# Pathophysiology of Acute Respiratory Failure in Children with Bronchiolitis and Effect of CPAP

# 27

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## 27.1 Introduction

Acute bronchiolitis is the most common lower respiratory tract infection (LRTI) during the first year of life. Respiratory syncytial virus (RSV) infection is the most prevalent virus found in these children, accounting for 60–80 % of cases. The rate of hospitalization is less than 2 %. Up to 8 % of those hospitalized require ventilatory support [1, 2].

Three clinical presentations of severe bronchiolitis have been described. Acute hypercapnic respiratory distress is the most frequent form, resulting from respiratory muscle fatigue associated with alveolar hypoventilation. Recurrent severe apnea occurs in 1.2–23.8 % of cases [3, 4]. The latest clinical presentation is predominantly alveolar and can lead to acute respiratory distress syndrome (ARDS) [5]. Obstruction of the bronchioles increases the work of breathing (WOB), which represents the energy required to overcome the increased airway resistance. Infants, especially those born prematurely, are more prone to respiratory muscle fatigue.

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Prematurity, young age, and preexisting chronic respiratory and cardiac diseases are the main risk factors for severe bronchiolitis [1, 6]. When the WOB increases or persists for a long period, ventilatory support is required to prevent severe hypoxemia or hypercapnic coma.

Noninvasive ventilation (NIV) is most often delivered by continuous positive airway pressure (CPAP) via nasal prongs or mask. Some studies have reported the use of assisted spontaneous breathing (ASB) and biphasic positive airway pressure (BIPAP) as other NIV modalities [7–12]. High-flow cannulas (HFCs) deliver positive end-expiratory pressure (PEEP) that can attain 3 or 5 cmH$_2$O, and some studies suggested that it could obviate the need for endotracheal intubation [7, 8, 13–15]. There is no strong level of evidence that NIV avoids intubation and is beneficial for patients compared to intubation. During the last decade, however, increasing numbers of clinical and physiological studies have reported a good experience of NIV as the primary ventilatory support mode. Currently, CPAP is widely used as the first ventilatory support in many centers, with a decreasing rate of intubation.

The objective of this chapter is to summarize the impact of NIV techniques in the management of children with severe bronchiolitis requiring ventilatory support. Physiological knowledge is first discussed followed by clinical studies assessing the impact of NIV on the intubation rate and outcome. We then address the technical and practical aspects of NIV application in children according to age and clinical condition.

## 27.2   Physiological Aspects and Impact of NIV on Ventilatory Mechanics

In a physiological study of 37 infants, Hammer and colleagues showed that RSV infection could lead to two pulmonary function abnormalities [5]. The most common is bronchiolitis, an obstructive airway disease characterized by increased airway resistance (respiratory system resistance, $R_{rs}$), air trapping [high functional residual capacity/total lung capacity (FRC/TLC)], reduced TLC, and low respiratory system compliance ($C_{rs}$) compared with normal values. Typically, chest radiography of these children shows bilateral perihilar infiltrates and hyperinflation. Of the 37 infants, 10 had a resistive profile, corresponding to the criteria of acute respiratory distress syndrome (ARDS), with very low $C_{rs}$ and $R_{rs}$. Radiography revealed bilateral alveolar consolidations. This form corresponded to RSV pneumonia.

The mechanism of apnea associated with RSV infection is not completely understood. Immaturity of central ventilatory centers is likely to be one of the explanations, which can explain the high prevalence of apnea in infants born prematurely and infants <2 months of age. The real incidence of apnea varies among studies, from 2.5 to 28.0 %, depending on the case mix. Among children admitted to the pediatric intensive care unit (PICU) the incidence is much higher [3]. It is probably important to distinguish primary apnea from apnea occurring after several hours of respiratory distress and a high level of WOB. The latter is likely to be due to muscle fatigue, which occurs more rapidly in young infants and those born prematurely.
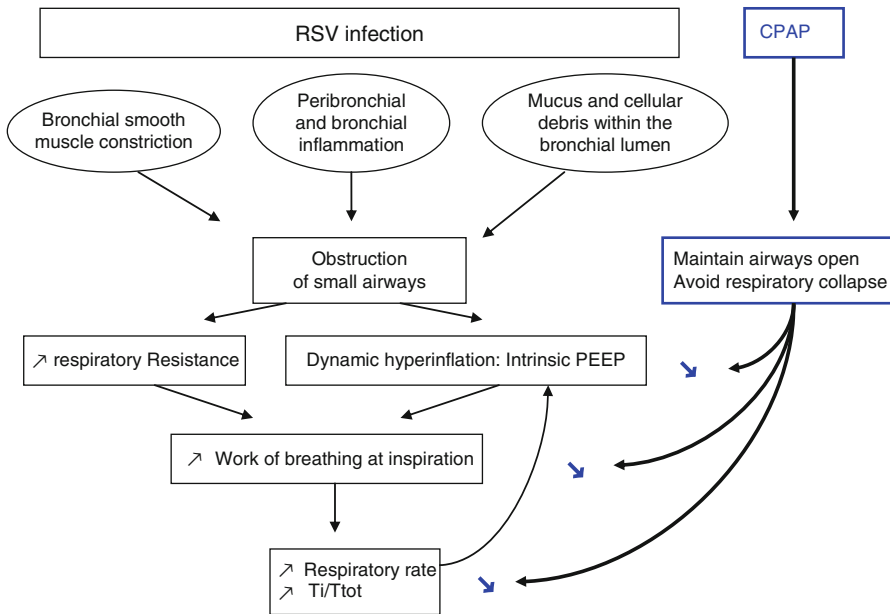
**Fig. 27.1** Pathophysiology of the classic form of bronchiolitis: obstruction of small airways, its impact on ventilatory mechanics, and the effect of CPAP application. *CPAP* continuous positive airway pressure, *RSV* respiratory syncytial virus, *PEEP* positive end-expiratory pressure, *Ti* inspiratory time, *Ttot* length of a respiratory cycle

