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REVIEW ARTICLE

Long-term non-invasive ventilation in pediatric neuromuscular diseases: challenges and advances

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ABSTRACT

Long-term non-invasive ventilation (LT-NIV) is one of the most advanced and complex long-term therapies offered to patients outside of a hospital setting. Its use has become increasingly important, especially for children with neuromuscular diseases (NMDs), where NIV plays a key role in correcting alveolar hypoventilation. Early identification of sleep-disordered breathing and a proactive approach to managing respiratory insufficiency are crucial for timely NIV initiation. Although polysomnography titration is the standard recommendation, recent advances in remote NIV monitoring and auto-adjusting modes now allow for home initiation and regular follow-up assessments to evaluate efficacy. NIV offers significant benefits, including better sleep quality, improved quality of life, and reduced mortality. Despite limited evidence, consensus guidelines support LT-NIV for the treatment of respiratory failure in patients with NMD, although further research is needed on improving personalized therapy to enhance patient outcomes and quality of life.

Keywords: Long-term non-invasive ventilation. Pediatrics. Home mechanical ventilation. Neuromuscular diseases.

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INTRODUCTION

Non-invasive ventilation (NIV) has become an increasingly important therapeutic option for respiratory support in pediatric care, offering a non-invasive modality for children with chronic hypercapnic respiratory failure who require intermittent ventilatory assistance or palliative care. Long-term NIV (LT-NIV), defined as the need for ventilation lasting more than 3 months, is delivered through an interface outside the airway, such as a mask (e.g., nasal mask, full-face mask [FFM], oronasal mask or nasal pillows)[1,2]. Since its initial application in the early 1990s, the use of NIV in children has expanded significantly. Several factors have contributed to this trend, including improved survival rates for children with complex medical conditions, a shift toward home-based healthcare, advancements in NIV technology and growing acceptance and increased familiarity among healthcare providers with NIV technologies. These developments have facilitated a transition from invasive mechanical ventilation to long-term NIV (LT-NIV) over the past two decades[3-10]. A study conducted in the United Kingdom between 1994 and 2010 showed a 30-fold increase in the prevalence of patients treated with LTV[11], from 0.2 to 6.7/100,000. In Italy, a prevalence of 4.2/100,000 was documented[12]; in Austria, 7.4/100,000 was reported[13]; in Canada, a 5-fold increase in incidence and a 3-fold increase in prevalence was described between 2005 and 2014[14], in France, there was a 14-fold increase in the number of patients under LTV between 2000 and 2019[15].

With the increasing number of infants and children living at home using NIV, understanding the benefits and risks of NIV is becoming important not only for specialists involved in this therapy but also for pediatricians and primary care physicians providing care to these children within the community and policymakers responsible for decisions about the provision of healthcare resources. This review will provide an overview of LT-NIV in pediatrics, with a specific focus on its role in managing children with neuromuscular diseases (NMDs).

GENERAL INDICATIONS FOR LT-NIV

Chronic alveolar hypoventilation is the major factor for initiating LT-NIV. This condition often arises from chronic respiratory failure, where the respiratory system fails to meet the body's gas exchange needs, resulting from the imbalance between the respiratory workload and ventilatory strength[16]. Decreased arterial oxygen partial pressure (PaO_2) may be treated with oxygen therapy, whereas elevated carbon dioxide partial pressure ($PaCO_2$) requires ventilatory support. LT-NIV can provide the support needed to improve gas exchange, alleviate symptoms, and enhance overall quality of life and improve survival[17].

