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Review

Non-invasive ventilation for children with acute respiratory failure in the developing world: Literature review and an implementation example

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SUMMARY

Over 2 million children die of acute respiratory infection every year, with around 98% of these deaths occurring in developing countries. Depending upon the clinical status of the patient, supplemental oxygen is usually the first line therapy. However this often proves inadequate for acute respiratory failure (ARF), in which case intubation and mechanical positive pressure ventilation are required. Adult intensive care successfully introduced non-invasive positive pressure ventilation (NIPPV) to treat ARF over a decade ago. This experience, coupled with the use of NIPPV in children with chronic respiratory insufficiency, has led to increasing use of NIPPV to treat ARF in paediatric populations. NIPPV can have similar or improved outcomes to IPPV, but with fewer complications. However there are no controlled trials of its use in children, and most data come from observational studies and retrospective reviews. In a developing world setting, where mortality from ARF is high and the risks of intubation are great and often not feasible, NIPPV can be a simple and cost-effective way to treat these patients. Its implementation in rural Northern Ghana shows NIPPV for ARF can be delivered safely with minimal training, and appears to impact significantly on mortality in those under 5 years.

INTRODUCTION

Acute respiratory failure (ARF) can be categorised into hypoxaemic ARF (type I) or the more common hypercapnic ARF (type II). The hypoxaemic type is usually defined by an arterial partial pressure of oxygen (Pa_{O_2}) of <7.8 kPa (60 mmHg) with a normal or low Pa_{CO_2}. These cut offs are to an extent arbitrary and the values must be put into the context of the child's pre-existing state and whether any supplemental oxygen is being given. In the absence of supplemental oxygen, a hypercapnic patient is always hypoxaemic. The primary issue is often ventilation-perfusion mismatch due to intrapulmonary shunting. It can be associated with virtually all acute lung diseases, categorised into acute asthma, infection (bronchiolitis and pneumonia) and pulmonary oedema [1]. In addition to treating the underlying cause, supplemental oxygen must be administered to a hypoxic child. However if that is insufficient to produce a satisfactory rise in oxygen saturation, mechanical ventilation may be required. In the hypercapnic or ventilatory type, as well as hypoxaemia, there is an arterial partial pressure of carbon dioxide (Pa_{CO_2}) of >6.5 kPa (50 mm Hg), usually accompanied by a fall in pH to <7.3. Whilst this may be a chronic issue (for example in children with neuromuscular disease or chronic upper airways obstruction), it may follow on from type I ARF, when the child's respiratory muscles start to fatigue leading to hypoventilation. In this instance, oxygen alone is insufficient and ventilatory support is required.

Traditionally mechanical support has been delivered following intubation, i.e. with invasive positive pressure ventilation (IPPV).

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Abbreviations: ARDS, Acute respiratory distress syndrome; ARF, Acute respiratory failure; BIPAP, Biphasic positive pressure ventilation; BiPAP, Bilevel positive pressure ventilation; CPAP, Continuous positive airway pressure; COPD, Chronic obstructive pulmonary disease; FiO_2, Fraction of inspired oxygen; IPPV, Invasive positive pressure ventilation; NIPPV, Non-invasive positive pressure ventilation; NIV, Non-invasive ventilation; PICU, Paediatric intensive care unit; Pa_{O_2}, Arterial partial pressure of oxygen; Pa_{CO_2}, Arterial partial pressure of carbon dioxide; SpO_2, Arterial oxygen saturation measured by pulse oximetry.

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However the use of non-invasive positive pressure ventilation (NIPPV) to treat ARF is increasing as NIPPV can have a similar or improved outcome to IPPV with fewer complications [1]. NIPPV tends to refer to biphasic and bilevel (BiPAP) respiratory support not delivered via invasive endotracheal intubation. Interfaces used include nasal pillows, plugs or masks; facemasks – which can be total (mouth, nose, eyes) or full (mouth & nose); mouthpieces; or helmets [2]. Some authors use the term NIPPV to include Continuous Positive Airway Pressure (CPAP) which is not strictly 'ventilation' although could be included under the umbrella of non-invasive respiratory support. Nevertheless an International Consensus has defined NIPPV as 'any form of ventilatory support applied without the use of an endotracheal tube, and was considered to include continuous positive airway pressure (CPAP), with or without inspiratory pressure support" [3]. The use in ARF has generally been restricted to paediatric intensive care units or high dependency units in the technologically-rich developed world, but because of cost issues and its relative simplicity making it accessible to trained healthcare workers other than doctors, there is great potential for its use in the lower income setting of the developing world. This review will look at evidence for the benefit of NIV in ARF, and how it may be applied in the developing world. We will also describe our experience of setting it up in a rural hospital in Ghana.