Obstruction of small airways is the main physiological phenomena of RSV infection in infants. It is the consequence of bronchial and peribronchial inflammation, plugging of airways by mucus and cellular debris, and bronchial smooth muscle constriction (Fig. 27.1). Consequently, the airway resistance and respiratory load increase. To preserve their pulmonary function, infants use their accessory respiratory muscles, increasing their WOB. They also increase their respiratory rate, but because of airway obstruction the duration of the expiratory period is too short to expire completely. Air is then trapped in the alveoli, generating dynamic hyperinflation and auto-PEEP. The inspiratory time/total respiratory time ($T_i/T_{tot}$) ratio increased as $T_i$ decrease (Fig. 27.1).

Cambonie et al. from Montpellier and Essouri et al. from Paris have documented these respiratory changes and have shown that application of CPAP via nasal prongs led to a decrease in the respiratory rate (RR), $T_i/T_{tot}$ ratio, and WOB assessed by esophageal and diaphragmatic pressure time products ($PTP_{es}$ and $PTP_{di}$) (Fig. 27.1, Table 27.1) [7, 16, 17]. These measures were obtained using an esophageal and gastric probe with balloons. The $PTP_{es}$ per breath was obtained by measuring the area under the diaphragmatic pressure ($P_{di}$) and the esophageal pressure ($P_{es}$) signal between the onset of inspiration and the end of inspiration. Essouri et al. showed in ten infants with severe bronchiolitis that the median level of auto-PEEP generated was 6.05 cmH$_2$O (range 3.9–9.2 cmH$_2$O) [16]. They showed that the decrease in

**Table 27.1** Main physiological studies on the effects of CPAP on respiratory mechanics and on clinical parameters

| Study | No. | Design | Age | Severity criteria | NIV type and setting | Main effects after CPAP | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | $FiO_2$ | WOB | RR | $pCO_2$ | Ti/Ttot | WCAS |
| Milési (2013) [17] | 19 | RCT | 52,5 | WCAS >4 RR 55 c/min $pCO_2$ 56 mmHg | Nasal CPAP 6 cmH$_2$O Infant Flow | ↘ | ↗ | → | ↘* | NA | ↗ |
| Cambonie (2008) [7] | 12 | Prospective No control | 43 | WCAS > 5 $pCO_2$ 64 mmHg | Nasal CPAP 6 cmH$_2$O Infant Flow | ↘ | ↗ | → | ↗ | ↗ | ↗ |
| Essouri (2011) [16] | 10 | Prospective No control | 45 | RR 78 $pCO_2$ 61.5 mmHg | Nasal CPAP 4-7-10 cmH$_2$O § | NA | ↗ | ↗ | ↗ | ↗ | NA |

*CPAP* continuous positive airway pressure, *FiO$_2$* inspiratory fraction of oxygen, *RCT* randomized clinical trial, *RR* respiratory rate, *Ti* inspiratory time, *Ttot* total respiratory time, *WCAS* Wilson clinical asthma score

*The level of pCO2 decreased significantly from baseline in the group treated by CPAP 6 cm H$_2$O whereas the level did not decrease significantly in the control group

§ Three levels of CPAP were tested 4, 7 and 10 cm H$_2$O

WOB was greater with a CPAP level of 7 cmH$_2$O compared to 4 or 10 cmH$_2$O. This suggested that application of extrinsic PEEP decreased the pressure gradient between the mouth and alveoli at end-expiration. It allowed air to pass through the airways, reducing the work required for the next inspiration. The Montpellier team in France confirmed these results and the role of CPAP in a randomized controlled trial (RCT). They compared ten children treated with nasal CPAP at 6 cmH$_2$O to nine children managed with oxygen alone [17]. The $T_i/T_{tot}$ and transcutaneous carbon dioxid partial pressure (TcPCO$_2$) were decreased in the CPAP group and the WOB was significantly reduced compared to that in control patients. This improvement of the WOB was correlated with the clinical improvement assessed by the modified Wilson Clinical Asthma Score (mWCAS).