In pediatrics, diseases for which LT-NIV is necessary can be classified into three categories according to the underlying pathophysiological abnormalities: increased respiratory load, ventilatory pump failure, and failure of neurologic control of breathing (Table 1). Historically, NMDs have been the most frequent cause for initiating LT-NIV. However, the patient profile has been changing, with an increase in children with upper airway obstruction, central nervous system, and

Table 1. Conditions that may benefit from home mechanical ventilation according to physiological impairment

Increased respiratory load	Obstructive sleep apnea
	Laryngomalacia
	Mucopolysaccharidoses
	Tracheobronchomalacia
	Bronchiectasis
	Bronchiolitis obliterans
	Kyphoscoliosis
	Chest wall deformities
	Lung hypoplasia
	Interstitial lung disease
	Bronchopulmonary dysplasia
	Heart failure
Ventilatory pump failure	Spinal muscular atrophy
	Muscular dystrophies
	Myasthenia gravis
	Diaphragmatic dysfunction
	Motor neuron disease
	Congenital muscular dystrophy
	Metabolic myopathies
	High-level spinal cord transection
Failure of neurologic control of breathing	Congenital central hypoventilation syndrome
	Acquired central hypoventilation through brain stem affection (e.g., tumor, trauma, bleeding, or encephalitis)
	Degenerative diseases or central nervous system tumors
	Stenoses of the craniocervical transition (e.g., Arnold-Chiari malformation)
	Syringomyelia

Adapted from Kwak et al.[74].

cardiorespiratory disorders. This can be explained by a more systematic screening of children with congenital malformations and/or genetic disorders for sleep breathing disorders and an increase in the number of interfaces and restraint systems available for pediatric population[9,18]. Praud et al. reviewed different series published between 2010 and 2020 and found that the most frequent diseases requiring LT-NIV in pediatric population were NMD, upper airway obstruction, rib cage deformities (including scoliosis), central nervous system disorders, parenchymal lung diseases, and obstructive sleep apnea syndrome[19].

RESPIRATORY FAILURE IN NMDS: PATHOPHYSIOLOGY AND DIAGNOSIS

Understanding the pathophysiology of respiratory muscle weakness in NMD is crucial for identifying early signs and determining the most appropriate time and method for screening. However, the clear predictors of when individuals with different NMDs will develop the different sequelae is not well understood. In addition, NMDs present at different ages and progress at variable rates, which makes it difficult to provide a single clinical guideline valid for all diseases.

In the normal state, there is an equilibrium between the respiratory load and the central drive plus the respiratory muscle strength. In NMD, this equilibrium is disrupted due to respiratory muscle weakness[16]. As the central drive to breathe increases, it stimulates the respiratory muscles, but the resulting imbalance leads to hypoventilation. This becomes particularly significant in "at-risk situations," which include sleep and acute illness, where the ability to compensate is further compromised. Therefore, a patient with progressive neuromuscular weakness will transition through four main stages: (1) normal ventilation; (2) at risk for hypoventilation during physiological stresses such as acute illness or surgery; (3) nocturnal alveolar ventilation; and (4) nocturnal and diurnal alveolar hypoventilation.

Sleep-disordered breathing (SDB) in children with NMD is highly prevalent compared to the general population, but the prevalence of SDB varies based on the type of NMD and the degree of neuromuscular weakness. The increased risk of SDB is due to several interrelated factors: (1) an increased upper airway resistance: muscle weakness can lead to impaired control of the upper airway making it more susceptible to collapse during sleep; (2) a reduced respiratory muscle strength: respiratory muscle weakness, particularly the diaphragm, diminishes the ability to generate adequate respiratory effort; (3) pulmonary restriction: conditions such as scoliosis and obesity can restrict lung expansion and reduce lung volumes, leading to a further decrease in effective ventilation[20]. Sleep-disordered breathing includes obstructive events, central events, and sleep hypoventilation, occurring alone or existing in any combination. Diurnal hypercapnia appears when inspiratory muscle weakness progresses, and daytime symptoms are often non-specific and are a late finding (Table 2). It can be challenging for young patients or those with cognitive delays to communicate their symptoms clearly, and patients are often asymptomatic. Therefore, patient reported symptoms and clinical evaluation is frequently insufficient for a reliable diagnosis of SDB[21-23].

Respiratory failure can also be accelerated by respiratory infections. Weakness in inspiratory, bulbar, or expiratory muscles impairs deep breathing and effective coughing, leading to difficulty clearing secretions. This increases the risk of recurrent atelectasis and pneumonia, which can reduce lung compliance and increase airway resistance and ventilatory demands[16,24].

