CHAMPION’S RESOURCE PACKAGE

High Flow Nasal Cannula (HFNC) Treatment Management for Viral Bronchiolitis - RCT
HFNC in Bronchiolitis

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Journal articles attached include:


Wing, R. et al - Use of High Flow Nasal Cannula Support in the Emergency Department reduces the need for intubation in Paediatric Acute Respiratory Insufficiency.

Schibler, A. et al - Reduced intubation rates for infants after introduction of high flow nasal prong oxygen delivery
Dear Nurse Champion

The Research team thank you in advance for becoming a champion for the High Flow Nasal Cannula randomised control trial (HFNC – RCT).

You and your fellow nursing and medical colleagues are part of a large multi-centre international trial in Australia and New Zealand that will provide results, which could change the clinical approach for the bronchiolitic infants presenting to your hospital, and many other hospitals both locally and internationally. Thus you are part of a very important study, which will influence the way in which infants with bronchiolitis will be clinically managed in the future.

This resource booklet will provide you with various information including but not limited to some background information on Oxygen therapy, effects of HFNC therapy on a babies work of breathing and some data following the pilot study at the Mater Children’s Hospital. Also attached are three recent journal articles that you may find as a useful resource.

As this project is a very large study we require your assistance as Champions, in the practical use of High Flow therapy and also ensure you have a greater understanding of the care of bronchiolitic infants and their needs to be a resource person for your colleagues in your department. This will include the bronchiolitic infant and their needs on either High Flow or low flow Oxygen therapy.

As a Champion, you will be provided with one-to-one education regarding the trial along with the AIRVO2 teaching. You will have this Champion booklet to refer to as your resource when teaching other nursing and/or medical staff about the trial. The research team will be liaising closely with you throughout the length of the study, in regards to the trial patients recruited, their documentation and care of these patients. Additionally we will require the emergency department Champion to record a
screening log book of other patients who are admitted with 'other respiratory illnesses'. Your feedback will be vital to us in order to move forward and improve processes within this study and to the other hospitals that will be recruiting patients.

We hope that you find this Champion Resource Package useful and ask that if you have any questions relating to any part of the study, that you contact one of the following study staff written below, via email or phone. We are always available to answer your questions and assist in any way we can to ensure the study is uncomplicated and easy to manage in your department.

Thank you for your ongoing support in this study and thank you in advance for your cooperation and dedication to this trial. It is greatly appreciated.

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HFNC in Bronchiolitis

Study Project

High Flow Nasal Cannula (HFNC) Treatment for Viral Bronchiolitis, a Randomised Control Trial to investigate if high flow oxygen therapy has a lower treatment failure rate in comparison to standard oxygen in both regional and tertiary centres.

Project Contact Details

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High Flow Nasal Cannula Study Coordinators (Central)

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DURATION OF THE STUDY

- September 2013 to December 2017
- Estimated number of patients: 1400 shared across 17 regional & tertiary centres

PARTICIPATING CENTRES

REGIONAL CENTRES

- Caboolture Hospital
- Gold Coast Hospital
- Logan Hospital
- Ipswich Hospital
- Nambour Hospital
- Redcliffe Hospital
- Redland Hospital
- Toowoomba Hospital
- The Tweed Hospital
- The Prince Charles Hospital

TERTIARY CENTRES

- Lady Cilento Children’s Hospital – Queensland
- Royal Children’s Hospital – Victoria
- Monash Health – Victoria
- Canberra Hospital – ACT
- Townsville Hospital – Queensland
- Starship Children’s Health – Auckland, New Zealand
- KidzFirst Middlemore Hospital – Auckland, New Zealand
Bronchiolitis is the leading cause of paediatric hospitalisation in Australia with approx. 10-15% of admissions requiring transfer to a paediatric intensive care unit (PICU) and subsequently at times requiring respiratory support. The aim of the study is to carry out a Randomised Controlled Trial (RCT) in order to prove that providing early introduction of high flow reduces the infant’s length of stay in hospital plus reduce or prevent the babies from deteriorating, which can lead to the need for mechanical respiratory support.

Bronchiolitis is a lower respiratory tract infection that occurs in infants and children less than 2 years of age. A virus, mainly Respiratory Syncytial Virus (RSV), usually causes it but other viruses can contribute to bronchiolitis namely adenovirus and human metapneumovirus. The virus causes inflammation of the small airways (bronchioles).

Viral bronchiolitis is the most common reason for non-elective admission to hospitals. There are currently 8-9000 admissions per year of bronchiolitis infants Australia-wide. Viral bronchiolitis is the most common reason for non-elective admission to PICU. There are 8-900 admissions per year to PICU of these infants. Of these bronchiolitis infants admitted to PICU, 35% receive non-invasive ventilation therapy and 28% invasive ventilation therapy Australia wide.

Currently in Queensland HFNC therapy is being used with great variety in its application in paediatrics within regional and tertiary centres and in various ways. Generally most centres believe they are using High Flow if the flow rate is > 2L/min (ranging from 0.5 to 2 L/kg/min). Some centres have a maximum flow rate of 8L/min. In general, all centres humidify and heat their HFNC circuits and most use blended Oxygen. This study aims also to standardise the use of HFNC and deliver best practice.
Infants have anatomical and physiological features that differ from the older child, teenager and adult. These include:

- Obligatory nose breathers easily obstructed with secretions
- High larynx which can cause increased resistance when breathing
- Ineffective use of accessory muscles (eg. Sternomastoid results in head bobbing rather than the increased chest expansion).

Why do infants rapidly get sick with a respiratory virus infection?

Infant’s ribs lie horizontally, which assists less with chest expansion. Physiologically, infants have very few type 1 muscles fibres (slow contraction muscle fibres) and hence fatigue more easily.

Infant’s bronchioles develop oedema, which causes them to narrow and close, and thus the infant finds it more difficult to breath.

Risk Groups include:

- Premature babies
- Infants younger than 6 months – lung and immune system not yet fully developed
- Underlying heart or chronic lung condition
- Contact with multiple children (child care centres)
- Exposure to cigarette smoke.
HFNC in Bronchiolitis

CURRENT TREATMENT BEING USED IN CENTRES

Currently there is no consistent treatment in managing bronchiolitis infants within Australia and around the world. Health professionals use various types of treatments, including HFNC and one or a collection of some of the following:

- Use of subnasal or mask Oxygen, nasopharyngeal, bubble and mask CPAP/BiPAP and invasive ventilation. More recently, HFNC therapy, in various forms, is taking over these other modes of treatment mentioned.

**AND/OR**

- **Bronchodilators** – can produce small shot-term improvements in clinical scores
- **Heliox therapy** – may significantly reduce a clinical score, no reduction in intubation rate, the need for mechanical ventilation, or in length of PICU stay
- **Nebulised 3% Saline** – may significantly reduce the length of hospital stay and improve the clinical severity score
- **Adrenaline** – some evidence to suggest that epinephrine may be favourable to salbutamol among outpatients
- **Steroids** – no evidence that infants with bronchiolitis benefit from use of steroids
- **Adrenaline and Steroids** – reduced hospital admission.

WHY USE BRONCHIOLITIS AS THE ILLNESS FOR THIS STUDY?

Bronchiolitis provides us with the ‘best playground for High Flow research’. The reasons are that bronchiolitis has a high economic burden with the highest number of non-elective PICU admissions (14.1%). There is a low mortality rate (~0) with this viral illness and the median length of stay is 3.37 days. It is a very homogenous population and includes a subgroup with well-defined risk factors such as prematurity and cardiac disease.
A randomised controlled trial (RCT) is a specific type of scientific experiment, and the gold standard for a clinical trial. RCTs are often used to test the efficacy or effectiveness of various types of medical intervention within a patient population. RCTs may also provide an opportunity to gather useful information about adverse effects.

The key distinguishing feature of the usual RCT is that study subjects, after assessment of eligibility and recruitment, but before the intervention to be studied begins, are randomly allocated to receive one or other of the alternative treatments under study. Random allocation in real trials is complex, but conceptually, the process is like tossing a coin. After randomisation, the two (or more) groups of subjects are followed in exactly the same way, and the only differences between the care they receive, for example, in terms of HFNC therapy or standard hospital Oxygen therapy for bronchiolitis infants (refers to low flow Oxygen humidified or not humidified), should be those intrinsic to the treatments being compared. The most important advantage of proper randomisation is that it minimizes allocation bias, balancing both known and unknown prognostic factors, in the assignment of treatments.

As there is limited research evidence that HFNC is effective this RCT will be able to test the efficacy of its used in infants with bronchiolitis. Using a power analysis, we are recruiting 1400 infants with bronchiolitis. A power analysis is a mathematical sum to ascertain how many infants should be recruited to the study to achieve adequate outcome variable numbers.
HFNC in Bronchiolitis

RANDOMISATION – WHEN AND WHO?

This is a large Randomised Control Trial (RCT) with specific criteria which includes:

1. Infants must be <12months (corrected age) and
2. Infants must have a clinical diagnosis of bronchiolitis and
3. Infants Oxygen saturations are <94% in room air on arrival into your emergency department.

In some instances an infant may not fully meet the criteria in the emergency department as their Oxygen saturations are >94% in room air, however they are still admitted to the ward for observation which may be related to a secondary illness at the time, for instance gastroenteritis or feeding problems. This infant could in fact meet the study criteria a few hours into their admission onto the ward or the next day in which case you can place them on the study and collect all the relevant documentation and equipment from the emergency department.

This large RCT is the first of its kind to be carried out in the world, and as such the study is attracting International interest as to the outcome of the results. We will be recruiting 1400 infants diagnosed with bronchiolitis meeting the above criteria, across 17 regional and tertiary hospitals across Australia and New Zealand. Ipswich Hospital and GCUH were both pilot hospitals for the study in 2013-2014. This provided the research team with relevant and good feedback from the staff to improve upon study materials and education and make alterations prior to expanding to the full 17 hospitals. We estimate that this study will run for 2-3 years.
What is Oxygen?

Oxygen is a commonly used therapy for hypoxemia in the management of bronchiolitis and other respiratory illness/disease in the paediatric population.

Oxygen is a drug, which should be administered with care at all times. If Oxygen is given in a too high quantity then Oxygen toxicity can occur, which can harm the lung, the brain and the heart. An example of how this knowledge has changed practice, is with newborns who are currently being resuscitated in room air due to the risks associated the adverse effects and toxicity of Oxygen.

The purpose of supplemental Oxygen is indicated to relieve the following:

2. Reduce myocardial stress due to hypoxemia that is the stress to the muscle tissue of the heart.

Signs and Symptoms of Hypoxemia

1. Confused, agitation
2. Hypertension
3. Tachypnoea
4. Cool, clammy skin
5. Tachycardia
6. Dyspnoea
7. Shallow and/or laboured breathing

Dangers of Oxygen include:

• Oxygen toxicity if exposure is high and prolonged
• Atelectasis (blockage of the bronchioles by mucus or by pressure on the outside of the lung, preventing normal Oxygen absorption to healthy tissues).
• Carbon dioxide retention causes respiratory drive depression
• Oxygen derived free radicals which is the end product of too much Oxygen causing cellular damage to the lungs.
ALVEOLI AND THEIR ROLE

The alveoli are found in the lung. The lungs contain about 300 million alveoli, each wrapped in a mesh of capillaries. The surface of an adult lung is equivalent to the size of a tennis court. The geometry of the alveoli is maintained by elastic lung tissue and surfactant. Surfactant is chemically similar to soap that we use for blowing bubbles. The alveoli are grouped together like a lot of interlinked caves, rather than existing as separate individual sacs. The alveoli have an innate tendency to collapse because of the bubble-like shape and high curvature – see Diagram 1.