## 27.2.1 Clinical Studies on NIV in Children with Severe Bronchiolitis

Beasley and Jones [18] and Soong et al. [19] were the first to report NIV use, especially CPAP, in infants with severe bronchiolitis. These preliminary studies showed that CPAP was able to decrease the PaCO$_2$ and RR of infants with severe bronchiolitis. Since 2004, numerous prospective or retrospective studies have been published and reported an increasing use of CPAP in this clinical setting (Table 27.2) [8–12, 17, 19–21]. However, there is no clear consensus on clinical use of CPAP compared to intubation and invasive ventilation [22].

### 27.2.1.1 Potential Advantages of NIV Techniques Compared to Invasive Ventilation

Complications of intubation and mechanical ventilation are well known. In infants, endotracheal intubation can be complicated by subglottic edema with a risk of evolution to tracheal stenosis. Mechanical ventilation of children with severe airway obstruction is challenging and may expose the airways and the lungs to high pressures or high volumes, causing lung injury. Most of infants who are mechanically ventilated require sedative drugs and sometimes muscle paralysis. The need for central venous access is common. These invasive procedures are associated with blood loss and expose children to nosocomial infection (e.g., pneumonia, urinary tract infection, bacteremia). The safety of sedative drugs in immature brains is not completely established. Hence, NIV represents a good alternative because its use rarely requires sedative drugs. On the other hand, the main risks of NIV are pneumonia aspiration in a child with an altered level of consciousness and potentially delayed intubation.

### 27.2.1.2 Clinical Effects of CPAP or NIV on Outcome

Most of studies have confirmed the results of early studies that CPAP and NIV improve gas exchange and the RR. Physiological studies suggested that application of CPAP improved gas exchange by decreasing the WOB and respiratory efforts, as assessed by the mWCAS.

**Table 27.2** Clinical studies on non-invasive ventilation in children with severe bronchiolitis

| Author (year) | Design | N | NIV mode | Interface | ETI avoided (%) | Clinical outcome | pH change | pCO₂ change | O₂ requirement | Infection | LOS, LMV | Major complication |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Thia (2008) [21] | RCT cross-over | 29 | CPAP | Nasal prongs | – | – | – | ↗ | – | NA | NA | 0 |
| Milési (2013) [17] | RCT, physio | 19 | nCPAP, 6 cmH₂O | Nasal prongs | 100 | ↘WOB ↘WCAS | NA | ↗ | ↗ | NA | NS | 0 |
| Cambonie (2008) [7] | Prospective, physio | 12 | nCPAP, 6 cmH₂O | Nasal prongs | 100 | ↘WOB ↘WCAS | NA | ↗ | ↗ | NA | | 0 |
| Javouhey (2008) [10] | Retrospective, Pre/post | 80 (15ᵃ) | CPAP, BIPAP | Nasal prongs or mask | 67 | | NA | NA | ↗ | ↘ᵃ | ns | 0 |
| Larrar (2006) [11] | Prospective, NC | 53 | CPAP | Nasal prongs | 75 | ↘RR | ↗ | ↗ | NA | NA | | 0 |
| Campion (2006) [8] | Prospective, NC | 69 | CPAP/BIPAP | Nasal prongs, facial mask | 83 | ↘RR | ↗ | ↗ | NA | NA | | 0 |
| Lazner (2012) [12] | Retrospective, NC | 61 | CPAP 4–6 cmH₂O Cuirass (P neg) | Nasal prongs or mask | 90 | ↘RR | ↗ | ↗ | ↗ | ↗ (compared to NR and IV) | | 0 |
| Essouri (2011) [16] | Prospective, physio | 10 | CPAP (4-7-10 cmH₂O) | Nasal prongs | 90 | ↘RR ↘WOB | NA | ↗ | | | | 1 bacterial coinfection, NIV failure, IV |
| Ganu (2012) [9] | Retrospective 10 years | 520 (285ᵃ) | CPAP | Nasal or facial mask | 83.2 | NA | NA | NA | NA | NA | ↘ᵇ | NA |

*LMV* length of mechanical ventilation, *LOS* length of stay, *NA* not available, *NC* not controlled, *NIV* non-invasive ventilation, *NR* non responder, *physio* physiological, *RR* respiratory rate, *WCAS* Wilson clinical asthma score, *WOB* work of breathing

ᵃThe rate of ventilator-associated pneumonia was significantly decreased during the NIV period compared to the IV period

ᵇMedian LOS was reduced in children in whom NIV succeeded compared to those with IV and those who failed NIV

Few studies have compared this approach to the classic invasive ventilatory strategy on clinical outcome, such as the duration of ventilatory support, length of PICU stay, length of hospital stay (LOS), or ventilator-assisted pneumonia (VAP). Javouhey et al. in a pre/post study design showed that NIV as the primary ventilatory support was associated with a significant decrease in the intubation rate: from 89 to 52 % [10]. The NIV failure rate was 33 %. This approach was associated with a decreased incidence of VAP and a decrease in the number of children with oxygen requirement for >8 days [10].

