Weaning From Noninvasive Ventilatory Support in Infants With Severe Bronchiolitis: An Observational Study

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Abstract

**Background:** The aim of the study was to analyze the weaning success, the type of weaning procedures, and weaning duration in consecutive infants hospitalized over a winter season in a Pediatric Intensive Care Unit.

**Methods:** A retrospective observational study in a pediatric intensive care unit in a tertiary center. Infants hospitalized for a severe bronchiolitis were included and the weaning procedure from continuous positive airway pressure (CPAP), noninvasive ventilation (NIV) or high flow nasal cannula (HFNC) was analyzed.

**Results:** Data from 95 infants (median age 47 days) were analyzed. On admission, 26 (27%), 46 (49%) and 23 (24%) infants were supported by CPAP, NIV and HFNC, respectively. One (4%), nine (20%) and one (4%) infants failed weaning while supported by CPAP, NIV or HFNC, respectively (p=0.1). In infants supported by CPAP, CPAP was stopped directly in 5 patients (19%) while HFNC was used as an intermediate ventilatory support in 21 (81%). The duration of weaning was shorter for HFNC (17 hours, [IQR 0-26]) than for CPAP (24 hours, [14-40]) and NIV (28 hours, [19-49]) (p<0.01).

**Conclusions:** The weaning phase represent a large proportion of noninvasive ventilatory support duration in infants with bronchiolitis. The weaning procedure following a “step down” strategy may lead to an increase in duration of weaning.

Background

Bronchiolitis is the most common lower respiratory tract infection in infants, with at least 20% of infants developing bronchiolitis in their first 12 months of life. Bronchiolitis is the first cause of hospitalization in infants with 1 to 3% of infants requiring a Pediatric Intensive Care Unit (PICU) admission for acute respiratory failure. Continuous positive airway pressure (CPAP) and noninvasive ventilation (NIV) are commonly used in infants with bronchiolitis and severe acute respiratory failure. High flow nasal cannula (HFNC) is a more recent type of ventilatory support which is increasingly used in moderate acute respiratory failure. In contrast with the abundant literature on ventilatory support in bronchiolitis, there is paucity of data on the weaning or discontinuation of ventilatory support in this population. Indeed, no study has analyzed the rate of weaning failure, as well as the weaning procedures and duration. These aspects of ventilatory support are nevertheless important because weaning failure may be associated with prolonged hospitalization and increased morbidity. The aim of the study was to analyze the weaning success, the type of weaning procedures, and weaning duration in consecutive infants hospitalized over a winter season in a PICU.

Patients And Methods

Study design
This single-center retrospective observational study was conducted from November 2018 to April 2019 in a 16-beds PICU of a tertiary pediatric center. Each year, approximately 100 infants with bronchiolitis are admitted to our PICU. The study was approved by the regional research committee (Comité d'Ethique du Centre d'Investigation Clinique de Clermont-Ferrand, France, IRB 5891) and follows the STROBE guidelines. Patients had been informed and non-opposition had been searched before data collection.

**Study population**

All consecutive infants younger than 6 months of age admitted to the PICU were eligible for inclusion if they had a clinical diagnosis of bronchiolitis and required 1/CPAP, 2/NIV or 3/HFNC (with an air flow rate > 1 L/kg/min) on admission. The PICU admission criteria were at the discretion of the attending physician without a local protocol. Usual criteria included: 1/severe acute respiratory failure defined as a Wang score > 7, hypoxemia (SpO\textsubscript{2}<92% in room air) and/or hypercapnia (PCO\textsubscript{2}>5.8 kPa in room air) despite medical treatment or 2/the presence of witnessed apnea, defined as any documented apnea observed by a caregiver or a parent. Exclusion criteria were: 1/patients on long term CPAP or NIV, 2/patients with an underlying cardiac or neuromuscular disease and 3/the presence of a pneumothorax on chest radiograph at admission.

**Data collection**

Demographic (age, sex and comorbidities) and clinical data during the PICU stay were gathered. Clinical data comprised the Wang and the m-WCAS (modified Wood's Clinical Asthma Score) bronchiolitis clinical severity scores, hemodynamic and respiratory parameters, ventilatory mode and settings and medical treatment. Biological data on admission, including venous pH, venous carbon dioxide (PvCO\textsubscript{2}) were also collected. All infants were screened for respiratory syncytial virus (RSV) at admission. The rate of intubation, the duration of ventilator support, and the PICU and hospital lengths of stay were analyzed.

