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Review

High-flow nasal cannula: Mechanisms, evidence and recommendations

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SUMMARY

The use of high-flow nasal cannula (HF) therapy as respiratory support for preterm infants is rapidly increasing, due to its perceived ease of use and other potential benefits over the standard 'non-invasive' respiratory support, continuous positive airway pressure (CPAP). The evidence from randomized trials suggests that HF is an alternative to CPAP for post-extubation support of preterm infants. Limited data are available from randomized trials comparing HF with CPAP as primary support, and few trials have included extremely preterm infants. This review discusses the proposed mechanisms of action of HF, the evidence from clinical trials of HF use in preterm infants, and proposes recommendations for evidence-based practice.

1. Introduction

1.1. High-flow nasal cannula: a new 'non-invasive' respiratory support

Nasal continuous positive airway pressure (CPAP) is the most widely used 'non-invasive' respiratory support for preterm infants around the world. In 2013, more than 85% of very preterm infants [<32 weeks of gestational age (GA)] registered to the Australian and New Zealand Neonatal Network (ANZNN) were treated with CPAP during their hospital admission [1]. CPAP delivers a continuous distending pressure to the lungs, usually set at between 5 and 10 cm of water (cmH_2O) when treating preterm infants. Gases are heated and humidified, and the delivered oxygen concentration may be altered with the use of a 'blender'.

Whereas CPAP is a well-studied and efficacious modality in preterm infants, it has some drawbacks. The need for the prongs to completely fill the nostrils may result in damage to the nasal mucosa and septum [2,3]. Excessive leak around the prongs or mask may lead to inadequate support, whereas too much pressure may cause air leak from the lung into the pleural space (pneumothorax), both of which may require intubation and mechanical ventilation [4]. CPAP may cause abdominal distension, sometimes called 'CPAP belly' [5], and the bulky interfaces used to maintain the prong position in the nose obscure the infant's face, which may interfere with bonding, suck feeding, and positioning. The effective application of CPAP requires skilled clinical care, and in smaller centers it may be difficult to acquire and maintain these skills.

In the last decade, an alternative form of non-invasive respiratory support known as high-flow nasal cannula (HF, Fig. 1) has become available. This form of respiratory support uses smaller binasal prongs than nasal CPAP, and a simpler interface. HF delivers gas flows >1 L/min [6]. This therapy has evolved from the practice of providing supplemental oxygen to preterm infants via small binasal prongs at flows <1 L/min using unheated and unhumidified gas, a practice thought to provide no respiratory support to the infant other than sensory stimulation that may contribute to reduction in apnea.

Commercially available HF systems that have been used in randomized trials of HF, such as the Vapotherm Precision Flow (Vapotherm, Inc., Exeter, New Hampshire, USA), Fisher & Paykel Optiflow™ Junior (Fisher & Paykel Healthcare, Auckland, New Zealand), and Comfort Flo® (Teleflex Medical, Research Triangle Park, NC, USA) systems, heat and humidify the delivered gas. Oxygen and air may also be blended with these systems to deliver a target fraction of inspired oxygen, similar to CPAP systems.

1.2. The increasing use of HF to treat preterm infants

HF has become a popular mode of non-invasive respiratory support in the pediatric population. In older infants and children,

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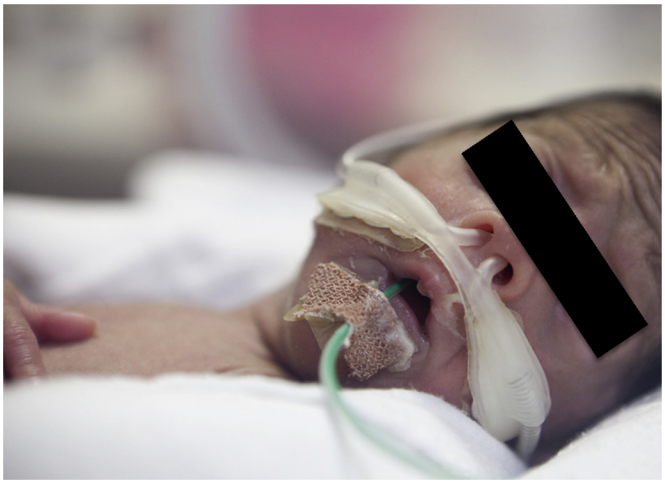

Fig. 1. A preterm infant treated with Fisher & Paykel 'Optiflow™ Junior' high-flow nasal cannula therapy.

there is increasing evidence of its use and efficacy, especially in treating those with viral respiratory tract infections [7–9]. In recent years, there have been more reports of the increasing use of HF to treat preterm infants. The ANZNN has recently reported 2013 data showing that 24% (2332 infants) of all tertiary neonatal intensive care unit (NICU) registrants had received HF, a marked increase from about 8% in 2009 [1]. HF use was predominantly in preterm infants born <30 weeks of GA: about 60% of these infants received HF during their hospital admission. Typical gas flows used ranged from 2–8 L/min.

