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Review Article

High-Flow Nasal Cannula Oxygen Therapy in Infants and Children Versus Other Non-Invasive Ventilation: A Review of Current Knowledge

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Abstract

Respiratory distress is the leading cause of hospitalisation in paediatric intensive care units. Non-invasive ventilation can be delivered via continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP) or high-flow nasal cannula (HFNC). HFNC protocols are based only on manufacturers' studies, with positive nasopharyngeal pressure as the primary endpoint. These protocols recommend the use of humidified air to prevent irritation of the airway mucosa. HFNC therapy may be better tolerated than traditional modes of non-invasive support, such CPAP and BiPAP in part owing to its smaller nasal prong interface allowing activities like breastfeeding with greater ease.

Keywords: *Paediatric Intensive Care; Continuous Positive Airway Pressure; High-Flow Nasal Cannula; Non-Invasive Ventilation; Preterm Infants*

Abbreviations

CPAP: Continuous Positive Airway Pressure; BiPAP: Bilevel Positive Airway Pressure; HFNC: High-Flow Nasal Cannula; SOT: Standard Oxygen Therapy; ICU: Intensive Care Unit; RR: Risk Ratio; MD: Mean Difference; CI: Confidence Interval; LOS: Length of Stay in Hospital; BPD: Bronchopulmonary Dysplasia; RCTs: Randomized Control Trials; PICU: Paediatric Intensive Care Unit; FiO_2: Fraction of Inspired Oxygen

Introduction

Respiratory distress is the leading cause of hospitalization in paediatric intensive care units [1]. Non-invasive ventilation can be delivered via continuous positive airway pressure (CPAP), bilevel positive airway pressure (BiPAP) or high-flow nasal cannula (HFNC). HFNC protocols are based only on manufacturers' studies, with positive nasopharyngeal pressure as the primary endpoint [2]. These protocols recommend the use of humidified air to prevent irritation of the airway mucosa [3].

When faced with a hypoxic child with respiratory distress, clinicians must choose from amongst standard oxygen therapy (SOT, up to 4 L/min), HFNC, BiPAP or CPAP. Factors influencing this decision are clinical outcomes, cost-effectiveness, and availability/tolerance of therapies [4]. HFNC therapy may be better tolerated than traditional modes of non-invasive support, such CPAP and BiPAP in part owing to its smaller nasal prong interface allowing activities like breastfeeding with greater ease [5].

Mechanism of action

Through various proposed mechanisms such as optimal humidification of inspired gases, reduction of inspiratory resistance, washout of airway dead space and generation of variable positive pressure, HFNC has been observed to decrease respiratory work of breathing and improve parameters of oxygenation and ventilation in a range of conditions such as bronchiolitis, asthma, and postcardiac surgery [6,7].

HFNC generates positive pressure throughout the respiratory cycles, hence maintaining lung inflation and promoting lung patency [8]. This mechanism serves to avoid the collapse of alveoli, preserve lung volume and capacity, and improve oxygenation. High-flow nasal cannula (HFNC) therapy has the additional benefit of mitigating the effort required for breathing by specifically reducing airway resistance during exhalation. [9]. The ongoing flow of gas generates positive end-expiratory pressure, hence maintaining partial lung inflation during the exhalation phase [10]. The reduction of oesophageal pressure changes during respiration, compared with standard nonocclusive oxygen facemask, indicates its capacity to ease inspiratory effort [11]. Airway pressure generated from a high-flow system varies and depends on flow amount, cannula and nares sizes, and degree of mouth opening in an experimental study [12].

Optimal flow in paediatric patients

There is a lack of guidance about optimal flow in paediatric patients. Important randomized controlled studies conducted in patients with acute bronchiolitis provided information about appropriate flow [13,14]. Patients younger than 24 months of age tolerated the flow of 1 - 2 Litre/kg/min (up to 20 L/min) and 3 L/kg/min. However, patients were uncomfortable with 3 L/kg/min despite the same efficacy [15].

Early protocols for non-intensive care unit (ICU) use of HFNC used age-based (e.g. 8L of flow for children under 12 months of age) flow rates and have been associated with increased ICU utilization [16,17]. More recently, there has been a shift toward the use of weight-based (e.g. 2L of flow per kilogram of body weight) flow rates, which have been studied in several recent randomized trials [18].

The transition to weight-based protocols was also associated with a trend toward allowance of higher maximum flow rates, consistent with flow rates used in recent published randomized control trials (RCTs) [14,18]. The protocolized use of HFNC in non-ICU settings has become common, with 1 survey conducted in 2017 finding that 37 of 77 (48%) responding sites used HFNC on the paediatric wards [19].