Ganu et al. reported their 10-year experience of NIV for infants with severe bronchiolitis in their PICU from The Children's Hospital at Westmead in Sydney. Among the 520 infants admitted for bronchiolitis, 399 required ventilator assistance—285 with a trial of NIV, mainly CPAP [9]. They reported a significant increase in the use of NIV (2.8 % increase per year) along with a decline in the intubation rate (1.9 % per year). The percentages of infants failing NIV decreased over the study period, from 31.8 to 13.5 %. This decline was also observed in centers in which NIV was widely used as the primary mode of ventilatory support [9]. In our center, for example, this percentage decreased from 33 to 5 % during the 2011–2012 epidemics (personal data). The median hospital LOS was longer for infants who were intubated and invasively ventilated than for those in whom NIV succeeded. The hospital LOS was also significantly longer for children who failed NIV than for those with invasive ventilation. The same tendency had been found in a previous study [10]. Even with no control study, these results suggested that a strategy using NIV (mainly CPAP) as the primary ventilatory support was able to obviate the need for tracheal intubation.

### 27.2.1.3  Use of High-Flow Cannulas

More recently, a system of oxygen delivery was developed using heated and humidified high-flow gases delivered via nasal cannulas that can generate PEEP. The level of PEEP provided depends of the flow and the leaks but can reach 3–5 cmH$_2$O. This system has been used in children with severe bronchiolitis, with results similar to those achieved with CPAP, including improved alveolar ventilation and decreased RR, obviating the need for tracheal intubation [14, 15, 23] (Table 27.3). Physiological studies showed that high-flow cannulas (HFCs) are able to improve lung mechanics and ventilatory function by a washout of the nasopharyngeal dead space, a decrease in airflow resistance, and improved mucociliary clearance [24].

An RCT pilot study performed in 19 infants with moderately severe bronchiolitis showed that heated/humidified HFC therapy at 4–8 L/min improved the SpO$_2$ compared to a head-box oxygen group at 8 h (100 % vs. 96 %, $p = 0.04$) and 12 h (99 % vs. 96 %, $p = 0.04$) [13]. The stability of PEEP is not guaranteed and the level of PEEP reached can be insufficient to counterbalance the WOB. An in vitro study from Sivieri et al. showed that the airway pressure varied widely with the degree of nares occlusion by the prongs and by the amount of mouth leakage [25]. At 6 L/min HFC with the mouth open the airway pressure was <1.7 cmH$_2$O. It was <10.0 cmH$_2$O when the mouth was closed. Complete nares occlusion can generate high airway pressure (up to 20 cmH$_2$O) when the mouth is closed.

**Table 27.3** Clinical studies on heated humidified high flow cannulas in children with severe bronchiolitis

| Author (year) | Design | $n$ | HFC set up | ETI avoided (%) | Clinical outcome | Ph change | pCO$_2$ change | LOS, LMV | Major complications |
|---|---|---|---|---|---|---|---|---|---|
| Schibler (2011) | Retrospective | 167 | 8 L/min | 96 | 4 % intubation<br>Decrease intubation rate from 37 to 7 %<br>20 % decrease of HR and RR 90 min after HFC | NA | NA | 2.33 (1.6–3.5) | 0 |
| McKiernan (2010) | Retrospective Pre/post study | 115 | 7 L/min (infant cannula) or 8 L/min (pediatric cannula) | 91 | Decrease intubation rate from 23 to 9 %: 68 % reduction of intubation (adjusted for age, weight, and RSV status)<br>Reduction of RR 1 h after initiation of HFC more important than without HFC | NA | NA | 4 vs. 6 days | 1 pneumothorax in each group Nasal, facial trauma |
| Abboud (2012) | Retrospective | 113 | | 81.4 | Risk factors of failure:<br>Low mean weight<br>High pCO$_2$ before and after HFC<br>Low RR before HFC<br>High PRISM score | | | | |

*ETI* endotracheal intubation, *HFC* high flow cannula, *HR* heart rate, *NA* not available, *PRISM* pediatric risk of mortality, *RR* respiratory rate, *RSV* respiratory syncytial virus

Further studies comparing CPAP and HFCs would be useful to understand which children should benefit from CPAP rather than HFC. The latter system has the advantage of being simple to apply, usable in emergency units, and minimally expensive. Criteria used to initiate HFC or CPAP should be better defined and validated. A selection bias cannot completely be excluded because the level of severity of the infants treated is difficult to compare among studies. Moreover, as criteria to initiate ventilatory support are not well defined, those used in the various studies are likely to be different. Some authors have included children with severe respiratory distress and severe hypercapnic acidosis, whereas others have put children on ventilatory support considering only the signs of retraction or the level of tachypnea.