Table 2. Symptoms and signs suggestive of chronic alveolar hypoventilation

Insomnia, nightmares, and frequent arousals
Nocturnal or early morning headaches
Shortness of breath during activities of daily living
Daytime fatigue, drowsiness and sleepiness, loss of energy
Decrease in intellectual performance
Loss of appetite and weight, impaired swallowing
Recurrent respiratory infections
Signs of cor pulmonale

Adapted from Praud[19].

The diagnosis of chronic alveolar hypoventilation is based on the identification of chronic hypercapnia. Due to the variability in the different NMDs, there have been a wide range of approaches to the assessment and management of hypoventilation, but recent literature emphasizes a more proactive approach, focusing on awareness of when a patient is at risk for hypoventilation and the timely use of polysomnography (PSG) for diagnosis[25-29]. PSG, including transcutaneous or end-tidal capnometry, is the gold standard test to evaluate for SDB and nocturnal hypoventilation, whereas nocturnal pulse oximetry is insensitive in detecting nocturnal hypoventilation. The presence of elevated bicarbonate (HCO_3) in a blood gas can suggest chronic hypoventilation, as the body initially compensates for impaired gas exchange, while elevated daytime carbon dioxide (CO_2) levels are typically a late finding[30]. Due to access to PSG is often limited, overnight ambulatory transcutaneous CO_2 ($TcCO_2$) monitoring has been suggested as a diagnostic tool because it is non-invasive, comfortable, cost-effective, portable, and feasible to implement in children on long-term ventilation[31,32]. However, there are some technical limitations as $TcCO_2$ monitoring can be affected by various factors, including skin temperature, perfusion, and the calibration of the device, which can lead to inaccurate readings if not properly addressed. Besides, when compared to PSG, it has been shown that is not sufficiently accurate as a clinical tool for the diagnosis of nocturnal hypoventilation in children with NMD[33,34]. On the other hand, end-tidal CO_2 ($EtCO_2$) monitoring is generally more user-friendly, often functioning as a plug-and-play device, which simplifies its implementation in clinical settings as it provides continuous, real-time feedback on respiratory status through non-invasive measurement of CO_2 at the end of exhalation, but it requires patients to tolerate a cannula which can be uncomfortable. Nevertheless, a randomized study that evaluated the diagnostic accuracy of an ambulatory polygraphy with end-tidal capnography, as compared to PSG for children with NMD, concluded that it had poor diagnostic accuracy to diagnose SDB and recommended not to be implemented in clinical practice as a diagnostic tool for SDB in children with NMD[35].

Nocturnal hypoventilation is a recognized criterion for the initiation of NIV, although the varying definition of this condition can be an additional challenge. In general, PSGs are scored and reported using the American Academy of Sleep Medicine (AASM) guidelines[36]. However, the AASM has different pediatric and adult diagnostic criteria with an option to use both criteria for children between 13-18 years of age. In addition, there is increasing recognition that the AASM scoring system for respiratory events is not well-suited for patients with NMD and may lead to the late recognition of disease. Paradoxical breathing, where the thoracic and abdominal movements are in opposition, may result from diaphragmatic dysfunction or intercostal muscle weakness and respiratory events are automatically scored as an obstructive event[37]. Progressive decrease in airflow along with reduced thoracic and abdominal movements, indicative of global inspiratory muscle weakness, is important evidence of respiratory disease but not typically scored as a respiratory event unless accompanied by a (micro)-arousal or desaturation. Consensus-based clinical practice guidelines for Duchenne Muscular Dystrophy and Spinal Muscular Atrophy recommend much less stringent criteria for the diagnosis of nocturnal hypoventilation to identify and treat hypoventilation earlier[28,29], as well as the European Respiratory Society (ERS) Statement on pediatric long-term non-invasive respiratory support[38] (Table 3).

