Using nasal high flow instead of nasal continuous positive airway pressure on the NICU

Most neonatal intensive care units use different types of nasal continuous positive airway pressure (nCPAP) to achieve non-invasive ventilation. The use of heated, humidified nasal cannulae to deliver nasal high flow (nHF) has gained support as an alternative to nCPAP, although there has been some conflicting evidence about how best to use it in a neonatal setting. This article will look at the safe and successful use of nHF as a direct substitute for nCPAP.

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Key points

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1. Nasal high flow (nHF) is an effective replacement for nCPAP in neonates.
2. nHF is safe and well tolerated in neonatal practice.
3. Optimal weaning of nHF requires further understanding.
4. Users should appreciate the mechanics of nHF, especially optimising 'flush'.

The non-invasive ventilatory management of preterm babies has evolved over recent years. It is now normal practice in many neonatal intensive care units (NICUs) for very small preterm babies to be managed either with very short-term ventilation (a few hours) or without mechanical ventilation. Fewer babies are now routinely given prophylactic surfactant in the delivery room, with greater use of support/rescue policies[1,2]. Evidence has shown that this approach is safe and reduces the rates of bronchopulmonary dysplasia (BPD) and death[3,4]. Most NICUs use different types of nCPAP to achieve non-invasive ventilation. There have been comparisons between the various types of nCPAP, including fixed and variable flow nCPAP, bubble nCPAP, biphasic and synchronised biphasic nCPAP (BiPAP) and non-invasive positive pressure ventilation (NIPPV)[5]. The Extubate trial[6] is currently investigating if BiPAP offers greater extubation success than nCPAP in babies less than 30 weeks' gestation although a previous, but underpowered, study found no difference[7]. NIPPV is no better than nCPAP according to a recent study[8].

An alternative to nCPAP has emerged during the past decade. The use of heated, humidified nasal cannulae (HHNC) to deliver nasal high flow (nHF) has gained support, although there has been some conflicting evidence about how best to use it in the neonatal setting. A recent article in this journal described its use at Leeds General Infirmary as a step-down from nCPAP[9]. This is arguably an illogical way to apply nHF and this article will address this issue and how and why the fear of pneumothoraces has not been realised in practice. An update from the most recent literature will also be provided alongside a discussion of why some of the published literature, including the current Cochrane review, appears to be flawed. The NICU at St Peter's has gained extensive experience in using nHF and some practical hints on how to use it successfully and safely will be described (**FIGURE 1**).

Background

From 2005 to 2008 a culture of non-invasive ventilation of extremely preterm babies was developed in St Peter's NICU based on a policy of prophylactic surfactant for babies less than 27 weeks' gestation and rescue surfactant for others, as needed. Babies deemed stable and breathing spontaneously were extubated

FIGURE 1 Safe and successful use of nHF on the NICU.

within a few hours of birth to BiPAP. They were sustained on BiPAP, which was then gradually weaned through a (fairly unscientific) combination of conversion to nCPAP, 'time off', nose-breaks with face mask and reduction in mean airway pressures. Despite emerging evidence that babies spent less overall time on nCPAP if they were weaned on pressure rather than 'time off'[10], there was still a real need to protect the nose from pressure effects caused by prongs and face masks.

Around this time, evidence for the efficacy of nHF in neonatal practice in the US was emerging. For example, in 2007 a large retrospective study demonstrated that the use of nHF compared with nCPAP appeared to be safe and resulted in fewer ventilator days, a reduction in BPD and a highly significant reduction in re-intubation after prophylactic surfactant and extubation[11]. A further study showed that nHF was as good as nCPAP in reducing the work of breathing and was well tolerated, with the potential to minimise nasal injury[12]. Evidence concerning distending pressure was mixed, however under circumstances where the prongs were correctly fitted, distending pressures were within normal limits. Regrettably, there were no UK clinical studies, despite nHF having been used in the neonatal population in the US for over five years. The next section will address the decision to use nHF instead of nCPAP/BiPAP at St Peter's.

nHF – differences and comparison to nCPAP

The NICU at St Peter's uses the Vapotherm™ Precision Flow© to deliver nHF. There are other different systems on the market which also deliver high flow, such as the Optiflow© by Fisher and Paykel Healthcare™. There are differences between the various high flow systems available that may be clinically important, but there has been very little direct comparison. One study demonstrated higher pressures in the Optiflow compared to the Vapotherm 2000i© system at flow rates <8L/min[13]. Another compared extubation success in 40 babies between 26 and 29 weeks' gestation between the 2000i and the Optiflow systems[14]. The failure rate of successful extubation by 72 hours for babies randomised to the 2000i was 9% and to Optiflow was 18%, which was not statistically significant due to the small size of the study. The HIPERSPACE trial compared nHF to nCPAP for post-extubation support in a multi-centre, randomised, non-inferiority trial[15]. It concluded that nHF is safe and non-inferior to nCPAP, with a trend to less re-intubation in the nHF group (p=0.12). The CHIPS trial presented similar results[16]. Another trial compared 432 babies over 28 weeks, showing that nHF was as safe and effective as nCPAP, with a significant reduction in nasal trauma[17].