**Ventilatory support**

The type and settings of the initial ventilator support were left at the discretion of the attending physician without a local protocol. In practice, the following step-up sequence was used according to the increase in patient severity: 1/HFNC, 2/CPAP, 3/NIV and 4/invasive ventilation. CPAP and NIV were performed with an ICU ventilator (Evita XL™, Dräger®, Germany or Servo I™ and U™, Maquet®, Solna, Sweden) with a facial or nasal interface according to the weight and clinical condition of the infant. HFNC was initiated at a flow rate of 2 L/kg/min with an ICU ventilator (Evita XL™, Draeger®, Germany), or with a specific device (Airvo 2™, Fisher and Paykel®, Auckland, New Zealand). Inspired fraction of oxygen (FiO\textsubscript{2}) was titrated in order to achieve a pulse oximetry (SpO\textsubscript{2}) > 94%.

**Weaning**

We defined weaning initiation as the time of the first step-down attempt in the ventilatory support, following the sequence NIV to CPAP to HFNC to standard oxygen. The rate of weaning failure within 48
hours after the weaning initiation, defined by the need to switch back to the previous ventilatory support whatever it was (CPAP, NIV or HFNC) or need to intubate the patient, was analyzed for every type of ventilatory support. The type of weaning procedure was defined as: 1/ **Other**: switch to another type of noninvasive ventilatory support; 2/ **Decrease**: decrease of the settings of the same ventilatory support or 3/ **Direct**: direct stopping of the ventilator support. Finally, the duration of the weaning process was analyzed, starting at the time of the first attempt and ending to the switch to room air or standard oxygen therapy.

**Statistical analysis**

Descriptive data were expressed as median values (with interquartile range, IQR) for continuous variables for homogeneous results presentation, and number and/or frequency (%) for categorical data. Differences in categorical variables were tested using the Chi-square or Fisher’s exact test. Differences in continuous variables were assessed by Student’s t test, Mann–Whitney test or analysis of variance test after verification of the eligibility conditions. P values of less than .05 were considered significant. All statistical analyses were performed using SPSS 26.0 (SPSS, Inc, Chicago, IL).

**Results**

**Study population**

Data from 95 infants were analyzed. No patient was excluded. On admission 26 (27%), 46 (49%) and 23 (24%) infants were supported by CPAP, NIV, and HFNC, respectively (Table 1). The median CPAP level was 6 cmH₂O (IQR 6-6) with a median fraction of inspired oxygen (FiO₂) of 30% (IQR 30-30). For NIV, the median expiratory level was set at 6 cmH₂O (IQR 6-6) with a median pressure support of 5 cmH₂O (IQR 4-6), a median back up rate (optionally) of 30 breaths/min (IQR 30-40) and a FiO₂ of 30% (IQR 30-40). A nasal interface was used in 93 infants and a total face mask in 2. HFNC was started at a median flow of 2 L/Kg/min, with a median FiO₂ of 30% (IQR 27-30). The demographic, clinical and biological characteristics of patients on admission are summarized in Table 1. Most infants presenting apnea were supported by NIV (p<0.001) and RSV-positive infants were more frequently supported by CPAP or NIV than by HFNC (p=0.02). The median length of hospital stay was 7 days (IQR 5-9) with a median PICU length of stay of 87 hours (IQR 67-116).

Table 1. Demographic, clinical and biological characteristics of the population according to the type of ventilatory support

| Values are median with interquartile (IQR) or numbers (%) |
|----------------------------------------------------------|
| **CPAP**: Continuous positive airway pressure; **HFNC**: High Flow Nasal Cannula; **LOS**: Length of stay; **NIV**: Noninvasive Ventilation; **PICU**: Pediatric Intensive Care Unit; **PvCO₂**: Partial venous carbon dioxide pressure; **RSV**: Respiratory Syncytial Virus; **SpO₂**: Oxygen saturation; **m-WCAS**: modified Wood's Clinical Asthma Score |