The transition to hypoventilation often involves a rapid shallow breathing pattern and increasing thoracoabdominal asynchrony, which can be detected in PSG when its interpretation is done in the context of the underlying NMD. Considering these, a new paradigm called Respiratory Insufficiency in Neuromuscular Disease has been described to consider the different stages of progressive respiratory insufficiency in NMD. This graded approach to hypoventilation, as opposed to defining it as present or not present, reflects

Table 3. Diagnostic criteria for hypoventilation and sleep apnea based on the AASM criteria[36], the Duchenne Muscular Distrophy (DMD) guidelines[28], the ERS Statement on pediatric LT-NIV[38] and the Delphi Study to Establish Consensus Criteria to Define and Diagnose Hypoventilation in Pediatric NMD[30]

Criteria	AASM criteria pediatric patients	AASM criteria adults and 13-18 y	DMD guidelines	ERS statement	Delphi study
AHI	OSA Mild: 2/h Mod: 2.1-10/h Severe: > 10/h Central AHI > 5/h	OSA Mild: 5-15/h Mod: 15.1-30/h Severe: > 30/h Central AHI > 5/h	> 5/h	> 10/h	
CO_2	CO_2 > 50 mmHg for > 25% of total sleep time	$PaCO_2$ > 55 mmHg for > 10 min $PaCO_2$ > 10 mmHg increase in $PaCO_2$ from awake to asleep with > 50 mmHg for 10 min	$TcCO_2$ > 50 mmHg for > 2% of total sleep time Sleep related ↑ CO_2 10 mmHg for 2% of total sleep time	Maximal $TcCO_2$ > 50 mmHg TcCO2 ≥ 50 mmHg > 2% of recording time	In order of preference: – $TcCO_2$ > 45 mmHg for > 25% of sleep – $TcCO_2$ > 50 mmHg for > 2% sleep or 5 min – $TcCO_2$ increase 10 mmHg above baseline for > 2% sleep
SpO_2			SpO_2 < 88% for 2% of total sleep time or for 5 min continuously	Minimum SpO_2 < 90% SpO_2 ≤ 90% < 2% of recording time	In order of preference: – Mean SpO_2 < 94% – SpO_2 < 90% for > 2% sleep – SpO_2 < 90% for > 5 min continuously

AHI: apnea-hypopnea index; OSA: obstructive sleep apnea; Mod: moderate; h: hour.

the importance of a proactive management to minimize respiratory morbidity, and it is based in a Delphi study with the aim to identify more sensitive criteria for identifying hypoventilation[30] (Table 3). In parallel, the American College of Chest Physicians clinical practice guideline on respiratory management of patients with NMD provides evidence-based recommendations[39]. The panel suggests using the AASM criteria for sleep-disordered breathing and hypoventilation for adult patients and the ERS criteria for pediatric patients.

Pulmonary function tests evaluate respiratory muscle strength. Current evidence and standard clinical practice indicate that pulmonary function tests (PFT) are commonly used to evaluate the progression of respiratory failure and to identify predictors of survival in patients with NMD. It is recommended to perform a spirometry with forced or slow vital capacity (FVC or SVC) and maximum inspiratory and expiratory pressure (MIP/MEP) or sniff nasal inspiratory pressure (SNIP) and peak cough flow (PCF). The following values are considered abnormal: FVC < 80% predicted, MIP < 60 cmH_2O, MEP < 40 cmH_2O, and PCF < 270 L/min in individuals ≥ 12 years of age[39].

Some studies have evaluated the ability of PFTs to predict the presence of SDB, using different cutoffs for FVC ranging between 40 and 70%, with variable sensitivity and specificity[40-44]. While there is no consensus on screening frequency, the British Thoracic Society guidelines for the management of pediatric NMD recommended to evaluate for SDB at least annually when individuals might be at risk: if FVC < 60% predicted, in children who have become non-ambulatory or who never attain ability to walk, in all infants with weakness symptoms of OSA or hypoventilation, in children with clinically apparent diaphragmatic weakness and rigid chest syndromes; and it is recommended to evaluate for more frequently if clinical deterioration or repeated infections or if symptomatic[45].

A holistic approach to SDB involves screening for key symptoms and signs, diagnostic tests including regular PFT assessment of respiratory muscle strength, awake oxygen saturations, and blood gases, as well as a history of pulmonary exacerbations. PSG should focus on identifying SDB as well as early REM-related physiological changes, including respiratory rate and work of breathing.

