

Noninvasive ventilation in children: a review

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Abstract

Objective: To assess the use of noninvasive ventilation (NIV) in children and its application in the acute and chronic setting of pediatric respiratory failure.

Sources: Search of pertinent articles within Pubmed, Cochrane and Ovid MEDLINE databases from 1950 to 2007, using the keywords "pediatrics", "noninvasive ventilation" and "positive airway pressure".

Summary of the findings: There is a paucity of published data on pediatric NIV. The majority of the data available are case reports or small case series, with a number of small, randomized studies reported.

Conclusion: Although the use of NIV is increasingly recognized in pediatrics, there are currently still no generally accepted guidelines for its use. In the chronic setting, its use has mainly been proven in obstructive sleep apnea and respiratory failure secondary to neuromuscular disorders. It would appear that the major challenge is ensuring compliance, and this can be enforced by patient/caregiver education, use of a suitable interface, heated humidifiers and by minimizing the side effects of NIV. In the setting of acute respiratory failure, it would appear from available data that success is usually predicted by the rapidity of response. Patients placed on NIV should be monitored closely and this mode of ventilation should be reviewed if there is a lack of response within a few hours after commencement of therapy.

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Introduction

Noninvasive ventilation (NIV) refers to the delivery of assisted ventilation without the use of endotracheal tubes or a tracheostomy. It can be delivered through negative pressure devices or through devices that provide positive pressure, either continuously or intermittently. Negative pressure devices, such as the iron lung or chest cuirass, were popular in the 1950s when poliomyelitis was epidemic. It made way for invasive mechanical ventilation in the 1960s.

In the 1980s, NIV became an accepted modality to treat adult patients with restrictive lung disorders, especially in the presence of hypoventilation, severe pulmonary dysfunction or sleep apnea.¹ It soon progressed to become a popular alternative for supporting acute respiratory failure in adults.²

Its use in pediatrics is now rapidly gaining acceptance.^{3,4} In the 1970s, the use of continuous positive airway pressure (CPAP) was introduced in neonates.^{5,6} NIV is now commonly used in children and this paper reviews the use of noninvasive positive pressure ventilatory support in infants and children in the acute and chronic setting.

Types of noninvasive positive pressure ventilation

Continuous positive airway pressure (CPAP)

In this mode, a continuous pressure is delivered to the lower airways through the pharynx by different types of airway interfaces, such as nasal prongs, face masks or head boxes. The infant flow system uses a "fluidic flip" action in the nasal prongs to help reduce the work of breathing. In

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inspiration, there is jet mixing and flow is directed towards the baby, but in exhalation, flow is directed away from the patient.⁷ In one study, a helmet device was used to support ventilation in children with leukemia.⁸ The positive pressure is created using various means; the simplest would be by putting the expiratory limb under a column of water (bubble system)⁹ or using mechanical ventilators or designated NIV devices.

CPAP improves oxygenation and reduces the work of breathing as it unloads the inspiratory muscles. It prevents alveolar collapse as it delivers a continuous distending pressure.

Bilevel positive airway pressure (BiPAP)

This pressure-targeted type of NIV gives respiratory support at two levels i.e., the inspiratory positive airway pressure (IPAP) and CPAP or end-expiratory pressures (less commonly, preset tidal volumes can be targeted). The terminology on various NIV devices may be different, but basically these devices can give full support to a patient with set rates and pressures.

In assisted spontaneous mode (pressure support), the patient has to trigger the breath. It is important to assess the suitability of such devices in children as the changes in flow or pressure created by a young child may not be enough to trigger such machines. Spontaneous/timed mode will give a combination of support for spontaneous breaths, as well as backup support should the spontaneous breaths be less than the backup rate. In such a modality, the support given to the patient would be higher than in CPAP.

Advantages and disadvantages of NIV

NIV delivers respiratory support without intubation, hence minimizing nosocomial infections such as sinusitis and pneumonia.¹⁰ Patients can talk, eat or drink while being supported by NIV. Using NIV also minimizes the need to use sedation, which is required in most intubated patients.