The delicate alveoli membrane’s main function is to absorb Oxygen from the air and eliminate carbon dioxide. The alveolar membrane is the gas-exchange surface (the tennis court). Inhaled Oxygen from inspired air diffuses through the walls of the alveoli and adjacent capillaries into the red blood cells. The Oxygen is then carried by the blood to the body tissues. In the tissue, Oxygen is used for energy production. Carbon dioxide is produced as a waste product, which is transported back into the lung via the blood. It then diffuses across the capillary and alveolar walls into the air to be removed from the body with expiration.

The body employs many defences to protect the lungs, including small hairs (cilia) lining the trachea and bronchi supporting a constant stream of mucus out of the lungs, and reflex coughing and sneezing to dislodge mucus contaminated with dust particles or micro-organisms.

Viral Bronchiolitis is an acute inflammatory disease of the lower respiratory tract, resulting in obstruction of the small airways/alveoli. Hence they have signs of reduced alveolar surface (atelectasis) resulting in an Oxygen requirement and airway obstruction (wheezing).

When is additional increased Oxygen delivery required and what does the clinician need to know?

Reduced alveolar surface - If the alveoli surface is reduced, then an Oxygen requirement for the patient can occur. To fix this problem, we need to reverse the atelectasis and consolidation in the lung. Continuous Positive Airway Pressure or
HFNC in Bronchiolitis

CPAP as it is commonly referred to can perform this function and fix this problem (blowing up the lung).

**Improving Shunt Fraction** – Shunt Fraction is the percentage of blood put out by the heart that is bypassed functioning alveoli and not completely Oxygenated and can arise when there is atelectasis occurring. CPAP can fix this problem.

**Poor Ventilation Inhomogeneity** - Ventilation Inhomogeneity is when part of the lungs are less well ventilated than others or even blocked. CPAP can fix this problem.

**Swelling Alveolar-Capillary Membrane** – If the alveolar-capillary membrane is thickened due to inflammation and secretion, Oxygen diffuses less well and less Oxygen is taken up into the blood. This problem can be fixed by giving more Oxygen into the inspired air (increase FiO2).

**In Brief -> Response of CPAP vs Oxygen**

- Improving **Alveolar Surface**
- Improving **Shunt Fraction**
- Is a Function of **Ventilation Inhomogeneity**
- Is a Function of **Alveolar-Capillary Membrane**

**Diagram 1**

- terminal bronchiole
- bronchiole
- small bronchi
- main bronchi
- trachea
- bronchus
- alveolus
- capillaries
- branch of pulmonary artery
- branch of pulmonary vein
- distal respiratory area (gas exchange region)
High Flow Nasal Cannula (HFNC) Therapy is heated, humidified gas mixture that is delivered via the AIRVO2 or other devices. Some regional centres have previously used a blender/flow meter and humidifier set-up for the same purpose. Since the inspired gas is humidified and heated, there is less stress to the mucosa.

HFNC therapy is a continuous flow of gas that is able to supply the patient’s resting minute volume and reduce the work of breathing for the patient. It provides positive airway pressure at levels similar to those provided by CPAP. HFNC therapy allows flushing of the dead space of the nasopharyngeal cavity, which allows improved ventilation. The inspired Oxygen concentration can be titrated to the patient’s needs.

Research has demonstrated that the maximal inspiratory flow the healthy and well infant achieves during regular breathing; which for each breath is 0.8 L/kg/min. An unwell infant such as an infant with bronchiolitis, generates an inspiratory flow higher than this, which is 1.0-1.6L/kg/min. The aim of HFNC therapy is to match this maximal inspiratory flow generated by the infant, so no additional air is entrained around the nasal prongs. For this purpose a safety margin up to 2L/kg/min is given, to ensure adequate flow is provided for these infants.

Weight of larger babies and High Flow delivery rate - all High Flow patients will use the Airvo2 with a flow of 2 L/kg/minute, except in some of the larger babies. In some instances infants are greater in weight than the average infant for 0-12 months. In these cases a maximum flow of 25 L/min is to be used and not higher. This is based on using the infant’s ideal weight rather than actual weight as a measure of how to deliver the flow for the larger babies. All study patients will use the Fisher and Paykel green infant cannula’s which the Airvo2 will allow a flow of up to 25L only.
HFNC in Bronchiolitis

HEART RATE & RESPIRATORY RATE

If the HFNC therapy is applied and the patient is responding, we can expect that the heart rate and the respiratory rate will drop. Our own data has shown that the heart rate will drop approximately by 15 beats and the respiratory rate by 5-10 breaths per minute. This change is normally observed within the first 1 to 3 hours after commencement of HFNC therapy. If there is no change in HR and RR, it is likely that the infant is a non-responder, i.e. that this patient is likely to need higher level of care in an HDU or PICU. The graph below (Diagram 2) shows the change of HR and RR in over 250 infants. The open circles are the responders and the closed triangles the non-responders.

Diagram 2

Infants with Bronchiolitis: Respiratory and Heart Rates

HF_only
HF N

Heart rate per minute

Respiratory rate per minute

Time [min]
HFNC in Bronchiolitis

WORK OF BREATHING

When we breathe in and out at rest, the speed of air flow is less than if we were running/jogging. With exercise we would suck more air in at a faster rate as the air flow requirement is greater. This is the same in the sicker child who will suck more air in and out as the lungs are sicker with alveoli that are closed with mucous plugs. As all children have a different lung and body size, it is more convenient to describe the air flow used in L/kg/minute and not in absolute L/min. In the adult world this difference is not usually made and absolute numbers are considered whereas in children due to the differing size a more accurate definition of the inspiratory flow needs to be made (it is like medication that you give per kilogram).

Research has demonstrated that in a healthy child the maximal air flow required with each breath in and out is 0.8 L/kg/min (as mentioned previously). For a 10 kg child this would be 8L/kg/min needed in a healthy child. If we deliver more than this flow, we will start supporting the lung and we will reduce the work of breathing.

In a sick child who is being administered with 2L/min of subnasal Oxygen this is not enough air flow to reduce the work of breathing. The child will be trying to entrap the air around the nasal prongs from the atmosphere to meet the require 8L/min or more for a 10 Kg child. If the child is sick then 8L/min would not even meet the requirement to match their inspiratory air flow with each breath.

This is where the 2L/kg/min is required to ensure more air flow into the lungs to reduce the work of breathing and allow the alveoli to open up and provide better ventilation. Therefore this explains why increasing Oxygen does not reduce the work of breathing, but adequate high flow does.

Work of breathing and Oxygen saturations are two different variables and the flow of air is what will open the alveoli and reduce the work of breathing rather than Oxygenation.
For all bronchiolitic patients, regardless of CONTROL or HIGH FLOW, feeding and fluid management should occur according to standard hospital practice.

For all patients on HFNC therapy, it is mandatory that a nasogastric tube is inserted and continuous enteral feeding occurs. NGT position confirmation should occur as per local practice (x-ray, pH) and is mandatory.

Regular de-venting of the stomach through aspiration of the NGT needs to be performed every 4 hrs (minimum). With regards to oral feeding, infants should not be orally fed whilst on HFNC due to potential risk of aspiration.

At this point in time there is no clear evidence that suggests it is safe to give oral feeds to infants on HFNC therapy. There is no research that has demonstrated its safety, so for this study all infants on HFNC therapy will have continuous NGT feeds.

It is recommended that infants remain on full NGT feeds for the duration of the HFNC therapy. If an infant is starting to improve, it is allowed to feed orally under the condition that HFNC therapy is turned down to LOW FLOW at 2L/min flow and 100% FiO2 using the AIRVO2 for the duration of the feeds. After a maximum of 20 minutes, oral feeds/breast feed should be stopped and HFNC restarted at previous settings.

It is vital to note that all consumables provided with the High Flow study are for the HIGH FLOW study arm only. When a patient is recruited and enrolled on the CONTROL arm then this is normal standard hospital practice and management of the infant with bronchiolitis, and therefore these CONTROL arm patients must use hospital purchased consumables, which includes nasal prongs.
HFNC in Bronchiolitis

For those hospitals which humidify their low flow Oxygen patients, they must also use the hospital purchased stock. Fisher and Paykel will be auditing the stock flow provided against the number of HIGH FLOW patients enrolled into the study so it is important to adhere to this process, so the hospital does not get costed for items misused from the HIGH FLOW stock area. At the completion of the study the five AIRVO2’s provided to your hospital will remain with your hospital as your own equipment stock.

DATA COLLECTION

Data collection is vital to the success of the HFNC study. This information is what will ultimately demonstrate to the believers and the non-believers of High Flow Nasal Cannula therapy in infants with Bronchiolitis that it does work or does not work and we will be able to provide rationales for both arguments if this is the case.

The uptake of HFNC therapy in paediatrics outside a Paediatric Intensive Care Unit in Australia is sporadic. This is, in part, due to a lack of ‘best practice’. Similarly, many centres do not use the HFNC therapy for bronchiolitis as there are opposing reports about its benefit and a lack of consensus on how to use it. This study aims to perform a multi-centre trial and to assess which patients with bronchiolitis benefit using this therapy.

The study will provide information on how to use the High Flow therapy and what conditions we should use the High Flow therapy and also instruct us on ‘best practice’ for High Flow therapy. Therefore it is of high importance that ALL data requested on the Data Form in the Patient Booklet is collected. If information is incomplete the research team will then liaise with the Champions for your centre to recall the patients chart and assist us in collecting the relevant information.

Without the information the study will not be successful. It is vital that we obtain all data that is requested and require your help as Champions in your department to follow up on this. It can be the nurse and/or the medical officer who completes the Data Form.
Consent is both important and necessary for the success of the High Flow Nasal Cannula Trial. There are three consent forms in the Patient Booklet. Two of them require a parent/guardian signature which the medical officer will get. A Registered Nurse can also obtain this signature if comfortable to do so. One copy (as labelled) to be filed in the patient's medical notes and one copy to the parent/guardian as labelled. As the Champion can you please check that signatures of both the parent/guardian and also the staff member are completed where instructed in the Patient Booklet.

Nursing ratio should be provided as per standard practice in hospital and current skill mix. It is imperative that the nursing ratio is not increased because of the patient on HFNC therapy. It is very important to note that all study patients, whether they are in the CONTROL or HFNC arm, are staffed as per current hospital practice for all patients requiring regular Oxygen therapy.

High Flow patients are not to be staffed at a higher nurse/patient ratio just because they are on High Flow. When looking at allocating staff to these patients it is important to look at each patient requiring an Oxygen requirement, rather than on High Flow. If you normally staff a patient with a higher Oxygen requirement and greater nursing care and observation frequency on a smaller nurse/patient ratio, then continue this practice, however if the patient is on less Oxygen requirement and less nursing care is required, then staff accordingly. The majority of these patients will be a 1:4 ratio as the study is only changing the way in which Oxygen therapy is provided to these infants. A patient who is admitted to your ward on HFNC therapy does not necessarily demand greater nursing care than a patient admitted on low flow Oxygen therapy.
HFNC in Bronchiolitis
They both require observations at the same time, both require basic care including suctioning of the nares, nappy changing, bathing etc. The only difference is one is being provided with Oxygen via nasal prongs at a low flow (via wall Oxygen) and one is being provided Oxygen via nasal prongs at High Flow (via a simple machine). The other difference is that one is being fed via NGT (HFNC and Low Flow Oxygen at times), and there are some simple additional cares that apply for a NGT.

