REVIEW

Non-invasive respiratory support therapies in the acute setting: how to improve the success rate of weaning

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ABSTRACT

Noninvasive respiratory support modalities such as noninvasive ventilation (NIV), continuous positive airway pressure (CPAP), and high-flow nasal cannula (HFNC) are commonly used in children with various acute respiratory conditions, characterized by oxygen dependence, hypercapnia, or both. The primary goals of noninvasive support in these patients are to reverse moderate respiratory failure while avoiding therapeutic escalation such as intubation and invasive ventilation, or to stabilize the clinical condition of a previously invasively ventilated patient to prevent extubation failure. Despite the strategic role of noninvasive respiratory support to reduce the impact of invasive mechanical ventilation, which requires admission in intensive care unit and exposes patients to higher risk of ventilator-associated complications, currently available evidence is not sufficient to establish solid guidelines or standardized protocols on initiation criteria, operating procedures, weaning strategies, and failure criteria, as well as to define the most appropriate settings in which to deliver noninvasive respiratory support. Further studies are needed to determine where and how to implement noninvasive respiratory support and which weaning strategies might provide the best outcomes in pediatric patients with acute respiratory failure.

IMPACT STATEMENT

Effective weaning from noninvasive respiratory support is essential.

KEY WORDS
Infant; noninvasive ventilation; HFNC, pediatric intensive care unit; weaning.

INTRODUCTION

In recent decades, there has been a progressive increase in the use of non-invasive respiratory support in pediatric patients with viral bronchiolitis, pediatric acute respiratory distress syndrome and other acute pathologies (1-6). However, the evidence currently available does not show that this phenomenon has always been accompanied by an improvement in the most important outcomes, such as the need for and duration of hospitalization in intensive care unit (ICU), the need for intubation and invasive mechanical ventilation, the length of hospital stay, or mortality (7, 8). On the contrary, some authors have found that the widespread use of NIV has significantly increased PICU admissions, without necessarily reducing the incidence of patients treated with intubation and invasive mechanical ventilation (9, 10). In 2024, Pelletier and colleagues conducted a large cross-sectional study on a sample of over

33,000 patients with bronchiolitis admitted to 27 PICUs from 2013 to 2022 (9). During this period, PICU admissions had increased by approximately 350 patients per year, effectively tripling the number compared to 2013. This figure was associated with an annual increase of approximately 368 patients treated with HFNC/NIV, corresponding to a 5-fold increase, while admissions requiring invasive mechanical ventilation remained essentially unchanged (9). In another recent multicenter study conducted in the United States, Slain and colleagues reported a marked increase in costs for infants with bronchiolitis over a 10-year period, with annual hospital charges doubling in 2018-2019 compared to 2009-2010 (10). Interestingly, the increased costs were attributed to a 333% increase in PICU admissions and were primarily related to the increase in the number of infants receiving high-flow nasal cannula (HFNC) or continuous positive airway pressure (CPAP) (10). Other cost-analysis studies have demonstrated that hospital costs for bronchiolitis are primarily related to ICU care (11, 12). Consequently, several centers have sought to reduce PICU admissions or at least admission duration, for example by promoting the implementation of NIV in general pediatric wards (13-15). Indeed, even if noninvasive respiratory assistance is still typically provided in PICUs, NIV treatment is increasingly being provided in general pediatric wards, which are appropriately equipped with both the necessary equipment and adequate medical and nursing resources. One of the main reasons for this is the avoidance of unnecessarily occupied intensive care beds, which can sometimes prove insufficient during epidemic periods, and the marked reduction in healthcare costs associated with PICU stays compared to lower-intensity wards, while maintaining a favorable safety and efficacy profile. However, managing noninvasive respiratory support outside the PICU requires specific medical and nursing skills, as well as the capability to transfer the patient to an intensive care unit in the event of clinical deterioration or poor response to treatment.

GOALS AND MODALITIES OF NONINVASIVE VENTILATION IN THE ACUTE SETTING

The three main objectives of noninvasive ventilation in children with acute respiratory illness are the following:

1) to noninvasively support mild or moderate respiratory failure, characterized by oxygen dependence, hypercapnia, or both.
2) To avoid therapeutic escalation with the need for intubation and invasive ventilation.
3) To promote the stabilization of a patient previously ventilated invasively, avoiding extubation failure.