### 27.2.1.4 Criteria for Ventilator Support in Children with Severe Bronchiolitis

Criteria to initiate ventilatory support in children are not well defined and have not been validated. Most epidemiological studies have shown that infants with low weight and age < 42 days were more likely to be admitted to a PICU and ventilated. Other factors predisposing to mechanical ventilation were factors linked to a medical history of lung and cardiac diseases, prematurity, and/or neuromuscular disease [2, 9, 20].

Evans et al. analyzed criteria for CPAP requirement in a retrospective cohort of 163 patients admitted to their center for severe bronchiolitis [20]. Among these 163 children, 28 required CPAP. The authors found seven predictors for CPAP requirement: young age, low gestational age, low $SpO_2$, high level of oxygen requirement, respiratory and heart rates (RR, HR), and Glasgow Coma Score (GCS). Using receiver operator characteristic (ROC) curve analyses, they identified several thresholds: age < 11 weeks, $SpO_2$ < 95 %, RR > 54, HR > 163, and GCS < 15. The strongest predictor was a low $SpO_2$. The authors found a negative correlation between $SpO_2$ and $O_2$ requirement ($r = -0.656$), a positive correlation between age and weight ($r = 0.836$), and a positive correlation between gestational age and birth weight ($r = 0.824$). They did not find blood gas analyses as predictors of CPAP requirement [20]. Their results were limited by the retrospective nature of the study and by the small sample size.

Mansbach et al. identified factors associated with CPAP and/or intubation requirement in a prospective multicenter study that included 161 children [26]. In the multivariate analysis, factors associated with CPAP and/or intubation requirement were age < 2 months [odds ratio (OR) 4.3, 95 % confidence interval (CI) 1.7–11.5], maternal smoking during pregnancy (OR 1.4, 95 % CI 1.1–1.9), birth weight < 5 lb (OR 1.7, 95 % CI 1.0–2.6), breathing difficulty began <1 day before admission (OR 1.6, 95 % CI 1.2–2.1), severe retractions (OR 11.1, 95 % CI 2.4–33.0), and room air $SpO_2$ < 85 % (OR 3.3, 95 % CI 2.0–4.8) [26]. Identifying patients at high risk of CPAP requirement is important because it can help the physician's decision about transferring the patient to the unit able to initiate the ventilatory support required.

Curiously, blood gas analyses have not been found to be good indicators of ventilatory support requirement except in the study of Campion et al., where a high

**Table 27.4** Criteria of ventilatory support selected by investigators in the French prospective multicenter study (at least two criteria are needed)

| Criterion 1 | Respiratory rate | RR > 70/min for age< 6 month |
| | | RR > 60/min for age ≥ 6 month |
| Criterion 2 | Oxygenation | $SpO_2 < 92\ \%$ whatever the level of $O_2$ requirement |
| Criterion 3 | Respiratory acidosis | pH < 7.3 and $pCO_2 > 70$ mmHg |
| Criterion 4 | Apnea | Apnea with $SpO_2 < 90\ \%$ and/or bradycardia < 90 if age < 6 month or < 80 for older |
| Criterion 5 | Neurological signs | Hypotonic and drowsiness in the absence of stimulation |

*RR* respiratory rate, *SpO$_2$* percutaneous oxygen saturation

**Table 27.5** Absolute criteria of intubation (one criterion is sufficient) defined a priori by investigators of the French multicenter study

| Criterion 1 | Respiratory arrest | Inability to maintain efficient ventilation with $SPO_2 > 90\ \%$ after 2 min of bag–mask ventilation |
| Criterion 2 | Refractory hypoxia | Inability to maintain $SpO_2 > 90\ \%$ during 1 h |
| Criterion 3 | Neurological failure | Altered level of consciousness with low reactivity or agitation not responding to oxygenation |

level of $CO_2$ before CPAP was predictive of NIV failure defined as the need for invasive ventilation [8]. Similarly, composite scores of respiratory distress failed to identify the group of patients requiring ventilator support. In two French studies, high PRISM scores were predictors of the need for invasive ventilation. However, as this score is calculated 24 h after admission, it cannot help the physician make clinical decisions [8, 11].