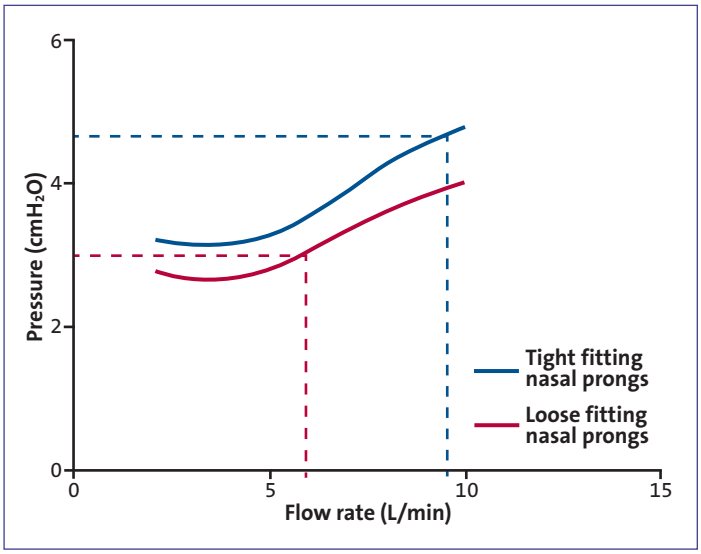

FIGURE 2 Adapted from Frizzola et al[19]. The graph shows increasing tracheal pressure in response to increasing flow rate using nasal prongs. At flow rates of 2-8L/min, the distending pressure varies between 2.5 and 4.2cmH_2O, even for tight fitting prongs. Where nasal prongs are applied correctly (ie loose fitting) the pressures are lower.

How does nHF work?

There are four key mechanisms that appear to underpin the efficacy of nHF when delivered through the Precision Flow system. This helps to explain the clinical experience of using nHF at St Peter's and the guidelines for starting, sustaining and weaning infants on nHF.

1. **Flush of the nasal passages and oropharynx.** In nHF, the respiratory 'dead space' in the upper airway is continuously replenished and exhaled gas instantly removed. This ensures that, for every breath taken by the infant, there is no re-breathing of expired gas. The higher the gas flow, the greater the flush, and there is evidence that low rates of nHF (<2L/min) are clinically ineffective and are unlikely to achieve adequate flush[18].
2. **Loose fitting nasal prongs.** This is one of the fundamental differences with nCPAP. nHF is an 'open' system, where prongs should not fit snugly in the nose and no attempts should be made to close the baby's mouth. By contrast, nCPAP is a 'closed' system where the mean airway pressure that is measured at the nose is achieved through the use of close-fitting and firmly applied prongs and, in some instances, mouth closing with pacifiers, chin straps or rolls.

   A study comparing the effects of tight and loose fitting prongs on blood gas levels of carbon dioxide ($PaCO_2$) and oxygen (PaO_2) in an animal model of acute lung injury showed that oxygenation reached a maximum at a flow of about 6L/min, regardless of whether the prongs were loose or tight fitting[19]. Loose fitting prongs were much more effective at all flows at removing carbon dioxide. This effect has also been confirmed using computational flow dynamics (unpublished data, Vapotherm Inc), so that the larger the unoccluded nasal opening, the more effective the flush effect. This is seen clinically in larger babies where the prongs occupy less than 50% of the nares and carbon dioxide removal can be highly efficient, such that lower flows can achieve effective flush. Loose fitting prongs are also more comfortable for babies. Nasal inflammation or injury from the use of nHF is never seen at St Peter's NICU. This has abolished the need for 'comfort breaks' or 'time off' or any other of the routines developed when using nCPAP to try to prevent nasal injuries, which have been described as frequent[20]. Babies on nHF look comfortable, including term babies.
3. **Reduced work of breathing.** A number of studies have compared the work of breathing in infants on nHF or nCPAP and concluded that they appear to be similar, even at flow rates as low as 2L/min[12]. In addition, the delivery of

optimally heated and humidified (conditioned) inhaled gas appears to be important. There is substantial evidence that lung compliance and mucociliary function are rapidly and adversely affected by inhaled gas that is not humidified or heated, and nasal inspiratory resistance increases[21]. The lungs also expend metabolic work to heat and humidify inhaled gas with every breath. The aim should be to use gas delivered at core temperature with 100% humidification[22].