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| Factors                              | Total n=95 | CPAP n=26 | NIV n=46 | HFNC n=23 | p  |
|-------------------------------------|------------|-----------|----------|-----------|----|
| **Demographics**                    |            |           |          |           |    |
| Male, n (%)                         | 54 (57)    | 14 (54)   | 24 (52)  | 16 (69)   | 0.36|
| Age, days, median (IQR 1-3)         | 47 (24-75) | 41 (20-61)| 39 (23-61)| 61 (43-107)| 0.09|
| Weight, median (IQR 1-3)            | 4 (4-5)    | 4 (4-5)   | 4 (3-5)  | 5 (4-6)   | 0.003*|
| **Comorbidities**                   |            |           |          |           |    |
| Respiratory, n (%)                  | 1 (1)      | 0 (0)     | 1 (2)    | 0 (0)     | 0.99|
| Prematurity, n (%)                  | 15 (16)    | 2 (8)     | 11 (24)  | 2 (9)     | 0.15|
| **Clinical status at admission**    |            |           |          |           |    |
| Wang Score, median (IQR 1-3)        | 9 (7-9)    | 9 (7-9)   | 9 (7-9)  | 9 (7-9)   | 0.81|
| m-WCAS, median (IQR 1-3)            | 7 (6-8)    | 7 (6-8)   | 7 (6-8)  | 7 (6-9)   | 0.78|
| SpO₂, %, median (IQR 1-3)           | 90 (90-94) | 90 (90-92)| 90 (85-91)| 91 (90-98)| 0.02*|
| Respiratory rate, breath/min, median (IQR 1-3) | 50 (40-60) | 47 (36-60)| 47 (39-60)| 55 (49-60)| 0.39|
| Heart rate, /min, median (IQR 1-3)  | 156 (143-170) | 155 (145-160)| 160 (140-171)| 160 (148-170)| 0.29|
| Mean arterial pressure, mmHg, median (IQR 1-3) | 66 (59-75) | 65 (60-74)| 63 (55-74)| 69 (59-80)| 0.24|
| Body temperature, C°, median (IQR 1-3) | 37.2 (36.8-37.9) | 37.1 (36.7-37.6)| 37.3 (36.8-37.8)| 37.4 (36.8-38.1)| 0.40|
| Witnessed apnea, n (%)              | 13 (14)    | 0 (0)     | 11 (24)  | 2 (9)     | <0.001*|
| **Radiological data at admission**  |            |           |          |           |    |
| Abnormal X-Ray, n (%)               | 52 (55)    | 11 (42)   | 28 (61)  | 13 (57)   | 0.32|
| **Biological data at admission**    |            |           |          |           |    |
| pH, median (IQR 1-3)                | 7.3 (7.3-7.4) | 7.3 (7.1-7.4)| 7.3 (7.3-7.4)| 7.3 (7.3-7.4)| 0.26|
| PvCO₂, mmHg, median (IQR 1-3)       | 53 (47-61) | 54 (51-62)| 55 (47-62)| 50 (37-59)| 0.44|
| RSV, n (%)                          | 81 (89)    | 24 (92)   | 42 (91)  | 15 (65)   | 0.02*|
Other treatments

| Treatment          | Group 1 | Group 2 | Group 3 | Group 4 | p-value |
|--------------------|---------|---------|---------|---------|---------|
| Antibiotics, n (%) | 37 (39) | 4 (15)  | 22 (48) | 11 (48) | 0.01*   |
| Caffeine, n (%)    | 18 (19) | 2 (8)   | 14 (30) | 2 (9)   | 0.03*   |

Outcome

| Outcome                             | Group 1         | Group 2         | Group 3         | Group 4         | p-value |
|-------------------------------------|-----------------|-----------------|-----------------|-----------------|---------|
| Hospital LOS, days, median IQR (1-3)| 7 (5-9)         | 8 (5-9)         | 7 (5-9)         | 7 (5-10)        | 0.94    |
| PICU LOS, hours, median IQR (1-3)   | 87 (67-116)     | 77 (65-93)      | 85 (67-119)     | 93 (76-124)     | 0.43    |
| Duration of ventilatory support, hours, median IQR (1-3) | 70 (54-104) | 70 (48-87) | 69 (57-104) | 72 (51-164) | 0.34    |

Weaning

The weaning process was initiated after a median of 44 (IQR 26-64) hours after PICU admission. At weaning initiation, patients had a median Wang score of 2 (2-5), a respiratory rate of 41 breaths/min (IQR 35-48) and a FiO₂ of 25% (IQR 22-30).