Several published surveys have helped to quantify HF use in the preterm population around the world. Hochwald and Osiovich [10] distributed a questionnaire regarding HF use to all 97 'academic' neonatal units in the USA: 69% of respondents reported using HF. Hough[11] surveyed the member NICUs of the ANZNN in 2011 and found that 63% were using HF. In 2009, Nath[12] undertook a telephone survey of all 214 neonatal units in the UK: 55% used HF. This survey was updated in 2011 by Ojha[13] for tertiary neonatal units in the UK: HF was used in 77% of responding units. Anecdotally, we are aware of several tertiary NICUs around the world that have replaced CPAP with HF as their preferred mode of respiratory support for preterm infants.

The increasing use of HF to treat preterm infants is due to its perceived benefits, as well as accumulating evidence of efficacy and safety. The simpler interface of HF is often described as easier to apply than CPAP, and there is evidence that HF is preferred by parents [14] and nurses [15]. Nursing staff in one center using HF for the first time as part of a randomized trial described HF as being easier to set-up and use, more comfortable and less likely to cause nasal trauma compared with CPAP [15]. Osman[16] measured pain scores and salivary cortisol concentrations, and found that preterm infants receiving HF were more comfortable than infants receiving nasal CPAP.

However, there have been complications when using HF in preterm infants. The most widely publicized was the *Ralstonia* contamination of the Vapotherm system that forced a temporary recall of this device in 2005 [17]. The Vapotherm system has since been subject to more stringent infection control measures and is back in widespread use. There has been a case report [18] of a preterm infant receiving humidified HF (2 L/min, device not reported) with concomitant subcutaneous scalp emphysema and pneumo-orbitis, which resolved after discontinuation of HF. A case series of pneumothoraces in older infants and children treated with HF was reported in 2013 [19].

1.3. Chapter outline

This Chapter evaluates the evidence for the use of HF in preterm infants, including studies of physiological effects and its mechanisms of action, and randomized clinical trials of HF use in different clinical scenarios. Several study authors have kindly provided unpublished subgroup data, and/or clarified their trial methodology and results.

2. Mechanisms of action of HF

2.1. Heating and humidification of delivered gas

The human nasal air passages warm inspired air from the ambient temperature to 37°C, and humidify it to 100% relative humidity (RH) [20]. At flows >1 L/min, delivery of unheated, unhumidified gas has potential adverse consequences, including mucosal injury and infection [21,22]. To this end, all commercially available HF systems deliver heated, humidified gas. Woodhead [23] demonstrated the clinical effectiveness of humidifying HF gas in a clinical crossover study of post-extubation support in 30 preterm infants: no patients 'failed' extubation during HF via the (heated and humidified) Vapotherm device, but seven 'failed' while receiving unheated, unhumidified 'high flow'.

Several benchtop studies have evaluated the heating and humidification performance of HF devices. Roberts [24] recently tested the Vapotherm 'Precision Flow' and Fisher & Paykel 'Optiflow Junior' devices at gas flows of 1, 4 and 8 L/min using a digital hygrometer in a neonatal manikin's 'nasopharynx', placed inside an isolette. At 1 and 4 L/min, the Vapotherm device produced slightly higher temperature (median ~34 vs ~33°C) and relative humidity, RH (median ~99% vs ~96%) than Optiflow Junior. At 8 L/min Optiflow Junior achieved higher temperature (median 36.3°C vs 34.3°C) and RH (median 88.8% vs 81.2%). Waugh [25] tested the previous Vapotherm 2000i and reported a temperature of 36.5°C and RH 99.9% at 5 L/min within the device circuit. Chang [26] found that gas delivered by the Vapotherm at flows 0–8 L/min was cooler (mean 34.0 °C vs 34.5°C, $P < 0.01$) but more humid (83% vs 76%, $P < 0.01$) than that delivered by nasal CPAP.

2.2. Distending pressure generation

HF may produce distending pressure in the lung, similar to CPAP pressures, however clinicians have raised concerns regarding the potentially unpredictable pressures generated by HF. Finer [27,28] noted that during CPAP the delivered pressure cannot exceed the set pressure, but the same cannot be said with HF, where pressure is neither set nor measured. Data on the pressure generated during HF are reassuring, but come from small observational, crossover, animal and *in vitro* studies, with different methods for estimating intrapulmonary pressures.

Evidence surrounding pressure generation with HF is somewhat conflicting. With regard to the relationship between leak and pressure generation, Kubicka [29] found that with the mouth open no pressure was generated, Sivieri [30] demonstrated very high pressures in an in-vitro model with simulated mouth closure, whereas Wilkinson [31] showed no relationship between pressure generation and mouth leak. Similar gas flows have been reported to produce pressures thought to be dangerously high [32], and pressures that are much lower than usually set with CPAP [33,34].