Noninvasive ventilation can vary in terms of modality, usually from high-flow nasal cannula (HFNC) and continuous positive airway pressure (CPAP), to more complex mechanical ventilation techniques, such as BiPAP, Pressure Support (NIV), Pressure Control (NIV), or Neurally Adjusted Ventilatory Assist (NAVA)-NIV (16-18). The choice of the most appropriate NIV mode must be calibrated to the clinical situation and the characteristics of the individual patient, based on numerous factors that can determine its effectiveness and safety, including the type of available care facilities. Another important aspect of NIV concerns the choice of the interface between the respiratory device and the patient, which should aim to achieve the best possible compromise between effectiveness and the child's comfort.

THE WEANING PROCESS

Once the acute phase of respiratory illness has passed, one of the most delicate aspects of the noninvasive respiratory support is the progressive weaning of the patient from respiratory assistance. The goal is to reduce ventilatory support while ensuring that the patient maintains adequate respiratory function. In recent years, research has focused on optimizing the weaning process from NIV, to prevent excessive prolongation of respiratory support while avoiding too premature attempts, which can jeopardize patient safety. Indeed, the weaning phase often proceeds in parallel with the patient's clinical improvement, allowing for rapid weaning from NIV. However, weaning attempts are sometimes unsuccessful, requiring problematic steps back, sometimes resulting in patient destabilization and the need for a new escalation of ventilatory support. In other cases, healthcare providers hesitate in the decision to suspend NIV support, with the risk of improperly prolonging the hospital stay, either in the PICU or other hospital departments, as well as increasing hospital management costs.

For pediatric patients undergoing invasive mechanical ventilation (IMV), numerous recommendations exist in the literature regarding weaning procedures and ventilator release criteria (19-21). This interest from the scientific community is justified by the risks associated with mechanical ventilation itself, but also by the potential failure of the extubation procedure, which can pose serious risks to the patient, sometimes with severe destabilization of vital signs, the need for emergency reintubation, subsequent increase in respiratory support, prolonged duration of invasive ventilation, and an increased incidence of related complications.

Conversely, as for the weaning process in children undergoing non-invasive mechanical ventilation, no unanimously agreed-upon guidelines are yet available, either nationally or internationally, so individual institutions, and sometimes individual providers, adopt highly variable methods for implementing it. Actually, this shortcoming is not justified, because weaning from non-invasive ventilation could also be a complicated process, requiring adequate monitoring and an individualized treatment plan, adapted to the patient's clinical characteristics.

The first phase of the weaning process from noninvasive ventilation is similar in many ways to that used in invasively ventilated patients. In both scenarios, it is essential to clinically assess the patients' readiness, that is, their ability to resume sufficiently autonomous breathing to allow them to be freed from mechanical respiratory support. This clinical assessment relies on various physiological parameters to determine whether the patient's condition is stable, respiratory parameters are improving and oxygen requirement is not excessive. Subsequently, a gradual reduction in support can be attempted, for example, by decreasing the peak and end-expiratory pressure values of NIV, or by de-escalate to less powerful respiratory support modes, such as HFNC. In any case, close monitoring should always be maintained to promptly identify any signs of respiratory distress, desaturation, or fatigue in the patient, by relying on a multidisciplinary medical and nursing approach.

It is important to emphasize that there is not yet sufficient scientific evidence to demonstrate the superiority of some weaning strategies over others, enough to allow for precise recommendations on when, how, and how to initiate and complete this fundamental process. Recently, some authors have attempted to provide useful guidance on weaning from NIV through expert consensus, quality improvement projects and clinical investigations (22-26).

Mortamet and colleagues used a modified Delphi method to reach expert consensus on the definitions and modalities of weaning from NIV in acute hospital settings (22). Involving 25 international experts from 10 different countries, the authors addressed various aspects of the definition of weaning and weaning failure, the criteria for initiating weaning, and the most effective operating methods to follow. However, out of 35 total statements, the authors were able to reach strong consensus on only 9, weak consensus on 10, and no consensus at all on 16 statements (22). The partial failure of this commendable effort by the panel of experts underscores the difficulty of developing a protocol containing criteria, operating methods, and weaning strategies in the pediatric population that are based on solid scientific evidence. In a recent cross-sectional survey, Suzanne *et al.* described the weaning practices from any type of NIV support in infants with severe bronchiolitis in 29 PICUs from five French-speaking countries (23). The authors reported the weaning procedures adopted in the participating PICUs, according to the mode of ventilator support, namely the BIPAP, CPAP and HFNC. Interestingly, most PICUs used the sudden weaning as the first-line weaning procedure, regardless the type of NIV support, while the choice of intermediate support as a weaning strategy was mainly used as de-escalation from BIPAP. However, given the design of the study, more research is still needed to assess the best weaning strategy in infants with severe bronchiolitis (23).