The use of nasal prongs may cause excoriation around the nose, and if there is a poor mask fit, air leaks can occur around the mouth causing inadequate ventilation as well as eye irritation. Nasal dryness can also occur due to high airflows, causing thick secretions. Aerophagia can occur with gastric distension, and if severe, may cause diaphragmatic splinting, and a gastric deflation tube may be necessary. Positive pressure ventilation can cause barotrauma and air leak syndromes.

The use of NIV requires proper knowledge for best results, as emphasized by the British Thoracic Society.¹¹ Correct prong or mask size and proper positioning to avoid extensive flexion or extension are important for effective ventilation. Different interfaces, such as the face mask or nasal prongs, will need to be properly strapped to the face of the patient.

Recently, helmet devices have been used, particularly in older children, to improve patient compliance and acceptance.^{8,12} Masks should be made of pressure-relieving material to minimize pressure sores around the face and there are masks that can be molded to the face to reduce leakage.

In a Cochrane review by Paoli et al.,¹³ a significant reduction in respiratory rate and oxygen requirement was found in preterm infants using short binasal prongs compared to those using single or long nasopharyngeal prongs. Hence, it may be preferable to use short nasal prongs for NIV in small babies. In some NIV devices, a single inspiratory tube delivers the preset pressures and it is essential to have expiratory valves around the mask or tube to allow for exhalation and to minimize air leaks and carbon dioxide rebreathing.

Contraindications for the use of NIV include congenital facial or airway abnormalities, which preclude the use of a tight fitting mask or prongs, severe cardiopulmonary instability, inability to protect an airway and intractable apneic episodes. It may also not be possible to apply NIV to patients with facial trauma or burns, or in patients with recent upper gastrointestinal surgery in case of gastric distension.

Application of NIV in the chronic setting

Home ventilatory support, especially through the use of noninvasive positive pressure ventilation in children, has increased substantially through the years. The indications for long-term noninvasive ventilation in children include a variety of obstructive and restrictive airway diseases as well as central hypoventilation syndrome. The two commonest indications in children are reportedly obstructive sleep apnea and respiratory failure due to neuromuscular disease.¹⁴ This technique has been shown to improve blood gases, survival and probably quality of life in those needing long term NIV. Long-term nocturnal NIV is reported to be well tolerated in children with a variety of conditions.^{15,16} The consensus statement for mechanical ventilation beyond the ICU in adults proposed the use of long-term NIV in chronically stable or slowly progressive respiratory failure with significant daytime CO₂ retention, or mild hypercarbia with symptomatic nocturnal hypoventilation, or significant nocturnal hypoventilation.¹⁷ Presently, there are still no generally accepted guidelines for the long term use of NIV in children. The vast majority of the studies are done in adults and case series constitute the main source of evidence in children.

Restrictive lung disease

The use of NIV began with restrictive lung disease, especially during the poliomyelitis epidemic. The majority of pediatric restrictive lung diseases are secondary to neuromuscular disorders. While the genetic defects of many

neuromuscular disorders affecting children are being identified and until genetic therapy becomes available, many succumb prematurely from respiratory failure. Respiratory failure results initially from recurrent chest infections caused by atelectasis, which progresses to nocturnal hypoventilation from muscle weakness, and reduced sensitivity to carbon dioxide during sleep. Sleep-related breathing disorders – nocturnal hypoventilation¹⁸⁻²¹ and obstructive sleep apnea,¹⁹ are well documented in children with neuromuscular diseases. Untreated sleep-related disorders can then lead to the development of respiratory failure through disordered ventilatory control resulting from adaptation and down-regulation of ventilatory responses to hypoxemia and hypercarbia.²²

It has been hypothesized that NIV works by several mechanisms in the chronic lung: 1) improving ventilatory mechanics; 2) resting fatigued respiratory muscles; or 3) enhancing ventilatory sensitivity to carbon dioxide.^{22,23} Investigations into a mixed group of patients with neuromuscular diseases showed that NIV improved daytime blood gases,^{16,24,25} ventilatory response to CO₂, but did not demonstrate improvement in pulmonary mechanics or respiratory muscle strength.^{24,25}