This outlines that there is really very little difference in the care of an infant on Low Flow Oxygen or HFNC therapy and the nurse/patient acuity should reflect this. **HFNC therapy patients do not demand higher nurse/patient ratios unless they have deteriorated and require escalation in their care.**
A troubleshooting guide is attached to each Study AIRVO 2 in your department.

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<tr>
<th>PROBLEM</th>
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| Incorrect L/minute on display screen for weight | • Work out correct L/kg/minute for specific patient weight (eg. 8 kg infant = 16 L/kg/min of flow with AIRVO2)  
• Press the ‘MODE’ button (side arrow button) twice (as the first press will give you humidification and the second press will give you L/minute).  
• Press the up and down arrows together for 5 seconds to release the lock.  
• Then increase or decrease the L/minute displayed using the up and down arrows.  
• Once reached correct L/minute, press the ‘MODE’ button again once for 1 second to lock. |
| Unable to increase Oxygen | • Check correct position of nasal prongs to ensure no occlusion exists, which includes secretions and/or positioning at nares.  
• Oxygen is manually increased using Oxygen flowmeter at wall (needs to be a 15 L/min flow meter and not less)  
• Actual Oxygen being delivered to the patient is shown on the display screen (eg. FiO2 of 30% may be 2 L/minute of flow at wall for a particular size of infant).  
• It’s important to observe the display screen FiO2 when increasing the Oxygen at the wall flow meter to achieve the FiO2 required to maintain SpO2. |
| Unable to decrease Oxygen | • Check correct position of nasal prongs to ensure no occlusion exists, which includes secretions and/or positioning at nares.  
• Decrease Oxygen at wall flowmeter whilst observing the display screen FiO2. With each small decrease on the wall you will see the FiO2 decrease on the display screen.  
• ROOM AIR = 21 % FiO2  
• FiO2 is Fraction of Inspired Oxygen |
| Machine alarming ‘Occlusion’ or ‘Blockage’ | • Check correct size of nasal prongs. Only green Optiflow nasal prongs for the High Flow study patients are to be used.  
• Check there are no kinks in the nasal cannula or circuit.  
• Check that the display screen shows a bird and butterfly, which represents ‘Junior Mode’ and if not, then AIRVO2 is in ‘Adult Mode’ and needs to be changed. To change to ‘Junior Mode’ hold the ‘Mode’ button (side arrow) down for 5 seconds until you see the bird and butterfly appear back on the screen. |
| Humidifier water level below maximum level (line allocated on chamber) | • Water is only required to cover the plate and does not have to reach the maximum line level allocated on the chamber.  
• There is a sensor floating ball in the chamber that prevents the humidifier from going dry (so long as there is a water bag attached with water in it). |
| Where does the AIRVO2 go once finished with its use? | • Return cleaned (wipe down with antibacterial wipes) and disinfected AIRVO2 to the paediatric ward. |
| Machine displays ‘Amber’ traffic light when switched on. Unsure if it can be used | • If ‘Amber’ traffic light is shown this means that the disinfection cycle has not been completed and needs to be done prior to using on a new patient.  
• A ‘Green’ traffic light indicates a disinfected and clean machine ready for a new patient. |
| How to disinfect AIRVO2 after use with patient? | • Remove all consumables using PPE from AIRVO2 and discard appropriately.  
• Attach red disinfection tubing (attached to the AIRVO2 pole) to machine.  
• Switch machine on  
• Machine will sense disinfection tubing and will automatically disinfect over a 55 minute period.  
• The display screen will show the time in minutes until completion. Once complete it will show a ‘tick’ symbol.  
• MUST switch machine off at on/off button prior to unplugging from wall otherwise it will alarm. |
<table>
<thead>
<tr>
<th></th>
<th>A baby recruited to the trial has a secondary diagnosis of gastroenteritis - can the baby be recruited or stay on the trial if the gastro started after admission?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>YES</strong></td>
</tr>
<tr>
<td></td>
<td>As the baby has a diagnosis of bronchiolitis, regardless of it being secondary to the gastroenteritis diagnosis.</td>
</tr>
<tr>
<td></td>
<td>A baby being recruited to the trial has also got Tracheomalacia - is the baby still eligible to be recruited?</td>
</tr>
<tr>
<td></td>
<td><strong>YES</strong></td>
</tr>
<tr>
<td></td>
<td>In the Exclusion Criteria “Upper Airway Obstruction” refers to babies with Croup and Anatomical upper airway malformations. An example of this exclusion criteria is Laryngomalacia. However, babies with Tracheomalacia and Bronchomalacia can be recruited to the Trial.</td>
</tr>
<tr>
<td></td>
<td>Bronchiolitis Vs Asthma in babies less than 12 months, should we include them into the trial?</td>
</tr>
<tr>
<td></td>
<td><strong>YES</strong></td>
</tr>
<tr>
<td></td>
<td>Differentiating bronchiolitis and early onset of asthma in the first year of life is difficult and some experts call any presentation similar to it a “reactive airway disease”, mainly defined by a response to a salbutamol trial, and rarely with a lung function test (except if this is available). Bronchiolitis and asthma is blurred in the first year of life, therefore again some experts state “do not diagnose asthma”, but experienced clinicians may detect already the first signs of a real asthma in the patient. In principle asthma as a pure diagnosis should not have an oxygen requirement in mild to moderate stage. This is somewhat a weak argument but never-the-less true. In all bronchiolitis trials there have been a good percentage of “reactive airways’ patients included and this is generally accepted as there is no clinical test to exclude them. A positive NPA will confirm to some extent the diagnosis of bronchiolitis.</td>
</tr>
<tr>
<td></td>
<td>Question</td>
</tr>
<tr>
<td>---</td>
<td>-------------------------------------------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>4</td>
<td>How do I give a Nebulizer to a baby on High Flow with the AIRVO2 machine?</td>
</tr>
<tr>
<td></td>
<td>For the duration of the nebulizer reduce the flow from the 2L/kg/min (i.e if a baby is 10kgs the baby will be on a flow of 20L/min) down to LOW FLOW at 2L/min. Do this by decreasing flow using AIRVO2 up and down arrows. Then increase the oxygen to 100% FIO2 by slowly increasing the wall flow meter and observing the AIRVO2 machine monitor screen for the FiO2 percentage increasing number to 100%. After the nebulizer is finished restart AIRVO2 at previous settings, changing both the L/min flow (i.e. back to 20L/min for a 10 kg baby) and decreasing the flow meter on the wall to meet the required FiO2 on the machine screen.</td>
</tr>
<tr>
<td>5</td>
<td>What colour nasal prongs can I use on the paediatric circuit?</td>
</tr>
<tr>
<td></td>
<td>The Paediatric Circuit is suitable for two sizes of nasal cannula, however for the purpose of the study you will use mostly Green and on rare occasions with smaller infants, the Purple nasal cannula. If you use purple nasal cannula then please document on the early warning tool form that you used the PURPLE cannula. Purple cannulas are used from the hospital stock presently until it is noted that there is a large volume used and a need for these cannulas in this study and for this population of infants.</td>
</tr>
<tr>
<td>6</td>
<td>Do I use corrected age or chronological age as 12 months?</td>
</tr>
<tr>
<td></td>
<td>Use only corrected age of infant when establishing if the patient meets inclusion criteria of less than 12 months of age. This means that if a baby is born at 32 weeks gestation (i.e. 8 weeks earlier than ‘planned’ birthdate), their corrected age is 8 weeks post their ‘actual’ birthdate.</td>
</tr>
<tr>
<td>7</td>
<td>How many times can the same patient be enrolled in the study?</td>
</tr>
<tr>
<td></td>
<td>A patient can have one enrolment per admission – if they are on the trial and weaned off CONTROL or HIGH FLOW but require further therapy, be that CONTROL or HIGH FLOW, always document the last time they came off CONTROL or HIGH FLOW in the data form. If the patient represents to the hospital again (and again) then they can be placed on the trial if they meet the inclusion criteria. New admissions require a new patient booklet and a new consent form to be completed.</td>
</tr>
<tr>
<td>Question</td>
<td>Answer</td>
</tr>
<tr>
<td>------------------------------------------------------------------------</td>
<td>------------------------------------------------------------------------</td>
</tr>
<tr>
<td>If the infant is weaned off FiO2 and then weaned off High Flow and then desaturates only when asleep with SpO2 ≥94% when awake; do we put the infant on High Flow only when asleep?</td>
<td>The infant needs to go back on High Flow immediately as per weaning protocol. This means the infant is on High Flow at both sleep and awake times. The infant may only required a flow of 2L/Kg/Min in room air (FiO2 21%). Aiming for sats between 94-98% if maintained for &gt;4hrs then turn High Flow off.</td>
</tr>
<tr>
<td>When High Flow is weaned and stopped, can we stop Nasogastric feeds and allow mum to breastfeed?</td>
<td>Yes.</td>
</tr>
<tr>
<td>When can I wean the infant’s FiO2 ((High Flow patient) or standard wall Oxygen (Control patient))?</td>
<td>When the infants SpO2 is stable between 94-98% you can then wean the patient’s oxygen. You do not need to wait until the SpO2 are at 98% - you can start to wean when the SpO2 are stable and ≥94%.</td>
</tr>
<tr>
<td>The baby has increased work of breathing however the saturations remain ≥94%? Can I commence on High Flow for the work of breathing?</td>
<td>No you cannot if you want to recruit this patient to the study. It is recognised that this is difficult for the medical and nursing staff to observe and not apply High Flow however this is the reason for the study taking place – to prove or disprove the effect and usefulness of High Flow against standard Oxygen therapy. The infant will have been working hard prior to presenting to the hospital whilst at home, and the infant will declare themselves by dropping their saturations at some point if this is going to occur. Admit the patient to the ward if you think this is what is needed and continue to observe and monitor SpO2.</td>
</tr>
</tbody>
</table>
High-flow nasal cannula oxygen therapy for infants with bronchiolitis: Pilot study

Sara Mayfield,1,2 Fiona Bogossian,2 Lee O’Malley1 and Andreas Schibler1,3

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Aim: To obtain data on the safety and clinical impact of managing infants with bronchiolitis on the ward with high-flow nasal cannula (HFNC) treatment.

Methods: A prospective pilot study was conducted of 61 infants aged <12 months with bronchiolitis and oxygen requirement presenting to the emergency department. HFNC was commenced at 2 L/kg/min, and fraction of inspired oxygen was titrated to oxygen saturation > 94%. A standard-treatment group (n = 33) managed with standard low-flow subnasal oxygen during the same time period was retrospectively identified.

Results: Admission demographics, heart rate (HR) and respiratory rate (RR) were similar in test and standard-treatment groups. Responders and non-responders to HFNC were identified within 60 min of treatment. Non-responders to HFNC requiring paediatric intensive care unit (PICU) admission showed no change in HR and RR, whereas responders showed decreases in HR and RR (P < 0.02). Patients receiving HFNC were four times less likely to need PICU admission than the standard treatment group (OR 4.086, 95%CI 1.0–8.2; P = 0.043). No adverse events such as pneumothorax, bradycardia, bradypnoea, emergency intubation or cardiopulmonary resuscitation were observed. No patients admitted to the PICU required intubation.

Conclusions: HFNC treatment in the paediatric ward is safe. Non-responders requiring PICU admission can be identified within the first hour of HFNC treatment by monitoring HR and RR. It is feasible to undertake a randomised controlled trial based on this pilot with the aim of decreasing PICU admissions.

Key words: bronchiolitis; high-flow nasal cannula; infant.