4. **Moderate upper airway pressures.** One of the concerns often raised is that high flow therapy can generate 'uncontrolled' or 'unmeasured' distending pressure. There is now experimental[19,23] and clinical evidence to show that upper airway pressures with nHF are similar to or lower than nCPAP (approximately 6cmH_2O)[12]. It is difficult to understand how significant pressure could build up in an open system. It has been shown that there is no increase in pressure at any flow rate, for any infant where loose fitting, small prongs are applied[24,25]. Even if the mouth is occluded, upper airway pressures are about 6cmH_2O[26].

Experimental data showed that tight fitting ('low leak') and loose fitting ('high leak') prongs gave only moderate distending pressures at flows up to 8L/min (**FIGURE 2**)[19].

At St Peter's the pneumothorax rate in 2006, when babies were extubated early to BiPAP, was compared with the rate during 2011, when babies were extubated to nHF. No babies in either year developed pneumothoraces while on either treatment, and pneumothorax is rare in non-ventilated babies of all gestations in St Peter's (<1%) and other units[17]. This reinforces the belief that nHF, used expertly, is safe. Clinical experience and evidence at St Peter's suggests that nHF does not give high or harmful levels of distending pressure.

Use of Precision Flow for nHF

The 'Vapotherm', as it is generally known in the NICU, is now the default for non-invasive ventilatory support for any baby at St. Peter's NICU, and has replaced nCPAP/BiPAP. nHF is not used as an additional step for weaning from nCPAP, as this appears to be an illogical use based on the available evidence and is likely to prolong the duration of respiratory support. Over the first few years of nHF use, there was a tendency to transfer babies who were failing to ventilate effectively on nHF onto synchronised BiPAP, in the hope that it would provide more aggressive back up to prevent re-ventilation. However, it was found that this was generally not effective – babies who had apnoeic episodes (usually due to a septic episode) could not be sustained on non-invasive ventilation of any type. It is now normal practice to just intubate and ventilate under these circumstances, as these episodes are usually transient. In fact, it has been observed that, despite rising activity rates, only 4.1% of babies were ventilated in 2010 (nHF era) compared to 8.5% of babies in 2006 (nCPAP era).

Anecdotally, it seemed that babies transferred into the unit who had been on nCPAP for a prolonged period were sometimes unable to manage on nHF. This could be because they may have chronically distended airways that cannot adapt to the lower pressures achieved on nHF.

Starting and sustaining babies on nHF

For preterm babies who have the largest ratio of dead space to lung volume, gas flows of 7-8L/min are routinely commenced. While this is above the level needed for optimal ventilation[19], it was recognised that the nares are often more than 50% occluded by the smallest prongs in the smallest babies and therefore using slightly higher flows enhances the efficiency of carbon dioxide removal.

Larger babies (>1.5kg) commence with flows of 6L/min but it may be necessary to reduce this within a few hours as hypocarbia can occur. The ventilatory effect with loose fitting prongs is so efficient that $PaCO_2$ levels less than 4kPa have been seen. The use of transcutaneous monitoring of carbon dioxide in the blood ($PaCO_2$) can be very useful in reducing the need for blood gas analyses and minimising 'over ventilation'.

Although successful extubation is hard to predict, it is expected most of the time at St Peter's. If a baby is stable a loading dose of caffeine is administered. Nasal prongs are applied prior to extubation; minimal handling and transcutaneous monitoring of carbon dioxide, are usual practice. Babies are always placed in the prone position, tilted upright. Initially the baby's breathing often appears 'jerky' and, in instances where the breathing pattern becomes smoother and more undulating, extubation is more likely to prove successful. Babies will often have frequent episodes of desaturation in the first few hours after extubation, but these episodes are usually transient and mostly self-limiting. Post-extubation blood gas analysis is not routinely performed unless there is concern.

Weaning

The purpose of weaning is to determine the minimum level of support that a baby requires. Once a baby is stable, weaning commences according to some principles learnt through experience.

- Babies should be weaned by a reduction in flow rate rather than oxygen level. However, when the fraction of inspired oxygen (FiO_2) is greater than 0.3, reducing the flow rate is questionable, especially in smaller babies.
- Even if they require some oxygen, stable babies should be weaned by a reduction in flow rate. As a guide, 30% oxygen is used in the unit.

	Duration of support (days)		
Gestational age at birth	**2006 (BiPAP/nCPAP era)**	**2010 (nHF era)**	**2011 (nHF era)**
24-27 weeks	31	22	18
28-30 weeks	10	16	10
>30 weeks	4	5	4

TABLE 1 Average duration of non-invasive support modality during different eras of modality use.