Weaning failure was observed in 11 (12%) infants with no difference between the three types of ventilator support (Table 2). Weaning failure occurred within the first 4 hours following the initiation of weaning in 9 (82%) infants. These infants had a longer PICU length of stay (141, IQR 81-236 versus 81, IQR 67-100 hours) as compared to those who had a successful weaning (p<0.001). However, they had a longer hospital length of stay (8, IQR 6-12 versus 7, IQR 5-9 days, p=0.01).

The weaning process followed the ventilator support strategy of the unit (step-up/step-down strategy). Indeed, 44/46 (97%) of the infants supported by NIV were switched to CPAP (n=42) or HFNC (n=2) (Figure 1). Twenty one of the 26 (81%) infants supported by CPAP were switched to HFNC whereas none of the infants supported by HFNC was switched to NIV or CPAP. A progressive decrease in settings was only observed in the infants supported by HFNC (14/23, 61%). Finally, the number of infants who had a direct weaning was greater in those supported by HFNC (9/23, 39%), than CPAP (5/26, 19%) and NIV (2/46, 4%).

The weaning duration was significantly shorter for HFNC as compared to NIV and CPAP (p<0.01, Table 2, Figure 2).

Table 2. Weaning failure and duration of weaning according to the type of ventilatory support

| Values are median with interquartiles (IQR) or numbers (%) |

CPAP: Continuous positive airway pressure; HFNC: High Flow Nasal Cannula; NIV: Noninvasive Ventilation
Factors & Total n=95 & CPAP n=26 & NIV n=46 & HFNC n=23 & p

| Duration between admission and weaning initiation, hours, median IQR (1-3) | 44 (26-64) | 45 (28-64) | 35 (20-52) | 63 (42-111) | 0.009* |
| Duration of weaning process, hours, median IQR (1-3) | 24 (14-45) | 24 (14-40) | 28 (19-49) | 17 (0-26) | 0.01* |
| Weaning failure, n (%) | 11 (12) | 1 (4) | 9 (20) | 1 (4) | 0.1 |

**Discussion**

Our study is the first to describe the weaning for noninvasive ventilator support in infants with severe bronchiolitis. Our results show that the rate of weaning failure was comparable between NIV, CPAP and HFNC, that weaning duration was shorter for HFNC as compared to NIV and CPAP, and that the switch to another type of ventilator support was observed for 97% of infants supported by NIV and 81% of those supported by CPAP as compared to none of those supported by HFNC.

Weaning from non-invasive ventilatory support is a key-question for several reasons. Indeed, as reported by Baudin et al. and Carron et al.\(^8,9\), CPAP, NIV, and HFNC may be associated with complications such as skin lesions, pneumothorax, gastric distension and air leaks\(^10\). It is therefore important to wean the patient from any type of ventilatory support as soon as possible. Given the limited bed availability during winter in PICUs, priority should be given to discharge as soon as possible from the PICU patients whose condition improves. Finally, reducing the duration of ventilatory support and PICU length of stay through a reduction in the weaning process duration contributed to limit health care costs.

By analyzing our practice, we observed that we used a similar weaning strategy as reported in preterm infants supported by CPAP or NIV: 1/ direct weaning, 2/ switch to another type of ventilatory support (such as HFNC), 3/ decrease of the ventilatory settings (inspiratory or expiratory pressure)\(^11-14\). However, we did not use a gradual increase in off-ventilation time as a weaning strategy, since it could more time-consuming for nurses.

As the choice of the initial ventilator support follows a “step up” strategy (from HFNC to CPAP and then NIV), the weaning procedure follows the same “step down” strategy in the opposite order. This strategy seems reasonable because of a similar rate of failure for the 3 types of ventilator support. The only observed difference was a slightly shorter duration of the weaning procedure for HFNC (17 hours) as compared to CPAP (24 hours) and NIV (28 hours) which may be explained by the lesser severity of the infants supported by HFNC as compared to CPAP and NIV. However, we may consider this “step down” strategy as too cautious, leading to a longer duration of weaning. We hypothesize that for most infants, a
direct weaning from NIV or CPAP is safe and that the use of HFNC as an intermediate type of ventilatory support is unnecessary and expensive.