What is already known on this topic
1 High-flow nasal cannula (HFNC) treatment is in use throughout many neonatal, adult and paediatric intensive care units (ICUs).
2 It is thought to provide incidental continuous positive airway pressure and reduce intubation rates.
3 There is potential for its use outside the ICU environment.

What this paper adds
1 Evidence is presented to guide a larger randomised controlled trial for the safety and feasibility of HFNC treatment use in the paediatric ward environment for the management of bronchiolitis.
2 HFNC treatment on the ward is safe.
3 Non-responders to HFNC can be identified early.

Bronchiolitis in infants is the most common reason for non-elective hospital admissions. Within Australia it accounts for an estimated 8000–9000 admissions per year. In 2011 the Australian and New Zealand Paediatric Intensive Care Registry reported 858 admissions of bronchiolitis to paediatric intensive care units (PICUs), reflecting approximately 10% of all bronchiolitis hospital admissions.1 There is a general trend in bronchiolitis management towards reduced intubation and ventilation and an increased use of non-invasive ventilation (NIV).2 The latest addition to the respiratory management of bronchiolitis is the use of high-flow nasal cannula (HFNC) therapy. Studies in neonates and recently in infants have shown that HFNC therapy delivers inadvertent continuous positive airway pressure (CPAP)3 and improves work of breathing (WOB).4–8 Since the introduction of HFNC treatment, a significant reduction in the need for mechanical respiratory support other than HFNC has been demonstrated.9–11 The striking advantage and efficacy of HFNC may be based on its simple application and minimal interference with patient comfort. However, the uptake of HFNC treatment in pediatrics has been sporadic. This is, in part, due to a lack of guidelines on ‘best practice’.

For the purpose of gaining some clinical data on the safety and clinical impact of HFNC use in a regular paediatric ward, we performed a case control study in infants with bronchiolitis aged less than 12 months of age. Secondary outcomes of this pilot study were to demonstrate a proof of concept for a future...
randomised controlled trial (RCT) and to present data on the decreased prevalence of respiratory deterioration and requirement for PICU admission.

**Methods**

**Study design**

A prospective pilot study was conducted, investigating the use of HFNC treatment in a paediatric ward setting. The use of an RCT design for this study was denied by the institutional ethics board, as there are no convincing data yet available for safety of HFNC use in regular ward settings. Inclusion of case controls who were admitted during the same period was retrospectively allowed by the ethics board for the purpose of comparison. These patients received standard oxygen therapy and are referred to as the standard-treatment group.

**Study protocol**

Prior to the study, staff education on the protocol and equipment was implemented utilising a structured education plan. The plan targeted both medical and nursing staff in the emergency department (ED) and paediatric ward. ED staff education focused on recognition and identification of candidates meeting inclusion and exclusion criteria, adherence to study protocol, notification to study investigator, understanding correct selection and application of equipment, commencement of HFNC treatment and ongoing assessment of the patient. Ward staff education focused on ongoing respiratory care, adherence to the study protocol, and understanding and recognition of deteriorating and improving infants.

Patients were screened from July 2011 to May 2012 in the ED of Mater Children’s Hospital, Brisbane, Queensland, Australia, for the following inclusion criteria: age <12 months, clinical diagnosis of bronchiolitis and oxygen requirement (\(S_O_2 < 94\%\) in room air). Exclusion criteria were the following: craniofacial malformation, upper airway obstruction (stridor), and impending PICU admission based on severity of illness (impending intubation, NIV, low level of consciousness, apnoea) or transfer elsewhere. Informed consent to the study was obtained for all patients receiving HFNC treatment.

Patients for the standard-treatment group were identified retrospectively through chart review and included all infants with the same inclusion and exclusion criteria as the study patients who were admitted during the same time period to the same paediatric ward. Informed consent was waived for this group.

**HFNC intervention**

After consent was provided by the parents or guardians, the infants had the appropriate-sized nasal cannula applied, and flow was commenced through a circuit (RT329, BC3780 and BC2745; Fisher & Paykel Healthcare, Auckland, New Zealand) at 2 L/kg/min to a maximum of 10 L/min. Fraction of inspired oxygen (\(F_O_2\)) was titrated (Bird Air–Oxygen Blender, CareFusion, Yorba Linda, CA, USA) to maintain oxygen saturation between 94% and 98%, and the humidifier (Fisher & Paykel Healthcare MR850) was auto-set at 37°C. All other areas of nursing and medical management for bronchiolitis remained unchanged for the study purpose according to standard hospital protocol and consultant directive. Patients were transferred to the paediatric ward after commencement of HFNC treatment. Once \(F_O_2\) could be reduced to 0.21, and oxygen saturations remained at 94% or higher, flow was turned off. If \(S_O_2\) dropped below 94%, flow returned at the same rate. If \(S_O_2\) did not improve, then \(F_O_2\) was increased and titrated to achieve \(S_O_2\) of 94% or higher. This weaning procedure was repeated until the patient was able to remain off HFNC treatment.

**Measures**

Physiological parameters including heart rate (HR), respiratory rate (RR), \(S_O_2\), temperature and a respiratory score for WOB were documented (from no distress to severe distress in three levels). Observations were recorded on admission and at regular time points until discharge. Hospital length of stay (LOS) and length of treatment (LOT) of either HFNC treatment or low-flow subnasal oxygen treatment were measured. Demographic data and comorbidities such as prematurity, chromosomal abnormality and repaired/unrepaired cardiac anomaly were recorded. Serious adverse events, as a measure of safety, were defined as cardiopulmonary arrest, pneumothorax, bradypnoea, bradycardia, requirement for CPR or emergency intubation in the ward/ PICU. Criteria for admission to PICU were the following: requirement for escalation of care, including cases of \(S_O_2 < 92\%\) despite 2 L/min \(O_2\) in the control group or \(F_O_2 > 60\%\) in the HFNC group; inability to manage the patient on the ward (nursing); and deterioration in physiological parameters (persistent tachypnoea (>60 breaths/min) and tachycardia (>180 beats/min) ). PICU admission in such cases was discussed and determined between the paediatric consultant and PICU registrar/consultant after patient review.

**Statistical analysis**

Demographic and clinical data, the number of adverse events and the number of PICU admissions were compared between the HFNC and standard-treatment groups using Fisher’s exact test and the independent-samples t-test where appropriate. For the relationship between physiological data and time among the different groups, a generalised linear model (GLM) was used. To describe the change of physiological data over time, an ANOVA was performed for repeated measurements with Bonferroni correction was used (SPSS 15.0, SPSS Inc, Chicago, IL, USA). Data are presented as mean and 95% confidence interval (CI), and a P value < 0.05 was considered significant.

**Results**

A total of 1111 patients were screened in the ED between July 2011 and May 2012, and 61 patients were enrolled for HFNC treatment. Subsequently, 33 patients were identified retrospectively as meeting the inclusion criteria and included in the standard-treatment group (Fig. 1). There were no statistically significant differences in the demographic and physiological characteristics of patients in the HFNC and standard-treatment groups on admission (Table 1).
There were no serious adverse events observed during the study in either group, and importantly, no emergency procedures such as intubation and mechanical ventilation were required.

Overall, among the four patient groups, there was a significant difference in the change of HR over time ($P < 0.001$, GLM) from admission (Fig. 2). The HR in patients remaining in the paediatric ward for both HFNC and standard-treatment groups dropped significantly within the first 60 min (responders). In responders in the HFNC group, mean HR changed significantly within 60 min from 158 beats/min (95% CI 154–164) to 144 beats/min (95% CI 138–150), whereas the mean HR of the non-responders increased slightly from 159 beats/min (95% CI 144–173) to 162 beats/min (95% CI 152–171) ($P = 0.02$).

Table 1  Demographic and physiological characteristics of high-flow nasal cannula and standard-treatment groups at admission

<table>
<thead>
<tr>
<th></th>
<th>HFNC group ($n = 61$)</th>
<th>Standard-treatment group ($n = 33$)</th>
<th>$P$ value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male, $n (%)$</td>
<td>39 (64)</td>
<td>19 (58)</td>
<td>0.66</td>
</tr>
<tr>
<td>Female, $n (%)$</td>
<td>22 (36)</td>
<td>14 (42)</td>
<td>0.66</td>
</tr>
<tr>
<td>Age (days), mean (95% CI)</td>
<td>157 (128–187)</td>
<td>146 (104–188)</td>
<td>0.66</td>
</tr>
<tr>
<td>Weight (kg), mean (95% CI)</td>
<td>6.8 (6.1–7.5)</td>
<td>6.6 (5.6–7.7)</td>
<td>0.78</td>
</tr>
<tr>
<td>Ex-prematurity (&lt;37 weeks gestation), $n (%)$</td>
<td>19 (31)</td>
<td>6 (18)</td>
<td>0.23</td>
</tr>
<tr>
<td>Other comorbidity, $n (%)$</td>
<td>3 (5)</td>
<td>2 (6)</td>
<td>0.58</td>
</tr>
<tr>
<td>NPA-positive, $n (%)$</td>
<td>55 (95)</td>
<td>32 (97)</td>
<td>0.54</td>
</tr>
<tr>
<td>Heart rate (beats/min), mean (95% CI)</td>
<td>158 (153–163)</td>
<td>159 (152–166)</td>
<td>0.75</td>
</tr>
<tr>
<td>Respiratory rate (breaths/min), mean (95% CI)</td>
<td>54 (51–57)</td>
<td>53 (50–57)</td>
<td>0.78</td>
</tr>
<tr>
<td>$\text{S}_\text{O}_2$ (%), mean (95% CI)</td>
<td>89 (88–90)</td>
<td>90 (89–92)</td>
<td>0.17</td>
</tr>
<tr>
<td>Hospital length of stay (h), median (IQR)</td>
<td>92 (59–141)</td>
<td>92 (48–124)</td>
<td>0.60</td>
</tr>
<tr>
<td>Salbutamol therapy, $n (%)$</td>
<td>16 (26)</td>
<td>8 (24)</td>
<td>0.83</td>
</tr>
<tr>
<td>Steroid therapy, $n (%)$</td>
<td>7 (12)</td>
<td>4 (12)</td>
<td>0.93</td>
</tr>
<tr>
<td>Antibiotic therapy, $n (%)$</td>
<td>12 (20)</td>
<td>8 (24)</td>
<td>0.60</td>
</tr>
</tbody>
</table>

†Includes trisomy 21, repaired and unrepaired cardiac anomaly, and tracheomalacia. ‡Viruses including respiratory syncytial virus, influenza, rhinovirus, enterovirus, adenovirus and human metapneumovirus. Fisher’s exact test and independent-samples t-test have been used as appropriate. CI, confidence interval; HFNC, high-flow nasal cannula; NPA, nasopharyngeal aspirate.

There were no serious adverse events observed during the study in either group, and importantly, no emergency procedures such as intubation and mechanical ventilation were required.

Overall, among the four patient groups, there was a significant difference in the change of HR over time ($P < 0.001$, GLM) from admission (Fig. 2). The HR in patients remaining in the paediatric ward for both HFNC and standard-treatment groups dropped significantly within the first 60 min (responders). In patients requiring PICU admission, the HR remained unchanged and even increased after admission (non-responders). Responders to care could be identified by their HR dropping by 15 beats (or 15–20%) from their baseline at admission. In the responders in the HFNC group, mean HR changed significantly within 60 min from 158 beats/min (95% CI 154–164) to 144 beats/min (95% CI 138–150), whereas the mean HR of the non-responders increased slightly from 159 beats/min (95% CI 144–173) to 162 beats/min (95% CI 152–171) ($P = 0.02$).
Similar to the change in RR after admission, the RR decreased significantly between the groups over time ($P = 0.05$, GLM) (Fig. 3). The RR decreased significantly for both the HFNC and standard-treatment responders after admission. The RR of the HFNC non-responders remained high, but in the standard-treatment non-responders it decreased after admission. In the responders in the HFNC group, RR dropped from 54 breaths/min (95% CI 51–57) to 51 breaths/min (95% CI 48–54), with a difference of 5 breaths/min. For the non-responders, the RR decreased from 54 breaths/min (95% CI 48–60) to 56 breaths/min (95% CI 48–69) ($P = 0.07$) at 60 min. However, differences in RR became significant at 180 min ($P < 0.05$).