LT-NIV IN NMD: PATIENT SELECTION

Children with NMD represent the largest group of pediatric patients requiring long-term respiratory support. As these children have unique and complex respiratory needs, it is essential that their care is managed by an expert, multi-disciplinary pediatric team. The role of NIV in this population is to assist the weakened respiratory muscles to correct alveolar hypoventilation by maintaining a sufficient tidal volume and minute ventilation. The long-term therapeutic goals include prolonging life, improving quality of life, and preventing further deterioration of pulmonary function or respiratory exacerbation. However, there is a lack of validated criteria to start NIV, regarding patient selection, optimal timing, and methodology[37].

After the screening assessment, initiation of LT-NIV should begin with shared decision-making involving the patient, family, and clinical teams to ensure that the treatment plan is tailored to the child's needs and aligns with both medical evidence and family preferences. Both parties must have a shared understanding of the purpose of LT-NIV but given the limited data on LT-NIV's long-term effects, benefits and risks should be discussed with an awareness of outcome uncertainty. The decision to proceed should include a plan for monitoring efficacy and considering alternative strategies if LT-NIV is ineffective. Finally, as LT-NIV is intended to occur in the home environment, practical factors such as the family's ability to manage the equipment, provide ongoing care, and address potential challenges are critical to the decision-making process[21].

The clinical indications for NIV can vary depending on NMD, patient age, and rate of disease progression (Table 4). In clinical practice, NIV may be initiated in an acute setting, after invasive or NIV weaning failure in the pediatric intensive care unit, in a subacute or chronic setting, or based on abnormal nocturnal gas exchange alone or abnormal gas exchange and respiratory events on a PSG[37]. In clinical practice, episodes of hypoventilation or paradoxical breathing, particularly during REM sleep, along with pulse oximetry readings below 90% or transcutaneous CO_2 levels above 50 mmHg, suggest insufficient respiratory muscle performance and should prompt consideration for initiating long-term NIV in children with NMD. While AHI thresholds of 5 or 10 events/h have also been suggested for NIV initiation, these may not fully capture the respiratory issues in patients with NMD, who may experience abnormal

TABLE 4. Clinical indications for NIV in children with NMD

Chronic setting	Hypoventilation or paradoxical breathing SpO_2 below 90% $PtcCO_2$ levels above 50 mmHg AHI 5-10 events/h FVC to < 80% of predicted with symptoms FVC to < 50% of predicted without symptoms SNIP/MIP to < –40 cmH_2O Preventing severe episodes of acute respiratory failure Supporting recovery after spinal surgery Promoting proper thoracic and lung development
Acute setting	After weaning invasive ventilation After NIV weaning failure

NMDs: neuromuscular diseases; NIV: non-invasive ventilation; AHI: apnea-hypopnea index; FVC forced vital capacity; SVC: slow vital capacity; SNIP: sniff nasal inspiratory pressure; MIP: maximum inspiratory pressure.

nocturnal gas exchange despite having a normal AHI. Therefore, overnight gas exchange abnormalities should be prioritized in this population[46]. Furthermore, any fall in FVC to < 80% of predicted with symptoms, or FVC to < 50% of predicted without symptoms, or SNIP/MIP to < –40 cmH_2O would support the initiation of NIV or further testing as clinically indicated for individual NMD[39]. Finally, NIV may also be indicated to prevent or mitigate severe episodes of acute respiratory failure, support recovery after spinal surgery, and/or promoting proper thoracic and lung development in infants and toddlers with NMD.

CONTRAINDICATIONS FOR LONG-TERM NIV

Although it is often stated that there are no absolute contraindications for LT-NIV, not all patients are suitable candidates. Certain conditions may prevent the initiation or adherence to LT-NIV, and in such cases, alternative treatments, such as invasive ventilation through tracheostomy, may need to be considered in consultation with the patient and their family[19].

