e-NIV failed, we observed an immediate increase in RR upon starting ventilation, indicating that for an extubated bronchiolitis patient given NIV electively, an increase in RR early on is a sign that the patient should be either very closely monitored or directly re-intubated. Unfortunately, However, multivariate analysis revealed that an increase in RR at 2 h is a non-significant marker for treatment failure ($P<0.055$), that may be due to the small sample size.

4.3.3. r-NIV group

Multivariate analysis did not show any trends for this group. Separate analysis in this study shows, that some variables such as RR probably have a different behavior as prognostic factors of NIV failure when used in initial NIV or elective NIV groups. Our data suggest that those studies mixing both populations

are perhaps reducing the chances to identify RR and HR as prognostic factors of NIV failure, so we strongly recommend separate analysis for each group for future research on NIV in pediatrics.

In conclusion, the most important conclusion of this study is that separate evaluation is advisable for i-NIV, r-NIV and e-NIV because multivariate analysis confirms that they are different samples both at the pre-NIV moment and in their outcomes. We also would like to highlight the usefulness of a simple and cheap interface as an endotracheal tube used as a nasopharyngeal tube for performing NIV in the smallest infants if better options like binasal prongs or nasal masks are not available. CPAP delivered through the Benveniste device has the worst efficacy compared with other ventilators used in other reports, except in e-NIV group. So, we should not perform CPAP with a homemade Benveniste device if leaks are not accurately compensated. Improved results with BLPAP in r-NIV group, suggests that an early BLPAP trial could be reasonable for those patients who are failing with CPAP. Clinical monitoring of these patients (especially for RR and HR) during the first few hours of NIV is critical for early detection of treatment failure. No changes in RR suggests failure of treatment in i-NIV group, on the contrary, it suggests success of the treatment in e-NIV group. Data on parameters such as PCO_2 and arterial PO_2 can complement clinical monitoring, although they should not take precedence over the use of clinical parameters. Subsequent studies are required to obtain better criteria for selecting the interface, ventilator and ventilation modes; and especially for well-defined criteria for extubation to elective NIV.

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