Fig. 2 Changes in heart rate (HR) in intervention and comparison groups after inclusion in the study. For both the standard-treatment responders and HFNC responders, the HR decreased significantly ($***P < 0.001, \text{ANOVA}$). HR remained high and did not change significantly for the patients requiring paediatric intensive care unit admission (HFNC and standard-treatment non-responders). Values are shown as mean and 95% CI.

Fig. 3 Changes in respiratory rate (RR) in intervention and comparison groups after inclusion in the study. For both the high-flow nasal cannula (HFNC) responders and standard-treatment responders, the RR decreased, but the decrease was significant only for the standard-treatment responders ($^*^*^*P < 0.05, \text{ANOVA}$). RR remained high in HFNC non-responders and decreased in the standard-treatment non-responders. Values are shown as mean and 95% CI.

Of the 61 patients in the HFNC group, 8 (13%) were admitted to the PICU (HFNC non-responders) compared with 53 (87%) who remained on the paediatric ward (HFNC responders). In the standard-treatment group, 10 patients (31%) required PICU admission (standard-treatment non-responders), and 23 (69%) remained on the paediatric ward (standard-treatment responders) (OR 4.086, 95% CI 1.0–8.2; $P = 0.043$). Between the responders and non-responders in both groups (HFNC and standard treatment) there were no physiological and demographic differences on admission (Table 2). Of those patients admitted to the PICU, one patient in the HFNC group and three in the standard-treatment group required a period of NIV. The remaining patients referred to the PICU received HFNC treatment only at 2 L/kg/min. No patients were intubated.

Hospital LOS was similar between the two groups ($P = 0.56$), with the median time being 92 h for both the HFNC and standard-treatment groups (95% CI 52–140). LOT was similar for patients admitted to the PICU and those who remained on the paediatric ward (standard-treatment group as well as the HFNC group ($P = 0.07$ and $P = 0.32$, respectively).

Discussion

The data from our study show that HFNC treatment can safely be used in a regular paediatric ward with a 1:4 nursing ratio, as no serious adverse event was observed. We determined that the safety of HFNC treatment can be monitored using clinical indicators such as HR and RR, providing a safe boundary for HFNC use in the ward. Responders and non-responders to HFNC treatment can be identified and described using HR and RR within 60 min of application. It is reasonable to anticipate that a future larger RCT may make similar findings of reduced PICU admission rates (4 times less likely) by following our protocol.

This pilot study was tested in a ‘real-world’ environment where standard care was not changed, only the oxygen delivery device. This approach allowed separation of oxygen delivery-specific aspects of the treatment and identification of responders and non-responders, which was important to demonstrate as a safety aspect of HFNC treatment. Infants responding to HFNC treatment showed decreased HR within the first hour of initiation. The RR also dropped in the responders, with a slight delay at 180 min. The non-responders to HFNC showed no change in HR and RR within the first 60 min of observation. Non-responders to HFNC may warrant medical review for potential PICU admission. A similar pattern was also observed in the standard-treatment group, in which responders and non-responders to standard treatment could be identified within 60 min. Interestingly, in the standard-treatment group the RR in the non-responders dropped within the first 60 min compared with the responders, but the differences were not statistically significant. This drop in RR may have been due to a mild degree of hypoxaemia or may be explainable by the low number of patients in the study. This concept of certain parameters differentiating responders from non-responders has been identified in other studies. One limitation of the study design is that the repeated measurement of HR and RR were robust descriptors but not necessarily predictors of response or non-response for both the intervention and comparison groups. Real predictors such as prematurity, heart disease and pre-existing...
Table 2  

<table>
<thead>
<tr>
<th></th>
<th>Value HFNC responders</th>
<th>P value</th>
<th>Value Standard-treatment responders (n = 23)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (days), mean (95% CI)</td>
<td>170 (70–270)</td>
<td>0.34</td>
<td>115 (111–206)</td>
<td>0.77</td>
</tr>
<tr>
<td>Weight (kg), mean (95% CI)</td>
<td>6.9 (4.8–9.0)</td>
<td>0.70</td>
<td>6.6 (5.7–7.8)</td>
<td>0.66</td>
</tr>
<tr>
<td>Ex-prematurity (&lt;37 weeks gestation), n (%)</td>
<td>1 (12)</td>
<td>0.26</td>
<td>0.08</td>
<td>0.77</td>
</tr>
<tr>
<td>Other comorbidity, (%)†</td>
<td>1 (12)</td>
<td>0.08</td>
<td>2 (4)</td>
<td>0.08</td>
</tr>
<tr>
<td>NPA-positive, (%)‡</td>
<td>7 (87)</td>
<td>0.47</td>
<td>43 (90)</td>
<td>0.47</td>
</tr>
<tr>
<td>Heart rate (beats/min), mean (95% CI)</td>
<td>159 (142–176)</td>
<td>0.98</td>
<td>157 (151–163)</td>
<td>0.75</td>
</tr>
<tr>
<td>Respiratory rate (breaths/min), mean (95% CI)</td>
<td>54 (47–61)</td>
<td>0.66</td>
<td>54 (45–50)</td>
<td>0.77</td>
</tr>
<tr>
<td>SPo2 (%), mean (95% CI)</td>
<td>88 (86–92)</td>
<td>0.39</td>
<td>89 (89–91)</td>
<td>0.17</td>
</tr>
<tr>
<td>Length of treatment (h), median (IQR)</td>
<td>7 (4.5–12)</td>
<td>0.07</td>
<td>7 (5–12)</td>
<td>0.32</td>
</tr>
</tbody>
</table>

†Includes trisomy 21, repaired and unrepaired cardiac anomaly, and tracheomalacia. ‡Viruses including respiratory syncytial virus, influenza, rhinovirus, enterovirus, adenovirus and human metapneumovirus. Independent-samples t-test has been used where appropriate. HFNC, high-flow nasal cannula; NPA, nasopharyngeal aspirate.

This experience is aligned with the trend towards use of early NIV in general. However, HFNC treatment did not shorten hospital LOS overall, and its associated physiological effect does not modulate the course of the underlying viral illness.

While hospital LOS was not shortened during the study, there are fiscal implications for reducing PICU admissions. The current cost for a 92-h combined PICU and ward admission in our hospital is estimated at A$15 517 per patient. The costs for the same patient on the paediatric ward are estimated at A$4992 per patient. It is predicted that the annual cost saving for our 19-bed PICU with 1400 admissions annually would be approximately A$1.2 million.

For a future RCT, the definition of high flow needs to be discussed. The original idea of delivering higher flow rates at >2 L/min originated from a need for better humidification of the delivered oxygen. In the past, this was achieved using higher flow rates. These higher flow rates created inadvertent CPAP. Previously published papers have explained some of the physiological effect of high flow with inadvertent CPAP. A study by Milesi et al. showed that flow rates of approximately 1.5–2 L/kg/min created a positive pharyngeal pressure during the entire respiratory cycle. Interestingly, a recent study by Mundel et al. in healthy adults has shown that during the inspiratory phase little or no positive pressure is delivered, and only during the expiratory phase is positive pressure observed. Further detailed physiological studies measuring changes on high flow, particularly of the intrathoracic pressures, are needed.

Generally, flow rates > 2 L/min subnasally in infants are regarded as high flows with a maximal limit of 8–10 L/min. This maximum of 10 L/min using our HFNC device was not based on any clinical or physiological rationale but solely on the decision of the device manufacturer. For this study, flow was titrated at 2 L/kg/min with a maximal flow of 10 L/min. In infants with a high RR, relatively high-flow rates are needed to match the maximal inspiratory flow of the patient. The choice of 2 L/kg/min is based on the fact that in the past with the older generation of continuous-bias-flow ventilators, the bias flow was set at 2 L/kg/min to match the high inspiratory flows.

Another finding was that we were able to wean the HFNC to room air (21% O2) before the HFNC was switched off, and no weaning of the flow rate was allowed. The oxygen in the control group was weaned from 2 L/min to off according to SaO2. This approach followed a shift in paradigm that considers that an early oxygen requirement can be treated with CPAP by recruiting previously collapsed lung regions. The weaning approach did not prolong the time of respiratory support or hospital LOS.
Limitations

This study may be criticised because of its non-randomised design. Our ethics review board denied us permission to perform a RCT and requested a pilot study investigating the safety of HFNC treatment first. After completion of the study, we were allowed to retrospectively analyse a case control group (standard oxygen therapy) of all infants with bronchiolitis who were admitted within the same time frame and fulfilled the inclusion criteria but were not enrolled in the study (due to the study investigator not being contacted). This group matched the study group in their demographic and physiological data on admission and were treated in the same paediatric ward using the same 1:4 nursing ratio and hospital bronchiolitis management protocol. The small number of patients in the study does not allow for a strong conclusion, and only a RCT will address the question of the effects of HFNC treatment in the ward environment.

Conclusion

This pilot study produced interesting results on the safety of HFNC treatment in a ward environment. It gives guidelines as to how a larger RCT may be conducted. Physiological parameters such as HR and RR correlate well with the response to treatment and hence potential PICU admission. With viral bronchiolitis being the most common reason for non-elective admissions to PICUs in Australia, using HFNC treatment in paediatric wards may result in substantial cost savings without impact on safety of patient care. It would be worthwhile to undertake a RCT and investigate the fiscal implications of reducing PICU admissions by utilising this treatment in the ward environment.

Acknowledgements

All phases of this study were supported by a Mater Children’s Hospital Golden Casket Grant (A$56,000), which supported the research nurse, and a Preston James Foundation Grant (A$60,000), which funded the nurse educator. Fisher & Paykel Health Care provided the HFNC circuits.

References

Use of High-Flow Nasal Cannula Support in the Emergency Department Reduces the Need for Intubation in Pediatric Acute Respiratory Insufficiency

Robyn Wing, MD, Catherine James, MD, Louise S. Maramda, PhD, and Carrie C. Arnshy, MD, MPH

Objectives: The objective of this study was to determine whether the use of heated, humidified, high-flow nasal cannula (HFNC) therapy is associated with a decreased need for intubation in patients presenting to a pediatric emergency department (PED) and admitted to a pediatric intensive care unit (PICU) with acute respiratory insufficiency (ARI).

Methods: A retrospective study of all patients admitted from the PED to the PICU with ARI from January 2006 through December 2009. Patients admitted before the availability of HFNC (cohort 1) were compared with those admitted after the availability of HFNC but before implementation of an institution-wide guideline on pediatric HFNC usage (cohort 2) and those admitted after the implementation of a pediatric HFNC usage guideline (cohort 3).

Results: After controlling for age, month of admission, type of respiratory illness, and severity of illness, there was an 83% reduction in the odds of intubation in the PED in cohort 3 compared with cohort 1 (odds ratio, 0.17; 95% confidence interval, 0.06-0.56; P < .0001). There was no significant change in mortality or median PICU length of stay after the introduction of HFNC.

Conclusions: High-flow nasal cannula used early in the development of pediatric ARI is associated with a decrease in the need for intubation and mechanical ventilation.