The most important contraindications for LT-NIV in children may include: (1) aspiration risk from above or the aspiration of oropharyngeal secretions. This can result from bulbar impairment or weakened muscles of the upper aerodigestive tract, leading to dysphagia and an increased risk of lung aspiration. Aspiration may result in severe acute or chronic sequelae. However, these risks can often be mitigated by treating sialorrhea, adjusting the texture of food, or using enteral feeding[47]; (2) aspiration risk from below, including aspiration of gastroesophageal contents, and the inability to clear secretions effectively, where a weak cough can prevent effective clearance of respiratory secretions, leading to a high risk of aspiration or respiratory infections. This issue is usually managed efficiently through techniques like manually assisted cough, inspiratory-air stacking, or the use of mechanical in/exsufflation[48]; (3) poor adherence or lack of cooperation from the patient which can be frequent in infants and young children, as well as in children with intellectual disability; (4) family or caregiver inability to manage the equipment, as full cooperation from the family is of the utmost importance for successful LT-NIV; (5) severe facial deformities or conditions that prevent proper mask fitting, leading to ineffective ventilation or discomfort; (6) uncontrolled seizures or other neurological conditions that interfere with the ability to tolerate the NIV mask or therapy; (7) acute clinical situations, as acute respiratory distress, where NIV might not provide sufficient support, requiring invasive ventilation instead[19].

STARTING NIV: DEVICES AND RECOMMENDED SETTINGS

The selection of appropriate modes, devices, and interfaces depends on the child's condition, weight, and level of respiratory support required. NIV should be performed with a ventilator with adequate alarms and an integrated battery, and patients with a high ventilator dependency (16-24 h of use) should have a backup device. Humidification is recommended to improve respiratory comfort and prevent drying of bronchial secretions. As breathing is less efficient during sleep, NIV is initially used at night, which is the most common approach in pediatrics. However, as respiratory muscle weakness progresses, NIV may be extended to daytime use, typically with a mouthpiece to allow for speech and eating.

The initiation process involves acclimatizing the patient to their treatment, ensuring they understand how the therapy works and its benefits, and selecting the most appropriate equipment, including titration of the mask and device settings to ensure optimal comfort, effectiveness, and compliance with the therapy. NIV may be initiated in the hospital, in an out-patient setting, or at home, although standard of care is the initiation and titration of NIV during an attended, in-laboratory PSG[38,49,50]. Recent technological advances in remote NIV monitoring coupled with the emergence of auto-adjusting NIV modes provide the possibility of safe NIV initiation in the home environment, although needs further validation[51-53].

A proper-fitting interface with minimal mask leakage is crucial for the successful initiation of NIV therapy. The currently available pediatric mask interfaces have likely contributed to the increased use of NIV in children. However, challenges remain, including limited size and shape options that accommodate growing faces, limited headgear choices, and the potential for both short- and long-term interface-related complications[9]. A nasal interface is the preferred interface, and a chin strap may be added if mouth leak is present. Oronasal and FFMs can be used for children who are mouth-breathers but may be challenging for patients who are unable to remove the mask independently due to neuromuscular weakness or developmental delay. Nasal prongs may be preferred by some patients and are also used in case of skin irritation or injury in the nose. When NIV is extended to daytime use, a mouthpiece may be used, allowing for speech and eating while still providing ventilatory support[37].

An important consideration when using NIV in young children is the risk of developing midface hypoplasia. Sustained pressure applied by the interface may lead to underdevelopment of the midfacial structures, contributing to midface hypoplasia over time. Careful monitoring of mask fit and the use of specialized interfaces are crucial to minimize this risk and support proper facial growth. FFMs can pose an asphyxia risk if there is no leak in the system. Vented interfaces are mandatory for NIV with a single circuit because they ensure that the patient can exhale freely while maintaining positive pressure for inhalation. Without a vented interface, there is a risk of insufficient exhalation or excessive pressure, which can lead to discomfort, respiratory distress, or even asphyxia. In addition, safety mechanisms are essential in these settings. NIV systems should be equipped with alarms or monitoring features that alert healthcare providers or nursing staff if there is any malfunction or failure in the system, such as a mask seal issue or a sudden rise in pressure. This ensures that immediate action can be taken to protect the child from potential respiratory compromise. Regular checks and clear protocols for response are critical for maintaining safety in this vulnerable population.

