

Andrew C. Argent  
Paolo Biban

## What's new on NIV in the PICU: does everyone in respiratory failure require endotracheal intubation?

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A. C. Argent (✉)  
School of Child and Adolescent Health, Institute of Child Health,  
University of Cape Town and Red Cross War Memorial Children's  
Hospital, Klipfontein Road, Rondebosch, Cape Town 7700,  
South Africa  
e-mail: andrew.argent@uct.ac.za  
Tel.: +27-21-6585369  
Fax: +27-21-6891287

P. Biban  
Paediatric and Neonatal Intensive Care Unit, Department of  
Paediatrics, Azienda Ospedaliera Universitaria Integrata Verona,  
Verona, Italy

Non-invasive ventilation (NIV) refers to the use of techniques of ventilatory support that do not include the utilization of invasive airways such as endotracheal tubes or tracheostomies. Thus, the full spectrum ranges from high-flow humidified nasal oxygen (HFHNO), through nasal continuous positive airways pressure (CPAP), to a wide range of positive (and negative) pressure support modes of ventilation.

Over the last decade, there has been a progressive increase in interest (in 2013 there were 230 publications on Pubmed including the search term NIV, vs. 14 in 1993 and 88 in 2003) and utilization [1] of NIV (both within and outside the intensive care unit) across the world. In adult intensive care, there has recently been particular focus on the use of NIV in: acute respiratory failure and ARDS [2]; patients with terminal conditions or following refusal of endotracheal intubation [3]; in patients who are being weaned off ventilator support [4];

and in patients following major surgery. A recent review has pointed out that there has been a substantial increase in the use of NIV across all diagnoses and in all settings of acute respiratory failure [5], and at the same time there has been substantial increase in the use of NIV for chronic ventilator support.

CPAP in various forms has been extensively used in neonatal care across the world for many years. More recent is the recognition that infants who fail nasal CPAP may be managed successfully without intubation, by use of additional forms of NIV [6]. HFHNO has also been utilized in the neonatal setting throughout the world [7], although there is limited evidence comparing this mode of support with alternative strategies.

In paediatrics, there has also been extensive interest in NIV, and in many centres there has been a dramatic increase in the utilization of NIV for respiratory support in a variety of settings from the emergency department [8], through transport services [9], to the intensive care unit [10, 11] (and other less well-equipped clinical areas) [7]. There is evidence that the increased use of nasal CPAP in bronchiolitis has been associated with a dramatic reduction in duration of PICU and hospital stay as well as costs [11].

While there has been increased focus on NIV (in multiple forms), there is very little formal study evidence to underpin the use of NIV in children. Currently, there are few randomized controlled studies of NIV in children (Table 1), and they do not compare conventional ventilation with NIV. A relatively recent systematic review [12] of the use of CPAP in children with bronchiolitis concluded that there is insufficient high-quality evidence to support the use of CPAP in this setting. There is currently a registered RCT collecting data (ISRCTN82853500) on the use of CPAP in immune-compromised children with acute respiratory distress. Thus, there is a real need for extensive international collaborative research to clarify the role of NIV.

**Table 1** Prospective studies with paediatric NIV since 2000

Design and population	Technique	Clinical effects	Adverse effects	Citations
<b>Prospective studies</b>				
Prospective observational study of 41 children admitted to the PICU with acute respiratory failure who were assessed as possible candidates for NIV	CPAP or NIV	21 patients required mask ventilation only with continuous positive airway pressure and 21 with biphasic positive airway pressure. The overall success rate of NIV was 57 %	Secretions obstructing the upper airways ( $n = 6$ ), skin pressure lesions on the nose ( $n = 4$ ), agitation ( $n = 4$ ), pneumothorax ( $n = 3$ ), atelectasis ( $n = 2$ ), serious gastric distension, apnoea, and pulmonary hypertensive crisis	Bernet et al. [16]
Prospective observational study of 119 episodes of NIV in a single PICU	CPAP or NIV delivered via nasal or oral-nasal mask, nasal prongs depending on patient. Provided with CPAP and if necessary inspiratory support	84 % of patients received successful support with NIV	Complications were noted in 20 % of patients. Skin lesions (without necrosis) were the most common complication. Others included pneumothorax, upper airway bleed and gastric distension	Mayordomo-Colunga et al. [17]
Prospective observational study of 47 children who required ventilator support over a 4-year period	Used a conventional volumetric ventilator with a NIV module	19 % of patients required endotracheal intubation and ventilation after a variable period of time, others successfully managed with NIV	The most common problem with irritation and erosion of the nasal bridge	Munoz-Bonet et al. [18]
Prospective observational study of 113 children who underwent NIV	A range of CPAP devices, conventional ventilators and BiPAP devices	Only 24 % went on to require invasive ventilation	No major complications noted	Nunes et al. [19]
Prospective observational study of 278 children admitted to a PICU in respiratory failure, or put on NIV following extubation	Nasal or nasal oral mask connected to a BiPAP ventilator	75.9 % of children avoided endotracheal intubation and ventilation	Pressure sores related to the mask and some children developed healthcare associated pneumonia	Lum et al. [20]
Prospective observational study of children with status asthmaticus	BiPAP machine via a mask system	72 children received NIV and 65 did not require endotracheal intubation and ventilation	One case of massive subcutaneous emphysema	Mayordomo-Colunga et al. [21]
Observational prospective study of 151 children with acute respiratory disease treated with NIV in a PICU	NIV was delivered by continuous (CPAP) or bi-level (BiPAP) positive airway pressure. The interface to the patient was chosen between nasal or mouth-nose mask, binasal short prosthesis and nasopharyngeal prosthesis (endotracheal tube with its extremity cut and placed on the nasopharynx). Conventional (and specific NIV ventilators: were used to apply NIV	NIV failure occurred in 34 patients (22.5 %). Risk factors for NIV failure were apnea, prematurity, pneumonia, and bacterial co-infection ( $P < 0.05$ ). Independent risk factors for NIV failure were apnea ( $P < 0.001$ ; odds ratio 15.8; 95 % confidence interval: 3.42–71.4) and pneumonia ( $P < 0.001$ , odds ratio 31.25; 95 % confidence interval: 8.33–111.11)	There were no major complications related with NIV	Abadesso et al. [22]
Prospective study on 25 children <18 months old with acute bronchiolitis	High flow oxygen therapy by nasal cannula	Improvement of cardio-respiratory parameters and of Wood-Downes Score 80 % reduction of PICU admissions compared with historical data	No adverse events were observed	Gonzalez Martinez et al. [23]
Prospective observational multicentre study of 390 episodes of NIV	CPAP or bilevel NIV delivered via nasal, nasal oral or face mask	NIV success rate was in excess of 80 %, with ARDS the most common reason for failure	Not reported	Mayordomo-Colunga et al. [24]