Key Words: humidified high-flow nasal cannula, acute respiratory insufficiency, acute respiratory failure, noninvasive ventilation, mechanical ventilation

(PEMC 2012;28: 1117-1123)

Respiratory illness accounts for more than 9 million visits to the emergency department (ED) annually in children aged 0 to 17 years, which accounts for 26% of all pediatric ED visits. Respiratory illness is also the leading reason for hospital admission among children and adolescents, accounting for nearly 1.5 million hospitalizations a year. With pneumonia, asthma, and bronchiolitis comprising nearly 11% of pediatric ED (PED) visits and 25% of pediatric admissions, the need for safe and effective treatment of acute respiratory insufficiency (ARI) and acute respiratory failure (ARF) in children is great. Traditional therapeutic options for ARI and ARF include endotracheal intubation with mechanical ventilation and noninvasive ventilation (NIV) with either continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BiPAP). Although mechanical ventilation through an endotracheal tube is a well-established and often life-saving procedure, it can be associated with many complications, including nosocomial pneumonia, ventilator-induced lung injury, airway injury from endotracheal tube placement, and complications from sedation. Noninvasive ventilation has proven to be a successful alternative in treating pediatric ARF but is often limited by patient compliance and tolerance. Heated, humidified, high-flow nasal cannula (HFNC) is a relatively new therapy for respiratory distress that allows the delivery of high-flow humidified gas via a nasal cannula. The flow of gas provided is able to fully supply a patient's resting minute ventilation. The optimal warm and humid condition achieved with HFNC enhance the liquefaction of secretions, improve mucociliary clearance, and inhibit inflammatory reactions and nasopulmonary bronchoconstriction reflexes triggered by cold and dry air. In addition, HFNC provides positive airway pressure at levels similar to those produced by nasal CPAP. Studies in newborns have demonstrated positive expiratory pressure created by HFNC in the range of 2 to 3 cm H₂O. A recent study in older children demonstrated that HFNC provided an average positive expiratory pressure of 40 ± 19.9 cm H₂O.

High-flow nasal cannula is proving to be a very comfortable and well-tolerated means of noninvasive ventilatory support. Experience of the use of HFNC in the adult population is limited, but has shown that it is better tolerated than face mask, reduces hypoxemia, and reduces respiratory rate. High-flow nasal cannula has also been shown to effectively decrease respiratory rate and overall work of breathing (WOB), increase oxygen saturation, and increase patient level of comfort in children. A retrospective study of infants with bronchiolitis admitted to the pediatric intensive care unit (PICU) demonstrated that the introduction of HFNC was associated with a 68% decrease in the need for intubation. No studies to date have evaluated the effects of HFNC use in infants or children with intubation rates in a more broad population of pediatric patients.

The goal of this retrospective study was to determine whether the use of HFNC was associated with a decreased need for endotracheal intubation and mechanical ventilation among infants and children with ARI presenting to a PED and subsequently admitted to a PICU.

METHODS

Study Design
We conducted a retrospective study of all patients presenting to the PED at the University of Massachusetts Children's Medical Center between January 2006 and December 2009 with ARI requiring admission to the PICU. This is a 160-bed urban tertiary care pediatric teaching hospital with approximately 28,000 PED visits annually. The PED is a separate section of the emergency department and is staffed by pediatric emergency medicine physicians. The PED sees all patients younger than 18 years who present to the ED. For the purposes of this study, we defined ARI as any acute respiratory illness severe enough to require PICU admission. Patients were excluded if they had a primary central nervous system cause of ARI, preexisting tracheostomy,
were on home NIV support, were intubated before arrival in our institution, or were not admitted through the PED because these patients were not potential candidates for HFNC therapy in the PED. Patients were divided into 3 cohorts based on the period during which they were admitted. Cohort 1 included patients admitted from January 2006 through December 2006, when HFNC was not yet available at our hospital. Cohort 2 included patients admitted from January 2007 through June 2008, after HFNC became available, but before implementation of a hospital-wide guideline on the use of HFNC in pediatric patients. During this period, HFNC was available in the PICU, but not readily available in the PED. Cohort 3 included patients admitted from July 2008 through December 2009, after the implementation of a hospital-wide guideline on the use of HFNC in pediatric patients. During this period, HFNC was readily available in both the PICU and the PED. There were no changes in other respiratory care policies or ICU admission, discharge, or intubation criteria during the study period. Data were collected by chart review and included patient age, sex, primary diagnosis, number of days of HFNC use, number of days of mechanical ventilation use, number of days of NIV (CPAP and BiPAP) use, location of initiation of advanced respiratory support, use of HFNC or NIV before or after intubation, PICU length of stay (LOS), PICU mortality, and Pediatric Risk of Mortality (PRISM III) scores. This study was conducted with appropriate oversight by the institutional review board.

HFNC SYSTEM AND GUIDELINE

The HFNC system used in our institution includes the Fisher & Paykel 855 humidifier and the Fisher & Paykel RT 329 Continuous Flow Circuit (for infant and pediatric patients) or the Fisher & Paykel RT 202 Continuous Flow Circuit (for adolescent and adult patients). The flow range of the RT 329 Infant/Pediatric Continuous Flow Circuit is from 2 to 10 L/min, and the flow range of the RT 202 Continuous Flow Circuit for adolescents/adults is from 5 to 50 L/min. Five different sizes of nasal cannulae are used with the system, including the infant cannula (maximum flow rate of 7 L/min), intermediate infant cannula (maximum flow rate of 7 L/min), pediatric cannula (maximum flow rate of 8 L/min), small adult cannula (maximum flow rate of 50 L/min), and large adult cannula (maximum flow rate of 50 L/min).

The HFNC system became available for use in our PICU beginning in January 2007. Over the period from January 2007 through June 2008, the equipment was not readily available in the PED, and the respiratory therapists, nurses, and physicians in the PED were not trained in its use. Therefore, HFNC use was largely limited to within the PICU, although there were occasions wherein HFNC was initiated in the emergency room, generally under the supervision of the pediatric intensivist. In July 2008, our institution implemented a formal guideline on the use of HFNC in pediatric patients (Appendix A), which was accompanied by an educational program for respiratory therapists, nurses, and physician staff in both the PICU and PED. The purposes of the guideline were to (1) extend use of HFNC to the PED, (2) provide guidelines on appropriate indications for HFNC use, (3) standardize the approach to initiating HFNC and adjusting the HFNC settings, and (4) provide instructions for proper setup and maintenance of the system. According to the guideline, indications for HFNC use include hypoxemia, increased WOB, inadequate mobilization of secretions, and poor compliance with oxygen therapy via mask. These indications are purposefully broad so as to have applicability to all respiratory illnesses. Although there were no quantitative data defined in the guideline, these indications were based on clinical assessment by the attending physician. Specific disease applications include bronchiolitis, congestive heart failure, pulmonary edema, pneumonia, pulmonary hypertension, interstitial lung disease, pulmonary fibrosis, asthma, cystic fibrosis, and pulmonary contusions.

Statistical Analysis

Comparisons between the 3 cohorts were carried out using analysis of variance for normally distributed variables, Kruskal-Wallis test for non-normally distributed variables, and $\chi^2$ test for proportions. The 3 study cohorts were compared together in 3-way comparisons, and where statistical significance was achieved, $P$ values associated with post hoc comparisons were adjusted using the Bonferroni method to account for multiple testing. Multivariable logistic regression was then performed to examine the association between the probability of intubation and study cohort, as a proxy of HFNC availability. The possible confounders accounted for in the logistic regression models included age, month of admission, type of respiratory illness, and PRISM III score. All data were analyzed with SPSS 19.0 statistical software (IBM, New York, NY).

RESULTS

There were 1246 admissions to the PICU for AKI/ARF during the study period (Fig. 1). Of these, 398 were excluded from the study: 240 had a primary central nervous system cause of AKI or ARF, 77 had preexisting tracheostomy or were on home NIV support, 46 were intubated before arrival at our hospital, and the remaining 442 were included in the study.

![FIGURE 1. Flow diagram of selection of the 3 study cohort populations.](image-url)
and 33 were not admitted via the PED. Eight hundred forty-eight patients were included in the study. One hundred ninety admissions were during the period from January 2006 through December 2006 (cohort 1). 289 admissions were during the period from January 2007 through June 2008 (cohort 2), and 369 admissions were during the period from July 2008 through December 2009 (cohort 3). Although the raw numbers of patients per month do differ among the cohorts, there was no statistical difference in the number of patients per month between the 3 cohorts (cohort 1 = 15.82 [95% confidence interval [CI], 9.18–22.49], cohort 2 = 16.86 [95% CI, 11.84–20.77], and cohort 3 = 20.59 [95% CI, 16.46–24.54]). The age, sex, admission type, primary diagnosis, and PRISM III scores were similar between the 3 cohort groups (Table 1).

Table 2 shows HFNC and mechanical ventilation utilization rates in the 3 cohorts. As expected, HFNC use in the PED increased dramatically following the introduction of the guideline. In the pre-guideline era (cohort 2), only 8% of ARI/ARF patients received HFNC support in the PED, compared with 19% in the post-guideline era (cohort 3, \(P < 0.0001\)). High-flow nasal cannula use also increased in the PICU, although to a lesser extent, from 18% to 23% (\(P = 0.06\)). A device utilization ratio measures the proportion of total patient-days in which the device was used. Overall, the HFNC utilization ratio nearly doubled from 0.19 in the pre-guideline era (cohort 2) to 0.35 in the post-guideline era (cohort 3, \(P < 0.0001\)).

An HFNC trial was considered "successful" if the patient did not require endotracheal intubation or NIV during their illness. The success rate of HFNC was similar before and after the implementation of the HFNC guideline, with 84% successful uses in the pre-guideline era (cohort 2) and 88% successful uses in the post-guideline era (cohort 3, \(P = 0.46\)).

### TABLE 1. Baseline Characteristics of the 3 Cohort Groups

<table>
<thead>
<tr>
<th></th>
<th>Cohort 1: HFNC Not Available</th>
<th>Cohort 2: Pre–HFNC Guideline</th>
<th>Cohort 3: Post–HFNC Guideline</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age, mean (SD), y</strong></td>
<td>4.6 (5.2)</td>
<td>4.1 (5.0)</td>
<td>4.8 (5.2)</td>
<td>0.16</td>
</tr>
<tr>
<td><strong>Female sex, n (%)</strong></td>
<td>85 (45)</td>
<td>135 (47)</td>
<td>145 (49)</td>
<td>0.14</td>
</tr>
<tr>
<td><strong>Primary diagnosis, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma/RAD</td>
<td>87 (46)</td>
<td>99 (34)</td>
<td>172 (47)</td>
<td></td>
</tr>
<tr>
<td>Bronchiolitis</td>
<td>43 (23)</td>
<td>77 (27)</td>
<td>84 (23)</td>
<td></td>
</tr>
<tr>
<td>Pneumonia</td>
<td>35 (18)</td>
<td>64 (22)</td>
<td>60 (16)</td>
<td>0.14</td>
</tr>
<tr>
<td>Croup</td>
<td>5 (3)</td>
<td>11 (4)</td>
<td>10 (3)</td>
<td></td>
</tr>
<tr>
<td>Other respiratory illness</td>
<td>20 (10)</td>
<td>38 (13)</td>
<td>43 (12)</td>
<td></td>
</tr>
<tr>
<td><strong>PRISM III score, median (range)</strong></td>
<td>0 (0–35)</td>
<td>0 (0–27)</td>
<td>0 (0–18)</td>
<td>0.29</td>
</tr>
</tbody>
</table>

Diagnoses included in the “other” category were pulmonary edema, pulmonary hemorrhage, pulmonary contusion, pneumothorax, acute chest syndrome, acute respiratory distress syndrome, and sepsis.