Interestingly, we found a longer weaning duration in patients supported by NIV and CPAP at admission as compared to those supported by HFNC, while the total duration of ventilatory assistance was similar. In facts, it means that patients were early switched to another mode of ventilation after admission in our step-down strategy.

To our knowledge, the weaning failure rate from non-invasive support has not been reported in the pediatric population. Yet, the impact of weaning failure on hospitalization duration and morbidity is very difficult to interpret. Unlike weaning from invasive mechanical ventilation, weaning from noninvasive ventilatory support is less challenging since the support can be easily put back in case of weaning failure, without incurring a high risk of deterioration to the patient. However, the consequences to pursue any type of ventilatory support can have an impact on hospitalization duration in PICU and therefore health care costs. Accordingly, as the concept of a targeted extubation failure rate in a cohort of mechanically ventilated patients, it could be relevant to apply the same concept for weaning failure rate from non-invasive support. This rate should therefore be not too low (which could mean that patients should have been weaned earlier) but not too high (meaning that patients still required the ventilatory support).

Interestingly, Betters et al. proposed a weaning protocol for HFNC in children admitted for acute respiratory failure in PICU\textsuperscript{15}. This protocol was based on a clinical score to discontinue HFNC, resulting in success rate from 70% on the first try to 90% on the fourth try. However, the population of patients included in this study was very heterogenous in term of age and diagnosis\textsuperscript{15}. As suggested by such studies, it could be useful to implement a weaning protocol from non-invasive ventilatory support in infants with bronchiolitis in order to reduce ventilatory support duration and to discharge patients from PICU more quickly.

Importantly, this study presents some important limitations that should be highlighted. First, this is a single-center study, while CPAP and NIV practices are very heterogeneous worldwide\textsuperscript{16}. Second, since we had no local protocol regarding ventilatory management of patients with bronchiolitis, this resulted in a wide heterogeneity in terms of ventilatory strategy, weaning procedures, criteria to initiate weaning and to consider weaning failure, making some of our findings difficult to interpret. Third, we acknowledge that the definition of weaning initiation may be controversial since not every switch from a type of ventilation to another can be considered as the beginning of weaning. However, as we described in our cohort, no patient experienced complication related to NIV, meaning that every switch from a type of ventilation to another can be explained by a significant change in the patient respiratory condition. Finally, the number of patients included is limited but we hypothesize that a larger population should provide some significant and more relevant findings. However, despite those limitations, our study provides some important and innovative data in this field.

**Conclusion**
The weaning phase represent a large proportion of noninvasive ventilatory support duration in infants with bronchiolitis. The rate of weaning failure was comparable between NIV, CPAP and HFNC and weaning duration was shorter for HFNC as compared to NIV and CPAP. The weaning procedure followed a “step down” strategy (from NIV to CPAP and then HFNC), an approach which may lead to an increase in duration of weaning. Future studies are warranted to define the best weaning strategy and to build protocols for weaning from non-invasive support.

Declarations

Ethical approval:

Yes

Consent for publication

N/A

Availability of data and materials:

All data generated or analysed during this study are included in this published article.

Conflict of interest

JC, CF, JD, IP, AB, BF and GM declare that they have no conflict of interest.

Funding:

None

Authors’ contribution:

JC, CF and JD wrote the manuscript, which was reviewed, edited, and approved by IP, AB, BF, and GM.

As the corresponding author, GM has final responsibility for the decision to submit for publication.

Institution where the work was performed

The work was performed at Grenoble Alpes University Hospital, Grenoble, France in 2019.

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**Figures**

*CPAP: Continuous Positive Airway Pressure; HFNC: High Flow Nasal Cannula; NIPPV: Non Invasive positive Airway Pressure*

**Figure 1**

Procedures used for weaning according to the mode of ventilatory support. The line-shaded bars represent the number of patients in whom a direct weaning strategy was used. The light grey bars represent the number of patients in whom a progressive strategy in decrease in parameters was used. The dark grey bars represent the number of patients in whom a progressive strategy using another type of support was used.
Figure 2

Duration of ventilatory support (light grey) and duration of weaning duration (dark grey) with interquartile, according to the type of respiratory support.