Table 1 continued

Design and population	Technique	Clinical effects	Adverse effects	Citations
Prospective observational study including 151 episodes of NIV in patients <6 months old, with need of respiratory support	NIV provided with two levels of pressure by different types of ventilators, using the nasopharyngeal tube as interface	NIV had a failure rate of 27 %. Successful NIV cases had significant shorter PICU and hospital stays. The effectiveness of NIV was higher when used in the elective post-extubation phase	Complications were observed in 4/151 (3 %) cases. One case of aspiration and three episodes of interface obstruction due to secretions	Velasco Arnaiz et al. [15]
<b>Prospective randomized control studies</b>				
Prospective randomized control study of 20 children with severe lower airways obstruction	Non-invasive mask ventilation. 2-h cross-over study of conventional therapy vs. NIV	Children with NIV had improved symptom scores	No major adverse reactions documents	Thill et al. [25]
Prospective randomized control study of 50 children in 2 PICUs with acute respiratory failure	Facial masks were used as an interface. A range of ventilators were used including conventional ventilators and BiPap or continuous flow generators	Patients were randomized to conventional therapy (oxygen provision together with nebulization) or NIV. The need for intubation was 28 % in the treatment group vs. 60 % in the conventional group	Mild skin erosion developed at the site of mask contact in five patients. Two patients developed conjunctivitis; one developed interstitial emphysema	Yanez et al. [26]
Prospective randomized controlled study of 20 infants with acute respiratory failure	Children were randomized to non-invasive ventilation via helmet or via facemask for periods of 90 min	Use of the helmet was associated with lower number of trial failures ( $P < 0.001$ ), less patient intolerance ( $P < 0.001$ ), longer application time ( $P < 0.001$ ), and reduced need for patient sedation ( $P < 0.001$ )	For both delivery methods, no major patient complications occurred	Chidini et al. [14]
Prospective randomized control study of 70 children who presented with respiratory distress	Nasal CPAP	Use of CPAP was associated with a decrease in respiratory rate	Not reported	Wilson et al. [27]

However, the research programme is potentially challenged by a number of issues including: selection of patients for NIV; the optimal timing and implementation of NIV; the interfaces used to provide care; the modes of NIV and the triggering modalities utilized to optimize delivery of NIV.

There is a need for predictive tools to select those patients who might benefit most from NIV. A recent multicentre study of children who required respiratory support for bronchiolitis [13] showed that it was possible to some extent to predict children who would require ventilatory support for bronchiolitis, and identified a subgroup who rapidly progressed to respiratory failure. However, as the range of indications for NIV expands, it is going to be difficult to focus research on the appropriate identification of children who are likely to benefit from NIV.

The quality of interfaces may play a crucial role in the success of NIV, regardless of the mode which is used to provide it. Although most interfaces have focussed on the use of nasal cannulae or face masks, there is recent evidence that helmets may be useful [14]. Velasco et al. [15] have recently reported their positive experience in using a

simple nasopharyngeal tube as the interface for bi-level NIV in young infants (6 months or less).

The range of modes of NIV that are applicable and available is also expanding and there is the potential to use tools such as the neurally adjusted ventilatory assist (NAVA), which is potentially capable of providing proportional and better synchronized support even in the presence of large air leaks, both in invasive and non-invasive modes, in neonatal, paediatric, and adult patients.

Finally, NIV is not new, but, as we reflect on the challenges of ventilator support for children (in multiple settings across the world), it would seem that this technique(s) has the potential to substantially improve the safety of ventilator support for children, and improve access to ventilatory support for both acute and chronic conditions. Given that respiratory problems are among the most important cause of childhood deaths across the world, it behoves us to explore the potential and collect the data.

**Conflicts of interest** Both authors have indicated that they have no conflicts of interest.

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