In a retrospective review by Duiverman, which included 114 adult patients with restrictive lung diseases (mainly post-poliomyelitis and idiopathic kyphoscoliosis), NIV improved both daytime blood gases and pulmonary function.²⁶

The differing results in the pulmonary function may be due to the differences in the natural progression of the diseases studied. Its use, in a small study of children with neuromuscular diseases, was associated with lower hospitalizations after initiation of NIV.¹⁸ The use of NIV has also been effective in improving polysomnography (PSG) indices as well as sleep architecture and sleep-related symptoms.^{20,21,25}

It therefore follows that NIV should be considered in patients who have evidence of nocturnal hypoventilation. The 1999 Consensus Conference Report²⁷ suggested the use of noninvasive positive pressure ventilation for restrictive lung disease in the presence of symptoms (fatigue, dyspnea, morning headache, etc) with one of the following parameters: PaCO₂ ≥ 45 mmHg, nocturnal oximetry demonstrating oxygen saturation ≤ 88% for 5 consecutive minutes; or progressive neuromuscular disease, maximal inspiratory pressures < 60 cm/H₂O or FVC < 50% predicted.

In a study involving Duchenne muscular dystrophy, Craig et al. found FEV1 < 40% predicted and PaCO₂ ≥ 45 mmHg, sensitive indicators of sleep hypoventilation. They advocated

the use of arterial blood gas in patients with FEV1 < 40% predicted, associated with PaCO₂ ≥ 45 mmHg, as a guide to initiate NIV.²⁸

In the pediatric population, lung function tests may be difficult to perform. Hence, clinical suspicion of sleep hypoventilation and early polysomnography would be important to identify children in need of NIV.

Obstructive sleep apnea

Obstructive sleep apnea (OSA) is an increasingly recognized disorder, occurring often in otherwise healthy children with a prevalence of around 2%.²⁹ In children with risk factors, such as Down's syndrome, the prevalence of sleep-disordered breathing can be as high as 80%. In otherwise healthy children, OSA is often related to adenotonsillar hypertrophy and the recommended first-line treatment would be surgical removal of the adenotonsillar tissues.

Children with craniofacial abnormalities or neurological problems such as Down's syndrome, Pierre-Robin sequence and cerebral palsy may be predisposed to OSA. In this group of patients where surgical/orthodontic procedures are not feasible and in the group of healthy children in which clinical improvement is not evident despite adenotonsillectomy, NIV nasal CPAP is currently the main treatment option.³⁰ It also serves as an interim measure in infants with OSA to allow growth before surgical correction is feasible.³¹

Children with OSA have abnormal upper airway patency during sleep. Abnormalities in upper airway collapsibility, cross-sectional area and genioglossus muscle activity have been demonstrated in this condition. CPAP helps to maintain airway patency by providing a continuous airflow to "stent" the upper airway and allowing for normalization of the genioglossus muscle activity.³²

When treating OSA, it is important to know that there are cardiovascular, behavioral and cognitive associated morbidities.³³⁻³⁷ The use of CPAP in OSA has been shown to successfully improve memory,³⁸ reduce pulmonary pressures,³⁹ and decrease hypertension and other cardiovascular risk factors.⁴⁰

Marcus et al. showed that both CPAP and BiPAP are highly efficacious in pediatric OSA.⁴¹ However, this study also showed a high dropout rate of one-third within 6 months of initiation, with no difference in adherence between CPAP and BiPAP. Massa reported a higher success rate (86%) with the use of CPAP in a group of younger patients with OSA using home acclimatization as a technique to recuperate otherwise poorly compliant patients.³⁰

Application of NIV in the acute setting

Although primarily proven in conditions such as acute exacerbations of chronic obstructive pulmonary disease,⁴²⁻⁴⁵ acute cardiogenic pulmonary edema⁴⁶⁻⁴⁸ and postoperative respiratory failure,^{49,50} the use of NIV in acute respiratory failure has also been described in immunocompromised patients,^{51,52} patients with pneumonia,⁵³ weaned from or with failed extubation⁵⁴ and asthma⁵⁵ with varying degrees of success.