RAD indicates reactive airway disease.

### TABLE 2. Respiratory Care Utilization and Outcome Data

<table>
<thead>
<tr>
<th></th>
<th>Cohort 1: HFNC Not Available</th>
<th>Cohort 2: Pre–HFNC Guideline</th>
<th>Cohort 3: Post–HFNC Guideline</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total patient ICU days</strong></td>
<td>795</td>
<td>1164</td>
<td>1145</td>
<td></td>
</tr>
<tr>
<td><strong>HFNC utilization</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HFNC started in PED, n (%)</td>
<td>0</td>
<td>22 (8)</td>
<td>69 (19)</td>
<td>(P &lt; 0.0001)</td>
</tr>
<tr>
<td>HFNC started in PICU, n (%)</td>
<td>0</td>
<td>51 (18)</td>
<td>86 (23)</td>
<td>(P = 0.08)</td>
</tr>
<tr>
<td>Total HFNC use, n (%)</td>
<td>0</td>
<td>73 (25)</td>
<td>155 (42)</td>
<td>(P &lt; 0.0001)</td>
</tr>
<tr>
<td>Total HFNC days</td>
<td>0</td>
<td>223</td>
<td>395</td>
<td>N/A</td>
</tr>
<tr>
<td>HFNC utilization ratio (HFNC days/total patient-days)</td>
<td>0.19</td>
<td>0.35</td>
<td>(P &lt; 0.0001)</td>
<td></td>
</tr>
<tr>
<td><strong>Mechanical ventilation utilization</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intubations in PED, n (%)</td>
<td>20 (11)</td>
<td>30 (10)</td>
<td>8 (2)</td>
<td>(P &lt; 0.0001)</td>
</tr>
<tr>
<td>Intubations in PICU, n (%)</td>
<td>10 (5)</td>
<td>15 (5)</td>
<td>22 (6)</td>
<td>(P = 0.90)</td>
</tr>
<tr>
<td>Total intubations, n (%)</td>
<td>30 (16)</td>
<td>45 (16)</td>
<td>30 (8)</td>
<td>(P = 0.005)</td>
</tr>
<tr>
<td>Total ventilator days</td>
<td>325</td>
<td>361</td>
<td>244</td>
<td>N/A</td>
</tr>
<tr>
<td>Ventilator utilization ratio (ventilator-days/total patient-days)</td>
<td>0.41</td>
<td>0.32</td>
<td>0.21</td>
<td>(P &lt; 0.0001)</td>
</tr>
<tr>
<td>PICU LOS, median (range), d</td>
<td>2 (1–65)</td>
<td>2 (1–68)</td>
<td>2 (1–39)</td>
<td>(P = 0.24)</td>
</tr>
<tr>
<td>Mortality, %</td>
<td>0</td>
<td>0.4</td>
<td>1.4</td>
<td>(P = 0.13)</td>
</tr>
</tbody>
</table>

*To be compared with Bonferroni-adjusted \(P = 0.017\).

N/A indicates not applicable; VAP, ventilator-associated pneumonia.
TABLE 3. Intubation Rate Comparison by Type of Respiratory Illness

<table>
<thead>
<tr>
<th>Type of respiratory illness</th>
<th>Cohort 1: HFNC Not Available</th>
<th>Cohort 2: Pre-HFNC Policy</th>
<th>Cohort 3: Post-HFNC Policy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 190</td>
<td>n = 289</td>
<td>n = 369</td>
</tr>
<tr>
<td>HFNC Use</td>
<td>Intubation Rate</td>
<td>HFNC Use</td>
<td>Intubation Rate</td>
</tr>
<tr>
<td>Asthma</td>
<td>87</td>
<td>0%</td>
<td>99</td>
</tr>
<tr>
<td>Bronchiolitis</td>
<td>43</td>
<td>0%</td>
<td>77</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>35</td>
<td>0%</td>
<td>58</td>
</tr>
<tr>
<td>Croup</td>
<td>5</td>
<td>0%</td>
<td>11</td>
</tr>
<tr>
<td>Other</td>
<td>17</td>
<td>0%</td>
<td>33</td>
</tr>
</tbody>
</table>

*To be compared with Bonferroni-adjusted P = 0.017.

The overall intubation rate in the period before availability of HFNC (cohort 1) was 16%. There was no significant change in the intubation rate during the period when HFNC was available, but there was no guideline for its use and availability in the PED was limited (cohort 2). Although the mechanical ventilator utilization ratio also decreased slightly during this period from 0.41 to 0.22 (P < 0.0001). In the period following the implementation of the HFNC guideline (cohort 3), the intubation rate decreased to 8% (P = 0.0006). This represents a 50% relative risk reduction and 8% absolute risk reduction from the pre-HFNC period, yielding a number needed to treat of 13. The decrease in the intubation rate was accounted for largely by a reduction in the number of intubations performed in the PED, where the intubation rate fell from 11% to 2%. The intubation rate within the PICU did not change significantly during the study period. Overall, mechanical ventilator utilization decreased by nearly half from 0.41 in the pre-HFNC era (cohort 1) to 0.21 in the post-guideline period (cohort 3, P < 0.0001).

Following the implementation of the HFNC guideline, the decreased need for intubation was observed across most ARI diagnoses (Table 3), with the exception of croup. However, these values did not reach statistical significance. Pediatric intensive care unit LOS and mortality rate were not significantly different in the 3 cohorts. In addition, mean duration of mechanical ventilation was similar among the cohort groups (10.8 ± 11.9 days in cohort 1, 8.0 ± 6.5 days in cohort 2, P = 0.19, and 8.1 ± 8.1 days in cohort 3; P = 0.31).

The results of the logistic regression analysis are shown in Table 4. After adjusting for other confounding variables (age, month of admission, type of respiratory illness, and PRISM III score), there was an 83% decrease in the odds of intubation in the PED, comparing cohort 3 to cohort 1 (P = 0.001). The overall odds of intubation (either in the PED or PICU) decreased by 28% (P = 0.02).

To examine whether the timing of initiation of HFNC made a difference in patient outcomes, we examined the intubation rate among patients who had HFNC started in the PED compared with those for whom HFNC was started in the PICU. Of patients who had HFNC started in the ED, shortly after presentation, 7.6% required intubation, whereas the intubation rate of patients for whom HFNC was initiated in the PICU, hours or days after presentation, was 18.1% (P = 0.047).

A possible concern is that the use of HFNC may delay intubation in children who truly need it and that this might contribute to longer ventilation courses and ICU stays for children who fail HFNC. To address this concern, we examined the duration of mechanical ventilation and PICU LOS among patients who failed HFNC. In our study population, 75 patients were intubated without receiving a trial of HFNC, and 30 were intubated after failing a trial of HFNC. Mean duration of mechanical ventilation and PICU LOS were similar whether the patient received HFNC before intubation or not (Table 5).

DISCUSSION

In this retrospective study, we demonstrate that the use of HFNC is associated with a decrease in the need for intubation and a decrease in mechanical ventilator utilization in children presenting to the emergency department and subsequently admitted to the PICU with ARI. To our knowledge, this is the first study that demonstrates the benefit of HFNC use in the PED in a broad spectrum of patients ages and diagnoses.

TABLE 4. Odds of Intubation After HFNC Implementation

<table>
<thead>
<tr>
<th></th>
<th>Cohort 2: Pre-HFNC Guideline</th>
<th>Cohort 3: Post-HFNC Guideline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Odds of intubation in ED</td>
<td>0.98 (0.39–2.45)</td>
<td>0.17 (0.06–0.50)</td>
</tr>
<tr>
<td>OR, adjusted (95% CI)</td>
<td>P = 0.97</td>
<td>P = 0.001</td>
</tr>
<tr>
<td>Odds of intubation in PICU</td>
<td>0.76 (0.28–2.06)</td>
<td>0.98 (0.40–2.45)</td>
</tr>
<tr>
<td>OR, adjusted (95% CI)</td>
<td>P = 0.59</td>
<td>P = 0.97</td>
</tr>
<tr>
<td>Overall odds of intubation</td>
<td>0.81 (0.38–1.74)</td>
<td>0.42 (0.20–0.89)</td>
</tr>
<tr>
<td>OR, adjusted (95% CI)</td>
<td>P = 0.59</td>
<td>P = 0.02</td>
</tr>
</tbody>
</table>

Presented ORs were determined comparing each cohort to cohort 1. Possible confounders adjusted for included age, month of admission, type of respiratory illness, and PRISM III score.

OR indicates odds ratio.
TABLE 5. Outcome Measures in Intubated Patients

<table>
<thead>
<tr>
<th>Patients Intubated Without</th>
<th>Patients Intubated After Failing Trial of HFNC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trial of HFNC</td>
<td></td>
</tr>
<tr>
<td>n = 75</td>
<td>n = 30</td>
</tr>
<tr>
<td>Mean duration of mechanical ventilation (SD)</td>
<td></td>
</tr>
<tr>
<td>9.2 (9.4)</td>
<td>8.0 (7.3)</td>
</tr>
<tr>
<td>P = 0.51</td>
<td></td>
</tr>
<tr>
<td>PICU LOS, median (range)</td>
<td></td>
</tr>
<tr>
<td>5 (1-65)</td>
<td>9 (2-68)</td>
</tr>
<tr>
<td>P = 0.76</td>
<td></td>
</tr>
</tbody>
</table>

In this study, the increasing use of HFNC was associated with lower intubation rates for patients admitted with asthma, bronchiolitis, and other respiratory illnesses (diagnoses included in the “other” category were pulmonary edema, pulmonary hemorrhage, pulmonary contusion, pneumomediastinum, acute chest syndrome, acute respiratory distress syndrome, and anaphylaxis). The intubation rate of patients with those diagnoses did not appear to be affected; however, only 1 patient with group required intubation during the study period. Further research is warranted to further elucidate the effectiveness of HFNC in various disease states.

The implementation of an institution-wide guideline with an accompanying educational program and greater availability of equipment proved to be an important part of the success of HFNC at our institution. Following the implementation of the guideline, HFNC use increased dramatically, and intubation rates concomitantly decreased. The overall reduction in intubation rates observed in this study was accounted for almost entirely by reduced need for intubation in the PED, whereas the intubation rate within the PICU did not change over the study period despite increased use of HFNC. In addition, the intubation rate of patients where HFNC was initiated in the PED, shortly after presentation, was 7.6% versus the intubation rate of patients where HFNC was initiated in the PICU, hours or days after presentation, was 18.5%. This suggests that for HFNC to be successful, it may be best to initiate HFNC early in the disease processes to best prevent the need for mechanical ventilation. It is interesting to note that the success rate of HFNC was similar before and after implementation of the HFNC guideline. Therefore, the decrease in intubation rates following implementation of the guideline seems to be due to the increased frequency of use of HFNC particularly early on in the disease processes, rather than the acquired skill of using this new modality of respiratory support.

One potential barrier to the use of HFNC could be the notion that it may increase PICU LOS or delay the initiation of endotracheal intubation and mechanical ventilation for patients with ARI, so that patients are then mechanically ventilated for a longer period or have a higher risk of mortality. Our study found no difference in PICU LOS, mortality rate, or mean duration of mechanical ventilation among the 3 cohorts.