Continuous Positive Airway Pressure, often used in children with obstructive sleep apnea, is considered inappropriate in children with NMD as it does not support ventilation and may further stress respiratory muscles worsening fatigue[20]. The most common ventilatory mode is Bilevel Positive Airway Pressure, where an inspiratory positive airway pressure (IPAP) and expiratory positive airway pressure (EPAP) are delivered. The IPAP and EPAP levels are adjusted to maintain upper airway patency, and the pressure support (PS = IPAP-EPAP) augments ventilation. NIV devices can be used in the spontaneous mode (the patient cycles the device from EPAP to IPAP), the spontaneous timed mode, which is the most commonly used (a backup rate is available to deliver IPAP for the set inspiratory time if the patient does not trigger an IPAP/EPAP cycle within a set time window), and the timed (T) mode (inspiratory time and respiratory rate are fixed).

The usual initial settings are 8 cmH_2O for IPAP and 4 cmH_2O for EPAP. IPAP can be increased at a maximum of 20 cmH_2O for patients < 12 years and 30 cmH_2O for patients ≥ 12 years but usually range from 10 to 14 cmH_2O and 4-6 cmH_2O of EPAP. The goal of NIV settings is to achieve a tidal volume of 6-10 mL/kg ideal body weight. A back-up rate is commonly used and is usually set at two to three breaths below the patient's physiological or spontaneous breathing rate[21,38].

Recommendations to improve patient comfort and patient-device synchrony include lowering the pressure if the patient awakens or complains and modifying the rise time. Adjustment or change in mask type or headgear should be performed whenever any significant unintentional leak is observed, or the patient complains of mask discomfort. During NIV titration with PSG, the pressure settings, backup rate, and inspiratory time are adjusted to maintain upper airway patency and support ventilation[54].

Volume guarantee modes have been developed to overcome hypoventilation despite optimal settings with pressure support mode. Volume-Assured Pressure Support (VAPS) is a newer hybrid mode of ventilation primarily used in adults, where multiple studies have shown it to be non-inferior to conventional pressure support ventilation. It is increasingly being utilized in children when other ventilation modes are insufficient or uncomfortable. In VAPS mode, the device automatically adjusts the pressure support to maintain a consistent tidal volume (or alveolar ventilation, depending on the manufacturer). The pressure delivered is modulated to ensure that the target volume is maintained, with the required pressure support varying based on lung mechanics, the patient's respiratory effort, and breathing control during sleep55. The use of VAPS has been supported in conditions such as congenital central hypoventilation syndrome[56,57], obesity hypoventilation syndrome, and NMD[58]. However, further studies are needed to assess its benefits and establish standardized recommendations for NIV therapy in the pediatric population. While VAPS is generally not recommended as an initial mode of pressure support ventilation, it may be considered as an alternative for patients on pressure ventilation modes who have uncontrolled nocturnal hypoventilation and issues with adherence[55,59,60].

MONITORING AND FOLLOW-UP

Despite there are no clear recommendations on how and when to optimally follow-up these patients, the efficacy of NIV should be assessed on the correction of alveolar ventilation, patient-ventilator synchrony, absence of leaks, and compliance with the therapy. Adherence to NIV therapy is crucial for the successful treatment of sleep-disordered breathing, and an outcome of interest as there are considerable challenges in establishing and maintaining the use of NIV in children[61].

Several studies have shown the persistence of respiratory events and/or abnormal nocturnal gas exchange requiring an intervention during systematic follow-up with PSG or polygraphy, performed 3-6 months after NIV initiation, even in asymptomatic patients[32,62,63]. An overnight monitoring of sleep, ideally with PSG with the optimal settings is recommended and can be postponed until the patient is well-adapted to NIV[37,49]. Although due to limited access to PSG, some centers use regular home recordings of SpO_2 and transcutaneous CO_2 as feasible strategy[32].

Leaks in the NIV system are critical to consider as they can impact the effectiveness of therapy. Total leak consists of both intentional leak, which allows for the flow of exhaled CO_2 through leak ports in the mask interface, and unintentional leak, which occurs due to issues such as poor mask seals, open mouth with a nasal mask, or damaged circuits. Unintentional leaks can significantly affect the efficacy of NIV, leading to poor tolerance, hypoventilation, sleep disturbances, and patient-ventilator asynchrony, and exposure to higher inspiratory pressures than necessary, potentially causing gastric distention, abdominal discomfort, vomiting, and aspiration[64,65].