- In larger stable babies, weaning can take place at least every 24 hours – usually in decrements of 1L/min, as tolerated.
- In smaller stable babies, weaning is attempted every 24-48 hours, usually in decrements of 0.5L/min.
- Small babies (<900g) should be maintained on flow rates of 4-5L/min to minimise their work of breathing and promote stability and growth. This decision should be reviewed regularly.
- If a baby is stable, routine blood gas analysis following a change is unnecessary.
- Babies on air at flow rates of 2.5L/min can be discontinued from nHF.
- Babies who still require oxygen at flow rates of 2.5L/min can be weaned to 2L/min. nHF flow rates below 2L/min are not used on the unit – the baby is placed on 'low' flow nasal cannulae.
- Contrary to the manufacturer's recommendation, the gas temperature should not be lowered with flow rates below 4L/min. While a baby is in an incubator, the environmental temperature ensures that, even at lower flow rates, the risk of condensation and 'spitting' of water at the nares is very small. For some babies in open cots, this may be a problem and the temperature may need to be reduced to 36°C at lower flows. This varies from case-to-case and should be determined on an individual basis.
- If a baby becomes less stable after an attempt at weaning, the previous flow rate should be reinstated. If instability continues, the cause should be determined.
- There is no need to give a baby 'time off' from prongs as nasal trauma is not an issue for babies on nHF.
- Prongs and circuits should be changed in accordance with the manufacturer's guidelines.

There is still a need for research to establish best weaning practice for babies receiving nHF, which is likely to depend on the clinical situation. There is a 'flow gap' between the lowest 'high' flow and the highest 'low' flow, which may be important for a small number of babies. The move from highly humidified, to poorly humidified gas when changing to low flow, may also be important.

Length of time on non-invasive support

The time spent on nHF was compared against the time spent on BiPAP/nCPAP, by gestational age (**TABLE 1**). Not only is the average duration on nHF lower than historical controls on nCPAP, but also the maximum-recorded duration of support on nHF is lower than nCPAP for the equivalent gestational age. However, the validity of this data has limitations because of difficulties associated with retrieving historical data.

One concern was the apparent increase in 2010 of babies from 28-30 weeks' gestation who appeared to be spending more time on nHF. However, an emphasis on ensuring that weaning protocols were followed appeared to improve the trend in 2011. One theory for this is that the babies looked so comfortable on nHF that staff (and parents) were reluctant to remove it! The data provides some reassurance that babies are generally spending less time overall on nHF than they did on nCPAP.

Parent and staff satisfaction

Parents are routinely surveyed about their views on the care provided in the NICU. As far as nHF is concerned, most parents see no other type of non-invasive respiratory support and have no comparisons to make. However, only positive comments have been received about nHF from parents whose babies received nCPAP as a result of transfer from or to other units that do not use nHF. Parents report that they like seeing their baby's face and expressions, seeing them move their heads and appearing comfortable on nHF. The nursing and medical staff were surveyed a year after the move from nCPAP to nHF and the results strongly indicated a preference for nHF. The junior medical staff were particularly in favour of ease of access to the head for ultrasound and head circumference measurements. The nursing staff liked the comfort for the baby and ease of set-up and use.

Conclusions, opportunities and suggestions

Using nHF as a replacement for nCPAP in the author's NICU over the past four years has led to the conclusion that this is a better way to achieve non-invasive ventilation for babies requiring respiratory support, either from birth or after extubation. It is not necessary or logical to use nHF as a step-down, as it can be used as a direct replacement for nCPAP. It is disappointing that there was no opportunity to draw on UK-based research to inform a decision to start using nHF and it is equally disappointing that the current Cochrane review contains only one study using 'low' high flow (1.8L/min) to draw a negative comparative conclusion against nCPAP[15].

There are still opportunities for neonatologists to participate in comparative clinical trials; different nHF systems still need to be evaluated, and clinicians need to study the evidence, then choose and use the modality properly. High flow for neonatal use needs definition and the usefulness of lower flows needs evaluating. Categories of nHF (4-8L/min), medium flow (>2-4L/min) and low flow (≤2L/min) might be useful.

High-quality healthcare is defined as being safe, having a positive clinical outcome and good patient experience[27]. The use of nHF at St Peter's combined with emerging evidence, demonstrates that clinical outcome and safety of nHF are, at least, equivalent to nCPAP and that the patient, parent and carer experience is better. Based on current understanding and experience, the author believes it is reasonable to conclude that, compared to nCPAP, nHF is a better-quality mode of non-invasive respiratory support for babies.

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