The criteria for initiating CPAP should differ from those used to initiate invasive ventilation. Unfortunately, no reported studies have made such a comparison of these criteria. Therefore, the ventilatory strategy for children admitted with severe bronchiolitis is based on little evidence. CPAP and HFC can be proposed as first-line ventilatory support in most cases, although HFC is probably insufficient in children with severe hypercapnic acidosis. Response to this first line of ventilatory support must be assessed within the first 2 h following its initiation. Nonresponders are at high risk of complications and often require invasive ventilation. NIV in BiPAP or ASB mode or in pressure control mode can be attempted provided that rapid assessment is done and strict supervision is observed.

For better selection of patients who will respond to CPAP, some studies have assessed risk factors of NIV failure. Most of these studies were retrospective and compared patients whose ventilatory support was NIV alone versus those who were intubated after an NIV trial [8, 10, 20, 27–29]. Failure was defined as the need for intubation. Most of these studies included children with all types of respiratory distress, not bronchiolitis alone. The level of $FiO_2$, ARDS and a high level of $FiO_2$ (over 80 %) 1h after starting NIV were found as factors associated with NIV failure in children with severe respiratory distress of various causes [27, 28]. Larrar et al. identified the absence of a reduction in $PCO_2$ as a predictive factor of NIV failure in a CPAP study. Abboud et al., in an HFC study, came to the same conclusion [11, 23].

A French prospective multicenter study noted that a minimal reduction in $CO_2$ and a low increase in pH measured 2 or 4 h after NIV initiation were strong predictors of NIV failure [30]. In that study, the various centers had defined criteria for ventilatory support and absolute criteria for invasive ventilation (Tables 27.4 and 27.5). The results suggested that early assessment of the response to NIV is crucial.

## 27.3  Practical Aspects of NIV Use and Risk Factors of Failure

Noninvasive ventilatory supports include a number of systems that deliver pressure support to the patient via an interface. The CPAP delivery system has to be reliable, with good stability of the pressure during all the respiratory cycle length. It also has to be easy to use and install in children. Interfaces are chosen according to their ability to be connected to the CPAP delivery systems while minimizing air leaks, dead space, and discomfort.

### 27.3.1  High-Flow Cannulas

To deliver heated/humidified oxygen, an air-oxygen flow generator is required combined with a heated humidifier. The circuit tubing and the size of the cannula differ according the age of the child. For infants weighing <10 kg, small-volume circuit tubing is required. Infant or pediatric cannulas can be used. Adult circuit tubing and cannulas are used for children weighing ≥10 kg.

### 27.3.2  Systems for Delivering CPAP

As children with severe bronchiolitis requiring ventilatory support are young (<42 days) and of low weight, CPAP systems developed for neonates are used, such as Infant Flow (EME, Electro Medical Equipment, Brighton, UK), Infant Star 950 (Nellcor Puritan Bennett, San Diego, CA, USA), and Bubble CPAP (Fisher and Paykel Healthcare, Auckland, NZ). In the latter system, a water column delivers PEEP. In PICUs, an ICU ventilator or CPAP machine may be preferred. No study has compared the stability of PEEP in these delivery systems. It is well known that PEEP stability can be affect by the level of leaks, the degree of mouth opening, and the level of airflow in the circuit.

The choice of the interface is crucial. The ideal interface is one that is easy to install, minimizes leaks, and does not cause skin or mucosal injury.

#### 27.3.2.1 Nasal Prongs
Low-resistance nasal prongs or cannulas are the interfaces most frequently used in infants with bronchiolitis. The nasal approach is preferred because infants predominantly breathe through the nose. In infants with bronchiolitis, the tolerance is reportedly good, although no study has specifically addressed skin or mucosal injuries in the context of bronchiolitis. As nasal breathing has to be preserved, nasal

obstruction, which frequently occurs during RSV infection, should be systematically treated and monitored. Nasal obstruction is a source of discomfort and agitation for children treated by nasal CPAP. Consequently, nasal lavage with NaCl 0.9 % every 3 or 4 h is recommended. The choice of the cannula's size is important to limit leaks and avoid nose injuries. It is recommended that nasal prongs of different sizes with different inter-nostril distances be readily available. To limit mouth leaks, a dummy is frequently used and sometimes a chinstrap is required. To avoid skin irritation or ulceration and to improve the patient's comfort, colloid ulcer dressings (e.g., Comfeel, Coloplast) are applied to protect the nasal bridge as well as the nostrils. In our experience, nasal prongs or cannulas are well tolerated by infants weighing up to 5 kg. For larger infants, nasal masks are often better tolerated.