In 2025, Huang *et al.* reported the results of a quality improvement initiative, which used a detailed protocol guide for initiating and weaning HFNC in 223 children with bronchiolitis, in the absence of other major comorbidities (24). With the application of a standardized protocol for HFNC treatment, the authors found a decrease of about one day in both the length of stay in the ICU and in the hospital, and a decrease of about eight hours in the overall duration of HFNC, without observing an increase in adverse events or hospital readmissions (24).

In the same year, Smith *et al.* optimized a weaning strategy in 642 patients with bronchiolitis, treated with HFNC in a PICU and a pediatric intermediate care unit at a children's hospital in USA (25). By iterative modifications to an HFNC weaning pathway that increased the frequency of flow weaning attempts, the authors were able to reduce HFNC duration and hospital LOS without increasing the need for escalation to NIV, ultimately recommending a 1L/Kg/min flow wean attempt every four hours (25).

Finally, in a multicenter prospective observational cohort study conducted in 5 PICUs in France, Mortamet and colleagues described three different NIV weaning strategies (26). Despite the limitations of its observational design, their study suggested that the use of HFNC as a de-escalation may improve comfort in patients with severe bronchiolitis, as well as reduce the length of PICU stay in centers where HFNC is also used in general wards (26).

WEANING FAILURE

In the study by Mortamet *et al*, the overall weaning failure rate was 18.5%, consistent with findings from other studies (9, 26). Therefore, according to the most recent data, weaning failure may occur in approximately one in five patients with bronchiolitis, prompting further research to reduce the incidence of this adverse outcome. It should be noted, however, that the definition of weaning failure can vary markedly between centers. For example, in a multicenter UK study, which demonstrated the non-inferiority of HFNC as a first-line modality of noninvasive respiratory support for acute conditions, compared to CPAP, Ramnarayan *et al.* used the same weaning failure criteria for both HFNC and CPAP, based on worsening respiratory distress and/or an FiO2 >40% (7).

Differently, in another multicenter study conducted in the USA, Pelletier and colleagues considered two distinct definitions of weaning failure, one for HFNC and one for NIV. Specifically, HFNC weaning failure was defined as when the patient, after being weaned to low-flow oxygen therapy or room air, had to resume HFNC or, worse, required escalation to NIV or invasive mechanical ventilation within 48 hours of stopping HFNC. Weaning failure during NIV was defined as when the patient, after being weaned from NIV to HFNC, or low-flow oxygen therapy or room air, had to resume NIV or, worse, required escalation to invasive mechanical ventilation within 48 hours of stopping NIV (9).

Although failure to wean from NIV or HFNC is generally considered less serious than failure to wean in an intubated patient, because healthcare providers can almost always easily return to the previous mode of respiratory support by waiting for the patient's condition to improve before making a subsequent attempt, failure to wean may be associated with a longer PICU or hospital stay, a prolonged need for sedation, and a delay in full feeding tolerance. Therefore, in the pre-weaning phase, it is essential to perform a thorough overall assessment of the patient. Ideally, patients should have stable vital signs, minimal oxygen requirements (*e.g.* FiO_2 <0.4), no signs of increased work of breathing, no recent episodes of apnea or bradycardia, and improving chest radiographs and ultrasound findings, if available. In younger patients, it may also be important to assess feeding tolerance.

The most commonly used strategies for successful weaning from noninvasive respiratory support are shown in **table 1**.

***Table 1**. Common strategies for weaning from noninvasive respiratory support.*

a) Gradual reduction of airway pressure, in the case of NIV or CPAP
b) Gradual reduction of flow/minute, in the case of HFNC
c) De-escalation from NIV to CPAP, or from NIV/CPAP to HFNC, and subsequently low-flow oxygen or room air
d) Gradual temporary suspensions of respiratory support (NIV/CPAP or HFNC) with phases of low-flow oxygen or room air
e) Sudden suspension of respiratory support and transition to low-flow oxygen or room air

Some centers use specific protocols to guide the weaning phase from NIV/HFNC, often based on both objective criteria, such as respiratory rate, oxygen saturation, and blood gas analysis, and more subjective clinical criteria shared by the medical and nursing team, such as respiratory distress, patient comfort, interface efficacy and acceptability, and feeding tolerance.