However, data in children are comparatively lacking. The largest series of pediatric patients with acute respiratory failure treated with NIV to date has been recently reported by Essouri et al.⁵⁶ This was a retrospective cohort study over a 5-year period of 114 patients that fell roughly into five different categories. Success in the use of NIV in their population of patients was largely dependent on the cause of respiratory failure as well as on illness severity, as reflected by their Pediatric Risk of Mortality (PRISM) and Pediatric Logistic Organ Dysfunction (PELOD) scores on day 1. This is not unexpected as adult data have shown that patient selection is important to the successful utilization of NIV.⁵⁷

Respiratory distress syndrome

With the advent of mechanical ventilation, survival of preterm infants has improved, though with increased morbidity in the form of bronchopulmonary dysplasia (BPD). Interest therefore changed to a “gentler” mode of ventilation that would have less volutrauma and barotrauma. The first reported use of NIV in this subset of patients occurred more than 30 years ago when Gregory et al.⁵ described the use of CPAP for the treatment of hyaline membrane disease (HMD). Physiologically, it establishes and maintains functional residual capacity, decreases upper airway resistance, inflates collapsed alveoli and promotes progressive alveolar recruitment, thereby reducing intrapulmonary shunting.^{58,59} Since then, it has become widely accepted and utilized. Its use in moderate to severe HMD in the INSURE (intubation; surfactant; rapid extubation) technique has seen a decrease in the need for mechanical ventilation.⁶⁰

In developing or third world countries where resources are scarce and where they are distributed in a manner of “survival of the fittest”, CPAP might prove to be a viable alternative option of ventilation in extremely low birth weight (ELBW) babies, being relatively inexpensive and easy to perform. A study done in South Africa⁶¹ showed a significant short-term survival, with a trend towards long-term survival in this subgroup of infants treated with CPAP.

More recently, interest has been shown in the use of nasal intermittent positive pressure ventilation (NIPPV). Theoretically, it may offer advantages over CPAP by improving tidal and minute volumes, as well as by stimulating the respiratory drive. A small study has shown an improvement in the work of

breathing in comparison to nasal CPAP.⁶² A number of small, randomized studies⁶³ and another retrospective case control study showed significantly less need for supplemental oxygen and decreased incidence of BPD.⁶⁴ Obviously, larger randomized studies need to be done to confirm these initial findings.

Apnea of prematurity

Clinical management of apnea of prematurity (AOP) has not changed in recent years, comprising pharmacological and non-pharmacological means. Methylxanthines and caffeine are the most widely utilized pharmacological agents. Nasal CPAP and more recently, NIPPV, are also well established in the treatment of AOP.^{65,66} Unfortunately, no randomized studies have been done to compare pharmacological versus non-pharmacological means of treating AOP.

Lower airway obstruction

Asthma and bronchiolitis are among the commonest causes for hospital admissions in infancy and childhood. Management has traditionally been aimed at relieving bronchoconstriction, airway inflammation, edema and secretions. Small minorities of patients fail medical treatment and require intubation and mechanical ventilation. This is associated with significant morbidity from barotrauma, hemodynamic instability, infections and increased length of hospital stay.⁶⁷⁻⁶⁹ NIV in these patients is therefore particularly attractive for obviating these undesirable complications.

Initial case reports indicated a favorable outcome from the use of NIV in pediatric asthma and this has recently been supported by two larger studies. Thill et al.⁷⁰ reported on 20 children with acute lower airway obstruction aged between 2 months and 14 years. These children were randomized to receive either 2 hours of noninvasive positive pressure ventilation followed by 2 hours of conventional therapy (group 1) or 2 hours of conventional therapy consisting of supplemental high flow oxygen, inhaled β_2 agonist and intravenous corticosteroids followed by 2 hours of noninvasive positive pressure ventilation (group 2). They found that the children receiving NIV had a significantly decreased respiratory rate and a lower clinical asthma score (CAS), as well as lower scores for each individual component of the CAS (accessory muscle use, wheeze and dyspnea). In contrast, this improvement disappeared with the initiation of conventional therapy in group 1 and was only seen when NIV was initiated in group 2.