The efficacy of NIV can be also assessed on the analysis of the ventilator's in-built software. NIV devices provide objective data including therapy usage days, average daily usage, leak data, tidal volumes, respiratory rate, and the residual apnea-hypopnea index, all of which can be wirelessly transmitted in real-time for remote monitoring. A typical review of ventilator data downloads includes confirmation of settings, adherence assessment, evaluation of leaks, and an analysis of treatment efficiency[64,66,67]. These data allow clinicians to adjust NIV settings in the home environment, enabling accurate and objective measurement of adherence. As most modern ventilators are now equipped for telemonitoring, this follow-up strategy is attracting growing interest. The development of telemonitoring for LT-NIV requires specialized tools, such as communicating ventilators and web-based platforms for data access, along with dedicated teams. With these resources in place, the efficiency of NIV delivery can be enhanced both at treatment initiation and during long-term follow-up, enabling the early detection of any deterioration in the underlying respiratory condition[68].

Finally, the ventilator settings and the interface need to be adapted to the child's growth and progression of respiratory muscle weakness, and in parallel, NIV should be associated with an efficient clearance of bronchial secretions or mechanical insufflation-exsufflation.

BENEFITS AND RISKS

LT-NIV offers substantial benefits for children with NMD, improving respiratory function, correcting nocturnal hypoventilation, reducing daytime $PaCO_2$ during spontaneous breathing, enhancing sleep quality, and positively affecting behavior, neurocognitive outcomes, feeding, weight gain, growth, and daytime symptoms. LT-NIV has also been linked to decreased mortality compared to supportive care across all NMD types and contributes to better overall quality of life[69-72]. By enabling effective management of respiratory failure at home, NIV reduces hospitalizations, benefiting both patients and healthcare systems. In addition, modern NIV equipment is more user-friendly, portable, and comfortable, making home use easier for families. While evidence supports the benefits of LT-NIV for various health outcomes, it is limited by risks of bias, as most studies are retrospective or observational, with few randomized trials[73].

The use of NIV in children comes with several risks and challenges. Potential complications include facial pressure ulcers, mask discomfort, mid-face hypoplasia with the use of nasal masks (especially in children when NIV is initiated in the pre-pubertal years), dryness in the eyes, nose or mouth, skin rash or irritation, nasal congestion, sinus infections, and/or aerophagia[19,74]. Adherence to NIV therapy can also be difficult, as children may resist wearing the masks, affecting the therapy's effectiveness. Ongoing support is necessary, as regular follow-up and adjustments are required to screen for commonly seen side effects and treat them in a timely manner. Besides, families must also be trained for emergencies such as equipment failure or sudden respiratory distress. Access to NIV technology and funding are critical considerations as well. Policymakers should allocate adequate resources to support families, including access to equipment and follow-up coordinated care between specialists and primary care providers.

CONCLUSION

Pediatric patients with NMD represent the largest group requiring LT-NIV, which is one of the most advanced and complex therapies provided outside of a hospital setting. Recommendations for managing NIV are primarily based on expert consensus due to the lack of randomized trials in this area. Understanding key factors in NIV management is essential for ensuring optimal outcomes for children, optimizing treatment, and assisting patients and families in navigating this complex therapy at home. Future research should focus on improving personalized treatment through advancements in lung function testing, hypoventilation screening, telemedicine, and AI-assisted NIV management, while emphasizing better access to ventilatory support and shared decision-making to enhance patient outcomes and quality of life. Achieving these outcomes requires a multi-disciplinary pediatric team to deliver personalized care, but also increased awareness of the benefits and risks of NIV among other specialists, primary care providers, and policymakers.

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CONFLICTS OF INTEREST

None.

ETHICAL CONSIDERATIONS

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The study does not involve patient personal data nor requires ethical approval. The SAGER guidelines do not apply.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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