HFNC vs other non-invasive ventilation methods

A recent 2024 Cochrane review comparing HFNC vs Standard Oxygen Therapy (SOT) (2012-2022, 8 studies, 2215 patients) reported that primary HFNC use reduced risk of treatment escalation by nearly half (45%) for an individual patient (risk ratio (RR) 0.55 (0.39 to 0.79) [20].

Prior to the introduction of HFNC, nasal CPAP/BIPAP were the key escalation therapies in patients failing SOT. In recent years, several large, high-quality studies, and subsequent metanalysis, have compared HFNC versus CPAP, in moderate to severe bronchiolitis. Key outcome parameters of interest include efficacy, safety, cost-effectiveness, availability and treatment compliance [4].

Pooled data meta-analysis (2 randomised controlled trials (2 RCTs) [33,36], 318 children) suggests no significant difference between CPAP and HFNC in hospital [mean difference (MD)=: _0.22, 95% confidence interval (CI) (0.91, 0.48), I^2 = 27%] or paediatric intensive care units (PICU) length of stay in hospital (LOS) (MD _ 0.15, 95% CI _ 1.27 to 0.98, p = 0.80) [21].

HFNC has similar rates of efficacy to other forms of non-invasive respiratory support in preterm infants for preventing treatment failure, death and chronic lung disease. Most evidence is available for the use of HFNC as post-extubation support. Following extubation, HFNC is associated with less nasal trauma, and may be associated with reduced pneumothorax compared with nasal CPAP. Further adequately powered randomised controlled trials should be undertaken in preterm infants comparing HFNC with other forms of primary non-invasive support after birth and for weaning from non-invasive support [22].

HFNC in premature infants

However, according to the results of a cohort study, infants born with a gestational age of less than 32 weeks used HFNC shortly after birth are being linked to higher rates of Bronchopulmonary Dysplasia (BPD). Additionally, infants born with a gestational age of less than 28 weeks had a higher failure rate of 60% when HFNC was used as first respiratory support. Additionally, compared to the CPAP group, it was noted that infants who received HFNC as their initial support mode needed escalation of care [23].

Other important clinical outcomes such as late onset sepsis, necrotising enterocolitis, patent ductus arteriosus, pneumothorax and retinopathy of prematurity were also more frequent in babies who received HFNC. Infants who received HFNC required respiratory support for longer and received in- hospital neonatal care for longer. Prolonged need for respiratory support with HFNC has been demonstrated in meta- analyses of (RCTs) [22] and observational studies [24,25].

The possibility of air leak syndromes with HFNC therapy is another drawback of applying the therapy in extremely premature infants. When an excess pressure accumulates in the airways and lungs, air leaks like pneumothorax and pulmonary interstitial emphysema can happen [26].

HFNC in paediatric intensive care units (PICU)

Wing., *et al*. studied 848 children with acute respiratory insufficiency requiring PICU admission. Overall intubation rates decreased from 15.8% to 8.1% ($p = 0.006$) with introduction of HFNC and establishment of a guideline for use, including a decrease from 21% to 10% ($p = 0.03$) among children with bronchiolitis. The overall decrease was largely accounted for by a decreased intubation rate in PICU, from 10.5% to 2.2% ($p < 0.001$), while rates of intubation after transfer to the PICU remained steady [27].

However, in a recent RCT among critically ill children requiring non-invasive respiratory support following extubation, HFNC compared with CPAP following extubation failed to meet the criterion for noninferiority for time to liberation from respiratory support [28].

Conclusion

HFNC has found a well-defined role in the treatment of children with acute hypoxemic respiratory failure, bridging the gap between the delivery of low-flow supplemental oxygen and traditional non-invasive ventilation (i.e. CPAP, BiPAP). Considering its ease of use, comfort, and the growing body of clinical evidence supporting its clinical equivalence to other non-invasive ventilation modalities, the use of HFNC is expected to continue to expand beyond the confines of the neonatal and paediatric ICUs [3].

The scholars recommend that further research be conducted to optimize the use of HFNC in extremely premature infants. Studies should focus on determining the best flow rates, FiO_2 levels, and duration of therapy, as well as explore the long-term effects of HFNC on neurological development and prevention of BPD. To facilitate this, standardized protocols and guidelines for its use should also be developed to ensure consistent and evidence-based practices [29].

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