Beers et al.⁷¹ reported on a retrospective review of 73 patients between the ages of 2 and 17 years seen in the emergency department with the diagnosis of status asthmaticus and treated with BiPAP. They found that 77% of these patients showed an improvement in their respiratory

rate and 88% showed an improvement in oxygen saturations. Although all 73 patients were initially destined for intensive care unit (ICU) admission, only 57 (78%) were eventually admitted to ICU, whereas the other 16 showed enough improvement and were admitted to general wards. Of the 57 patients admitted to the ICU, only two eventually required intubation and mechanical ventilation.

They postulated that BiPAP relieved the fatigued muscles of respiration and obviated the need for autopoitive end-expiratory pressure (PEEP). The positive pressure generated also had a direct bronchodilator effect, recruiting smaller airways and collapsed alveoli, thereby improving the ventilation perfusion mismatch.

These are promising initial studies and larger, prospective, randomized studies would contribute more to determine the safety and efficacy in the use NIV in asthma.

Upper airway obstruction

The use of NIV in the acute setting of upper airway obstruction in pediatrics has not been widely available in the literature.

Padman et al.⁷² reported in his series of 34 patients treated with BiPAP for respiratory insufficiency, three patients with upper airway obstruction. one with post-extubation stridor and two with upper respiratory tract infections. All three responded to BiPAP with improvements in respiratory rate, heart rate and oxygen saturations, and the dyspnea score improved by at least 2 standard deviations. None required intubation.

Essouri et al.⁷³ reported on a series of 10 infants with severe upper airway obstruction secondary to laryngomalacia (n = 5), tracheomalacia (n = 3), tracheal hypoplasia (n = 1) and Pierre-Robin sequence (n = 1). All of the 10 patients were randomized to either BiPAP or CPAP, and all showed a significant decrease in respiratory effort as well as a drop in esophageal and transdiaphragmatic pressures. However, patients on BiPAP displayed patient-ventilator asynchrony. This is probably not unexpected as the patients were young infants with a median age of 9.5 months, and the flow trigger on the BiPAP devices may not have been sensitive enough for their needs. In addition, CPAP alone would probably have sufficed in overcoming the airway obstruction without the need to augment respiratory efforts.

Pneumonia

Adult studies have not shown a convincing argument in favor of NIV in the setting of community-acquired pneumonia.⁵³ Existing pediatric studies may be more promising. Fortenberry et al.⁷⁴ reported on a series of 28 patients with acute respiratory failure, with the most common primary diagnosis being pneumonia. Use of BiPAP in this series of patients showed an improvement in respiratory

rate, oxygenation, carbon dioxide clearance and pulse oximetry saturations. However, it was noted that over 30% of the patients had an underlying neuromuscular or immunocompromised state where the use of NIV is more proven.

Padman et al.⁷² had 13 patients, out of his series of 34, with the diagnosis of pneumonia, and the use of BiPAP showed an improvement in respiratory rate, heart rate, dyspnea score and oxygenation in all the patients.

Essouri et al.⁵⁶ had the largest series of pediatric community-acquired pneumonias treated with BiPAP (23/114). BiPAP was successfully utilized in 87% of these patients with a significant improvement in respiratory rate and carbon dioxide clearance within 2 hours after initiation of NIV.

Acute respiratory distress syndrome (ARDS)

The use of NIV in ARDS in adults has not been shown to be useful⁷⁵ and might be contentious as it may delay intubation. In pediatrics, there is again a paucity of data.

In the study of Essouri⁵⁶ et al., the success rate of NIV in their group of patients with the diagnosis of ARDS (n = 9) was rather dismal. The definition of ARDS was based on the American-European Consensus Conference on ARDS, and NIV was initiated in the least severe of their patients ($\text{PaO}_2/\text{FiO}_2 > 150$) as the more severe patients were systematically intubated and mechanically ventilated. Even so, 78% of these patients failed NIV and required intubation and there were two deaths. Multivariate analysis in their study showed that a diagnosis of ARDS was an independent predictor for NIV failure.