### 27.3.2.2 Small, Nonleaking Masks for Neonates

During the last decade, manufacturers have designed small nasal masks specifically intended not to leak. They allow us to put small infants on CPAP with standard ventilators in the PICU. These masks are also available for the Bubble CPAP system and the Infant Flow CPAP generators. It is also possible to use a nasal mask with intentional leakage to connect infants to a CPAP or BiPAP machine. The Resmed Sullivan Infant Bubble mask (ResMed, Waterloo, Australia) is used for the smallest infants and the Small Child Profil Lite mask (Philips Respironics, Murrysville, PA, USA) for the others. Skin protection can be used to minimize skin irritation. The choice of the headgear or bonnet fitted to the head's form and size is important to avoid mask displacement, which can increase leaks, and fastening the mask too tightly on the face, which could increase the risk of skin injuries.

### 27.3.2.3 Bucconasal Masks, Facial Masks, Helmets

Bucconasal masks are used only when the leaks are interfering with synchronization of the infant with the ventilator for NIV. When the mouth is open or if the nose is obstructed, application of nasal CPAP becomes ineffective. A major concern is the absence of specific bucconasal masks for infants. Most often, anesthesia masks or adult nasal masks are used. However, in these cases, the risk of skin injury is much higher than with nasal masks, particularly laceration or ulceration of the nasal bridge. Skin protection with colloid dressings must be used to prevent these injuries. Progress in the design of bucconasal masks is needed to enable NIV in infants and young children. Helmets represent an alternative in children weighing >5 kg. They cannot be used in smaller children because the helmet compresses the chest, reducing its efficacy. Some experiences with helmets have been reported even in small children. They report rather good tolerance and improvement of alveolar ventilation [31, 32].

## 27.4    Ventilator Settings: Level of CPAP

Essouri and colleagues showed that a CPAP level of 7 cmH$_2$O was better than either 4 or 10 cmH$_2$O in 10 children admitted to a PICU for severe bronchiolitis [16]. The decrease WOB, assessed by PTP$_{di}$ and PTP$_{es}$, was more significant with 7 cmH$_2$O.

This level was closest to the auto-PEEP level (6.3 cmH$_2$O) and is consistent with the level of CPAP used in the main clinical studies (Table 27.2). Based on these results, starting with a level between 6 and 8 cmH$_2$O is recommended.

For HFC, the recommended flow by the manufacturer is 1–2 L/kg/min. In a retrospective study, Schibler et al. used a fixed flow of 8 L/min but did not explain the reason for this choice [15]. In practice, we start with a flow of 1 L/kg/min and increase it to 2 L/kg/min according to the tolerance of the child. As already noted, the optimal level of flow is unknown and depends of the degree of nares obstruction and mouth leakage.

Concerning the BiPAP or ASB ventilation modes, as no study has been performed comparing different ventilatory settings we are not able to make any recommendations. The studies that have reported the use of BiPAP or ASB in patients with bronchiolitis used a level of PEEP varying from 4 to 8 cmH$_2$O and inspiratory pressures between 10 and 20 cmH$_2$O. The level of pressure support varied from 4 to 12 cmH$_2$O. NIV pressures >20 cmH$_2$O are associated with a high risk of gastric dilatation by gas. To minimize this phenomenon, a nasogastric tube is routinely inserted to deflate the stomach when necessary. In our clinical practice, when an infant is switched from CPAP to NIV on pressure support, we start with a level of PEEP equal to the level of CPAP used and then add pressure support of 6 cmH$_2$O above PEEP or an inspiratory pressure of 6 plus PEEP. Then, after assessing the efficacy and tolerance, we adapt the ventilator setting or the interface, avoiding exceeding 20 cmH$_2$O. The inspiratory pressure is titrated by 2 cmH$_2$O increments to a level where the RR, signs of WOB, and blood gases are improved.

The main problem with NIV in pressure support mode, such as BiPAP, is asynchrony. The sensitivity of ventilatory triggers is sometimes insufficient for young infants, who are unable to trigger a ventilatory cycle. On the contrary, when the sensitivity of the trigger is too high, and when the leaks are important, auto-triggering may appear, generating discomfort and asynchrony. Control of leakage is another factor contributing to synchrony: If the ventilator is unable to compensate for the leaks, the inspiratory time can be prolonged into the period when the child wants to expire. These causes of asynchrony are a source of discomfort and poor tolerance of NIV in infants.

No study has been performed comparing different ventilatory modes with different ventilators in infants who suffer from severe bronchiolitis. Neurally adjusted ventilatory assistance (NAVA) is a promising mode that would limit the incidence of asynchrony. Liet and colleagues reported three cases of infants with severe bronchiolitis treated with this mode during invasive mechanical ventilation and showed that NAVA was able to improve synchrony, decrease the oxygen requirement, and decrease peak airway pressure from 28±3 to 15±5 cmH$_2$O [33].