THE BURDEN OF ARF

ARF develops in minutes to hours, and is more frequent in infants and children than in adults [4]. There are a multitude of causes, which can be reviewed in many text books [5]. However in the developing world, infection is paramount. Worldwide, a conservative estimate has suggested 2 million children die of acute respiratory infection every year, a figure that excludes sepsis and pneumonia in neonates [6]. Inevitably, around 98% of these deaths occur in developing countries [7]; estimates from 2000 suggest 70% were in Africa or SouthEast Asia [8]. From 2000-03, 19% of worldwide deaths in children under five were caused by pneumonia and 10% by neonatal sepsis and/or neonatal pneumonia [9]. Worryingly, in one of the few studies that were able to look at trends in mortality by cause, in Morocco between 1987 and 1997, despite a halving in overall infant and child mortality, there was little change in the rates of death due to pneumonia (report by Garenne M in French, quoted by Mulholland) [6]. Indeed, pneumonia kills more children every year than AIDS, tuberculosis, malaria and measles put together [10].

An important risk factor for respiratory deaths is malnutrition, which in itself is said to be an underlying cause in over half of all deaths in children under 5 years [9]. Poorly nourished children are more likely to develop respiratory fatigue and consequently ARF. Another factor is severe chronic anaemia which, by impeding oxygen transport, makes it more likely for hypoxaemia to develop during respiratory infections. Chronic anaemia is common in developing countries due to a variety of factors including malnutrition, helminthiasis, sickle cell anaemia, and chronic malaria [11].

There are many strategies to prevent deaths from childhood pneumonia in the developing world. These include use of vaccination (to *Haemophilus influenzae* type b, pneumococcus and measles), improvement in nutritional state, and possibly reduction of indoor air pollution [10]. If the child develops pneumonia, early recognition (of tachypnoea) and prompt treatment with antibiotics (often just oral amoxicillin for 3 days) can save lives [12]. If the pneumonia is severe, these children need to be managed in a district hospital. Use of oxygen saturation monitoring and oxygen concentrators to deliver supplemental oxygen when appropriate (SpO_2<90%), led to a 35% reduction in risk of death from pneumonia in a rural setting in New Guinea [13]. This is not surprising given hypoxaemia (SpO_2<90%) has been shown to be associated with a 4.3- fold increase in mortality in Kenyan children under 3 years with pneumonia [14]. With the development of type II respiratory failure, oxygen alone will be insufficient, and only mechanical ventilation will save the child, hence our interest in non-invasive ventilation.

USE OF NIV FOR ARF IN THE DEVELOPED WORLD

Positive pressure ventilation is often used to provide respiratory support for children with ARF as it increases the tidal volume hence helps to recruit lung tissue and maximise lung volumes, reversing hypoxemia and hypercapnia. This is most frequently provided invasively via an endo- or nasotracheal tube, unless the child has a tracheostomy. However, following experience in patients with chronic respiratory insufficiency, the benefits of NIPPV for ARF are being increasingly recognised. Inevitably, experience in ARF has initially come from adult intensive care, where NIPPV has been successfully used for over a decade in a multitude of conditions, including exacerbations of chronic obstructive pulmonary disease [15], acute exacerbations of asthma [16] and cardiogenic pulmonary oedema [17].

One review over 15 years ago quoted 29 studies enrolling 748 patients successfully treated with NIPPV for hypoxaemic ARF [18]. Gas exchange can be maintained and there is a decrease in the necessity for endotracheal intubation, with the additional benefit of shorter length of stay and fewer serious complications [19]. In particular NIPPV is associated with a lower rate of ventilator-associated pneumonia and sinusitis than invasive ventilation [19,20]. The risk of secondary lung injury and barotrauma from positive pressure ventilation is lessened although not abolished with NIPPV. It also stops the risk of upper airway trauma including vocal cord damage and subglottic scarring with subsequent stenosis. Additionally it enhances the patient's comfort and aids eating and drinking, coughing and talking [21]. It also reduces the need for sedation although that can sometimes be needed for agitated or scared patients (assuming the agitation is not due to hypoxaemia) [21]. Contraindications to the use of NIPPV include congenital facial or airway abnormalities (precluding use of a tight fitting mask or prongs), severe cardiopulmonary instability, inability to protect the airway, and intractable apnoeic pauses [22]. Other problems include facial trauma or burns, and patients with recent gastrointestinal surgery (in case of gastric distension with air) [22].

Paediatric experience: Evidence for the paediatric use of NIPPV is limited because there are no consistent guidelines, and few prospective randomised controlled trials. The majority of published work is in the form of non-controlled trials and small case series yet its use is increasing [23]. Nevertheless, the results of available studies are encouraging. An excellent review from Najaf-Zadeh and Leclerc has summarised studies up until 2011, categorising the use of NIPPV (including CPAP) in children with acute airway obstruction (including asthma, bronchiolitis, malacia) and parenchymal lung disease (including pneumonia, acute respiratory distress syndrome (ARDS), acute chest syndrome) [1]; there were 13 studies in the first group and 7 in the second. They also categorised specific circumstances of its use, including in the post-operative period (6 studies), for facilitation of ventilation weaning and post-extubation management (2 studies), and in immunocompromised children (6 studies) [1]. A randomised controlled trial of NIPPV plus standard therapy versus standard therapy in 50 children with ARF (mostly due to bronchiolitis or pneumonia) carried out in Argentina and Chile, confirmed the improvement in cardiopulmonary parameters, and the intubation rate was 28% in the NIPPV group vs 60% in the other [24]. There has