It would seem prudent not to delay definitive intubation and mechanical ventilation in this particular subset of patients for a trial of NIV, as results in both adults and children have thus far been poor.

Post-extubation respiratory failure/weaning from extubation

In initial adult studies, the use of NIV for post-extubation respiratory failure showed rather mixed results. However, a large multicenter trial⁷⁶ showed no benefit and in fact a significantly higher mortality rate in the NIV group. The time interval between development of respiratory failure and reintubation was also significantly higher in the NIV group in comparison to the control group. It would appear that delayed recognition of the failure of NIV in this group of patients contributed to the above results. The patients in this particular study were also unselected and the authors felt that careful selection of patients (i.e., hypercarbic respiratory failure) might still benefit from NIV.

In pediatrics, Bernet et al.⁷⁷ reported on a series of 11 patients who were extubated to NIV after cardiac surgery.

Seven patients responded well to NIV (64%) and four required reintubation. However, it was uncertain in the report if patients received CPAP or BiPAP, but this would be informative.

In the study of Essouri et al.,⁵⁶ respiratory failure after extubation (n = 61) formed the largest group and is the largest series reported. A large proportion of the patients (n = 33) were post-liver transplantation. The success rate of NIV in this group of patients was reported as 67% with 33% of patients requiring reintubation. Seven out of the 61 (11%) patients that required reintubation died, but none of the deaths was attributed to the use of BiPAP or to delayed reintubation.

Although it has been shown that a requirement for reintubation after failed extubation in adults is associated with a poorer outcome and a higher mortality rate,^{78,79} this has not been demonstrated in children.

Immunocompromised patients

Acute respiratory failure is commonly seen in this group of patients, caused by infections, pulmonary localization from primary disease, or even post-chemotherapy cardiogenic pulmonary edema. A number of adult and pediatric studies have reported a poor outcome and a very high mortality rate in immunocompromised patients requiring mechanical ventilation.^{80,81}

NIV is therefore particularly attractive as it avoids the infectious and bleeding complications of invasive ventilation in these patients, who are frequently neutropenic and thrombocytopenic.

There are a number of pediatric case reports⁸²⁻⁸⁴ on the successful utilization of NIV in hematological malignancies and in acute respiratory failure.

The study of Essouri et al.⁵⁶ reported on 12 oncology patients with acute respiratory failure treated with NIV. Success rate was as high as 92% with only one patient requiring intubation.

This high success rate could be attributed to the fact that there was a high vigilance in the detection of infection and respiratory distress in this group of patients, and treatment therefore tended to be initiated early and aggressively, thereby improving outcome.

Conclusion

The use of NIV is well established in adults, and its use in children is also increasingly recognized in both the acute as well as in the chronic setting.

Nocturnal NIV has been proven useful, especially in sleep-disordered breathing. The major challenge for its use in children as a form of home ventilation lies in compliance. This can be maximized by adequate patient/caregiver education,

careful choice of a suitable interface, use of heated humidifiers and by minimizing the side effects of NIV.

Although the groups of pediatric patients who may benefit from NIV are still not clearly defined in acute respiratory distress, larger studies show that success is usually predicted by the rapidity of response.

Essouri et al.⁵⁶ noted that there was an improvement in the breathing pattern and gas exchange as early as 2 hours after initiation of NIV in the NIV success group. Bernet et al.⁷⁷ noted that there was a significant difference in oxygen requirements in the responder group compared with the nonresponder group after 1 hour of NIV. These findings have also been echoed in adult studies.⁸⁴ Caples et al.⁵⁷ found that “predictors of success include younger age, unimpaired consciousness, moderate rather than severe hypercarbia and acidemia, and prompt physiologic response improvement in heart and respiratory rates and gas exchange within 2 hours”.

In practical terms, we should therefore monitor patients on NIV closely, and the maintenance of this mode of ventilation in acute respiratory distress should be reviewed if there is a lack of response within a few hours after initiation of therapy.

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