It has been shown In 15 neonates and children that NAVA decreased patient–ventilator asynchrony and the peak inspiratory pressure [34]. The percentage of time in asynchrony was lower in the NAVA group (8.8 %) than in the pressure (33.4 %) and flow (30.8 %) trigger groups (ventilated either in pressure control or pressure regulated volume controlled). Moreover, the peak inspiratory pressure was 1.9–2.0 cmH$_2$O lower in NAVA than in the pressure and flow groups, respectively ($p < 0.05$ for both) [34].

We reported our experience of NAVA in NIV mode in 18 infants with severe bronchiolitis. The tolerance and the feasibility were good, and 16 of 18 infants had NAVA mode success, thereby avoiding invasive ventilation (personal communication). As no study comparing classic NIV to NAVA NIV has been reported, this technique cannot be recommended but represents a new mode to be considered when asynchrony is detected frequently with classic NIV.

## 27.5    Discussion

During the last decade, ventilatory support for children with severe bronchiolitis has radically changed. Nasal CPAP is become the first mode of NIV for children who meet the criteria for ventilatory support. Numerous studies have suggested that this strategy is associated with a decreased need for intubation and invasive ventilation. Although the level of evidence of improved outcomes related to this strategy is low, in the absence of prospective controlled studies the data published have shown that children can be safely managed less invasively without prolonging the PICU stay. Some studies suggested that responders to nasal CPAP had a lower length of PICU stay than those who were intubated.

Physiological studies have provided some evidence that a CPAP level of 6–7 cmH$_2$O is able to decrease the WOB and improve alveolar ventilation in children with obstructive bronchiolitis [7, 16, 17]. The application of extrinsic PEEP to the airways at a level greater than the level of auto-PEEP generated by dynamic obstruction of small airways allowed reduction of efforts made by the child to initiate the next inspiratory cycle. This mechanism is responsible for the clinical improvement observed in the children after initiation of nasal CPAP. The responders are those whose RRs are reduced and CO$_2$ levels and heart rates are decreased within 2–4 h of starting NIV with CPAP. Early identification of those who will respond is crucial so as not to delay applying NIV with two levels of pressure or intubation with invasive ventilation.

More recently, the HFC, which is able to deliver humidified/heated oxygen, has been reported to be another alternative to nasal CPAP [14, 15, 23]. This system has been shown to generate a low level of PEEP, induce washout of nasopharyngeal dead space, match inspiratory flow rates in infants, and improve mucociliary clearance [24]. Children with apnea and those with severe hypercapnic acidosis are more likely to fail HFC and can be treated by nasal CPAP. As no study has been conducted comparing HFC to nasal CPAP, no recommendation can be drawn. There is a crucial need of studies to better distinguish groups of children who will respond to HFC, to CPAP, or to NIV because the level of expertise and equipment differ significantly between these modes. HFC can be initiated in the emergency or intermediate care units, whereas CPAP and NIV should be reserved for use in an intermediate care unit or an ICU according the level of the teams' experience. Stratification of respiratory distress severity is required for better patient selection at admission. We know that patients with a medical history of chronic lung, heart, or neuromuscular diseases are at higher risk of complications and failure of HFC or CPAP. Young

infants, particularly those born prematurely and those with low weight, are more likely to require ventilatory support [1, 6]. However, the clinical score, biological markers, and blood gas criteria associated with ventilatory support and with CPAP failure, are not well defined and require further study. Moreover, as no study has been performed on NIV at two pressure levels in bronchiolitis, there is no evidence that NIV after CPAP or HFC failure can obviate the need for intubation and invasive ventilation. Only a multicenter prospective study comparing different ventilatory strategies would be able to determine the best ventilatory support treatment.

Technically, manufacturers have improved their products to facilitate CPAP application. Nasal masks and nasal prongs of different sizes are now available, allowing us to fit the equipment to the child's facial and head morphology. The objectives of these interfaces are to facilitate setup, limit the dead space, and reduce air leaks. Experience and the use of specific nursing protocols are factors associated with a high success rate of NIV techniques, suggesting that only teams with a high level of training and experience should apply NIV.

**Key Major Recommendations**
- Nasal CPAP and HFCs are the best first option for ventilatory support of children with severe bronchiolitis. Their use may avoid intubation and invasive mechanical ventilation.
- There is an insufficient level of evidence of the efficacy of NIV on mortality or morbidity criteria.
- NIV with pressure support is an option when CPAP fails.
- Early assessment (within the first 2 h) of responders to CPAP or HFC is required to prevent secondary critical deterioration.
- Improved blood gas levels after CPAP is a good indicator of response to CPAP.
- Infection, apnea, and young age are associated with NIV failure.
- Nasal cannulas are the most appropriate interface for infants weighing <5 kg.
- The optimal CPAP level to prevent muscle fatigue is probably around 7 cmH$_2$O.

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