Some possible causes of weaning failure are described in **table 2**.

***Table 2**. Common cause of weaning failure from noninvasive respiratory support.*

1. Early weaning attempts, which can lead to increased work of breathing, desaturation, and fatigue, leading to respiratory failure
2. Suboptimal ventilator-patient interaction, resulting in asynchrony and patient discomfort
3. Interface-related difficulties, such as poor mask fit or skin lesions, both of which reduce efficacy and tolerability.
4. Lack of standardized protocols, leading to discretionary choices by operators, resulting in inconsistent results and increased risk of failure
5. Inadequate treatment of anxiety, agitation, and pain, which can hinder successful weaning
6. Poor ability to recover the patient's native respiratory function, due to the severity of the underlying disease

CONCLUSIONS

Non-invasive respiratory support has become an essential therapeutic option for infants and children affected by various acute respiratory diseases, bronchiolitis being the most frequent and investigated. However, widespread use of NIV has been associated with a dramatic increase in hospital operating costs, without always being linked to a corresponding improvement in key outcomes, such as the need for and length of hospital and PICU stays, the need for intubation and invasive mechanical ventilation, length of hospital stay, or mortality. Currently available evidence does not allow for the development of widely shared guidelines or standardized protocols on initiation criteria, operating procedures, monitoring methods, weaning strategies, failure criteria, and the most appropriate settings in which to deliver noninvasive respiratory support. Future randomized trials are needed to definitively determine where and how to implement NIV support and which weaning strategies might provide the best outcomes in pediatric patients with acute respiratory failure.

COMPLIANCE WITH ETHICAL STANDARDS

Conflicts of interests

The Authors declare no conflicts of interest.

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Ethical approval

Human studies and subjects

N/A.

Data sharing and data accessibility

Data are available upon motivated request to the Corresponding Author.

Publication ethics

Plagiarism

Authors declare no potentially overlapping publications with the content of this manuscript and all original studies are cited as appropriate.

Data falsification and fabrication

All the data correspond to the real.

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MINI REVIEW

Impact of Early-Life Rhinovirus and Respiratory Syncytial Virus Infections on Recurrent Wheeze and Asthma Development

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ABSTRACT

Early-life viral lower respiratory tract infections (LRTIs), particularly those due to rhinovirus (RV) and respiratory syncytial virus (RSV), play a pivotal role in the developmental origins of pediatric respiratory disease. RV and RSV are among the most prevalent causes of bronchiolitis and early wheezing globally. Longitudinal evidence and mechanistic studies have increasingly shown that these infections do not merely cause acute morbidity but also set the stage for chronic airway inflammation, wheeze, and asthma. Notably, new cohort data (INSPIRE study, and other European birth cohorts) (1) and reviews from 2025 by Hartert and Zar (2, 3) build on this paradigm and reinforce the need to understand early viral exposures as critical modifiers of airway trajectory. This narrative review draws on recent epidemiologic, mechanistic, and interventional evidence, supplemented with recent findings, to detail how RV and RSV exposures in infancy contribute to lasting respiratory morbidity.

KEY WORDS
LRTIs; RVS; bronchiolitis; wheeze; asthma.

EPIDEMIOLOGY: RISK OF RECURRENT WHEEZE AND ASTHMA

A growing evidence base confirms that early-life RV wheezing episodes are strong predictors of later asthma. Initial risk estimates from landmark birth cohorts report odds ratios (ORs) of approximately 3.3 for asthma after RV bronchiolitis, increasing to OR >7 when early allergic sensitization is present (4). A Swedish cohort found that 63% of toddlers hospitalized with RV bronchiolitis were diagnosed with asthma by age 11 (5). On the RSV front, multiple longitudinal studies underscore a similar, albeit slightly less strong, association. A U.S. birth cohort reported that infants who evaded RSV infection in the first year had a 26% lower risk of developing asthma by age five (6), translating to preventable 15% of early asthma cases according to ARDS estimates (3). Reinforcing this, a 2024 meta-analysis found a two- to twelve-fold increase in asthma risk following RSV bronchiolitis (7). A 2025 systematic review focused on early viral LRTIs echoed this, reporting a moderate (OR 3.02) increased asthma risk after RSV infection and a higher but more variable risk after RV infection (2). These and other data (8) firmly establish RSV and RV as significant moderators of long-term respiratory health.