The finding that mechanical ventilator utilization decreased by nearly 50% during this study period has important implications for the cost associated with hospitalization for ARI. The cost of mechanical ventilator support is substantial, and these are additional costs associated with the provision of sedation, which is generally required for intubated patients, as well as costs for the treatment of ventilator-related complications. In contrast, HFNC is a less expensive modality, is less labor intensive for the respiratory therapist, does not require sedation, and is likely associated with fewer complications.

Patients tolerated HFNC quite well. Although other forms of NIV (BiPAP and CPAP) are technically difficult to use in children because of poor mask fitting, inadequate ventilation due to leaks, eye irritation, and nasal dryness due to high flow, we found that HFNC was generally well accepted and tolerated by patients. Of the 226 patients treated with HFNC during the study period, there was only 1 potential major complication attributed to HFNC use (complication rate = 0.4%). This occurred in an infant admitted for treatment of pneumonia who developed bilateral pneumomediastins within several hours of intubation of HFNC. This complication occurred during period 2, before the implementation of our HFNC guideline and education efforts for all respiratory staff, which, we hypothesize, may have led to placement of improperly fit cannula.

STUDY LIMITATIONS

This study has the limitations of a descriptive retrospective study. We attempted to control for severity of illness using the PRISM III score; however, this is a relatively insensitive marker of the severity of respiratory illness. Unfortunately, there is no universal severity-of-illness score for the variety of illnesses included in our comprehensive study. Laboratory data, such as blood gas measurements, are not obtained in all ARI patients presenting to the PED and admitted to the PICU. The lack of objective data to calculate severity of illness limits the strength of our study. A prospective study in which the severity of respiratory compromise could be quantified through careful measurement of oxygen saturations, respiratory rate, and WOB may provide more information. Although the admission rates in all 3 cohorts do not significantly differ and the 3 cohorts are homogeneous, as evidenced in Table 1, there were clearly more PICU admissions during cohort 3. The increase in PICU patients in cohort 3 was likely accounted for by the summer 2009 H1N1 epidemic rather than the increasing use of HFNC. Although HFNC use does not necessitate admission to the PICU at our institution, the patients with respiratory illness severe enough to warrant use of HFNC would have been admitted to the PICU in the pre-HFNC cohort era. There was no change in staffing of the PED during this study. The decision to admit the PICU has always been based on severity of illness. Furthermore, regardless of the PICU admission rate, the mechanical ventilation utilization rate, which accounts for total PICU patient-days, decreased in both cohorts 2 and 3.

CONCLUSIONS

We conclude that HFNC use early is the development of pediatric ARI is associated with a decreased need for endotracheal intubation and mechanical ventilation.

REFERENCES


APPENDIX A: UNIVERSITY OF MASSACHUSETTS HNFCL GUIDELINE

Guideline Name: High-Flow Nasal Cannula Guideline for Pediatrics

Purpose
To provide guidelines for the application and management of patients utilizing the Fisher & Paykel high-flow, high-humidity nasal canula.

Statement
The Fisher & Paykel S50 humidifier, in addition to the F&P adult or infant/pediatric continuous-flow single-limb heated circuit, allows delivery of high-flow saturated gas (44 mg H2O) at body temperature (37°C) via a nasal cannula. The combination of increased flow capabilities and 100% relative humidity at body temperature allows treatment of a broad range of indications that potentially can result in mucusolytic therapies (i.e., CPAP, BiPAP, or ventilation). The high-flow system may be used in both ED and ICU patients.

Optimal humidity maintains the mucociliary transport system and consistency of secretions. This will result in:
- liquefying of secretions
- improved mucociliary clearance
- reduction in risk of airway occlusions/improved airway patency
- reduction in lung infections as a result of increased clearance of pathogens

Relative high flows will be well tolerated at optimal humidity levels and will result in:
- decreased laryngitis
- reduction in WOB and energy consumption
- reduction of rebreathed deadspace
- improved deadspace tidal volume ratios

Indications:
- hypoxemia
- increased WOB
- inadequate mobilization of secretions
- poor compliance with oxygen therapy via mask

Disease Applications (Not Limited to):
- Respiratory syncytial virus
- Congestive heart failure/pulmonary edema
- pneumonia
- bronchiolitis
- pulmonary hyperinfection
- interstitial lung disease
- pulmonary fibrosis
- asthma
- cystic fibrosis
- pulmonary contusion

Benefits:
- neonatal, pediatric, and adult applications
- flow rate of 0.3 to 50 L/min controlled by external source
- optimal humidity (atmospheric pressure
- vapor phase humidity versus water particles minimizes particle-borne infection
- improved comfort and compliance

Potential Complications:
- pneumothorax
- gastric insufflation
- eye irritation (from misplaced cannula)

Cannula Flow Ranges
- infant—maximum flow rate 7 L/min
- intermediate infant—maximum flow rate 7 L/min
- pediatric—maximum flow rate 8 L/min
- small adult—maximum flow rate 50 L/min
- large adult—maximum flow rate 50 L/min

Infant/Pediatric Application
The flow range of the RT 329 Infant/Pediatric Continuous Flow Circuit is from 2 to 10 L/min. Maximum flow possible is 8 L/min using the pediatric cannula (BC3750) and pediatric flowmeter. Note: The size of the nasal cannula selected, which is determined by fit, will dictate the size of the circuit used and the maximum amount of flow that the patient may receive. Specific maximum flow capabilities will be based on the limitation size cannula used (i.e., infant, intermediate infant, pediatric, or small/large adult).

Proper cannula fit will allow excess flow to escape. Note: Never completely occlude the nose when selecting cannula size.
**Equipment for Infant/Pediatric High Flow**

- Fisher & Paykel S80 Humidifier on the appropriate stand
- Temperature probe and pigtail
- Fisher & Paykel RT 329 Continuous Flow Circuit
- Nasal interface (infant 7 L/min, intermediate infant 7 L/min or Pediatric 8 L/min)
- 500-mL water bag for inhalation
- Pressure relief valve
- Oxygen connecting tubing
- Blender with standard flow outlet
- Flotec Flowmeter (0-8 L/min)

**Setup**

1. Slide the humidification chamber onto the humidifier base. Remove the blue caps.
2. Hang the water bag. Unwind the water feed set and spike the water bag. The bag should be at least 20 inches above the chamber. Ensure that the water feed set is not kinked and that water is present in the chamber.
3. Connect blue circuit to one side of the humidification chamber. Do not use the extension piece (incubator extension) included in the bag with the circuit.
4. Connect the pressure relief with the adapter to the other side of the humidification chamber.
5. Connect one end of the oxygen connecting tube to the pressure relief adapter.
6. Connect the other end of the oxygen connecting tube to the outlet of the flowmeter attached to the blender via the nipple adapter.
7. Set the flowmeter at the desired flow rate.
8. Turn the humidifier on, and let it warm up to temperature on the invasive mode (≥37°C). Once it is warm, place the appropriate-size cannula in the patient’s nose. There are 3 pediatric cannula available: infant (provides flow rates up to 7 L/min), intermediate infant (provides flow rates up to 7 L/min), and pediatric (provides flow rates up to 8 L/min).
9. The blender settings and flow rate provided to the patient will vary depending on the needs of the patient. Do not set flow rate for less than 2 L/min on infant/pediatric size cannulas.

**Setting Recommendations for Infant/Pediatric/Adult Application**

The system may be used for any of the above listed indications. The blender setting and the flow rate will depend on the severity of the patient’s distress and illness. Patients with an abnormal chest film (pneumonia or bronchiolitis) may benefit from the use of higher flows. Refer to the blender settings and oxygen flow rate to decrease the patient’s WOB and achieve the desired saturation.

- Set blender at 100%.
- Increase the flow in 0.5- to 1-L increments until desired O2 saturation and a decreased WOB are observed. (Further increase in flow rate may not be necessary once these 2 goals are achieved.) Do not exceed the maximum limit for the cannula size selected.
- Monitor patient’s respiratory rate, WOB, O2 saturations, arterial blood gases.
- Decrease FiO2 as tolerated according to above criteria.
- When patient goals are achieved, flows may also be decreased in 0.5- to 1-L increments as tolerated. The patient may be switched back to traditional O2 delivery once the FiO2 is reduced to 40% or less, and the liter flow is reduced to 2 to 4 L in infants/children using infant/pediatric cannulas and to 10 to 15 L in adults/adolescents using adult cannulas.

**Equipment for Adolescent/Adult High Flow**

- Fisher & Paykel S80 Humidifier on the appropriate stand
- Temperature probe and pigtail
- Fisher & Paykel RT 203 Continuous Flow Circuit
- Nasal interface (small or large)
- 500-mL water bag for inhalation
- Oxygen connecting tubing
- Blender with standard adult high-flow outlets
- Flotec Flowmeter (0-40 L/min)

**Setup**

1. Slide the humidification chamber onto the humidifier base. Remove the blue caps.
2. Hang the water bag. Unwind the water feed set and spike the water bag. The bag should be at least 20 inches above the chamber. Ensure that the water feed set is not kinked and that water is present in the chamber.
3. Connect the blue circuit to one side of the humidification chamber.
4. Connect the oxygen connecting tube to the other side of the humidification chamber.
5. Connect one end of the oxygen connecting tube to the adapter on the humidifier.
6. Connect the other end of the oxygen connecting tube to the outlet of the flowmeter via the nipple adapter.
7. Set the flowmeter at the desired flow rate.
8. Turn the humidifier on, and let it warm up to temperature on the invasive mode (≥37°C). Once it is warm, place the appropriate-size cannula in the patient’s nose.
9. The blender setting and the flow rate provided to the patient will vary depending on the needs of the patient.

**Adult/Adolescent Application**

The flow range of the RT 202 Continuous Flow Circuit for adolescents/adolescents is from 5 to 50 L/min. Maximum flow possible is 40 L/min limited by the adult flowmeter. Specific maximum flow capabilities will be based on the limitation of cannula used.

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**Daily Maintenance**

The patient circuit and humidifier will be changed every 7 days according to manufacturer recommendations. The circuit will be changed sooner if visibly soiled.
Reduced intubation rates for infants after introduction of high-flow nasal prong oxygen delivery

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Abstract Purpose: To describe the change in ventilatory practice in a tertiary paediatric intensive care unit (PICU) in the 5-year period after the introduction of high-flow nasal prong (HFNP) therapy in infants <24 months of age. Additionally, to identify the patient subgroups on HFNP requiring escalation of therapy to either other non-invasive or invasive ventilation, and to identify any adverse events associated with HFNP therapy. Methods: The study was a retrospective chart review of infants <24 months of age admitted to our PICU for HFNP therapy. Data was also extracted from both the local database and the Australian New Zealand paediatric intensive care (ANZPIC) registry for all infants admitted with bronchiolitis. Results: Between January 2005 and December 2009, a total of 298 infants <24 months of age received HFNP therapy. Overall, 36 infants (12%) required escalation to invasive ventilation. In the subgroup with a primary diagnosis of viral bronchiolitis (n = 181, 56%), only 6 (4%) required escalation to invasive ventilation. The rate of intubation in infants with viral bronchiolitis reduced from 37% to 7% over the observation period corresponding with an increase in the use of HFNP therapy. No adverse events were identified with the use of HFNP therapy. Conclusion: HFNP therapy has dramatically changed ventilatory practice in infants <24 months of age in our institution, and appears to reduce the need for intubation in infants with viral bronchiolitis.

Keywords high-flow nasal cannula · Oxygen delivery · Infant

Introduction

Respiratory distress and hypoxaemia in infants are treated with various forms of non-invasive respiratory therapy [1]. In addition to oxygen therapy, continuous positive airway pressure (CPAP) is used to reduce the work of breathing and improve functional residual capacity, since regional atelectasis of the lung is a common feature in infants breathing near their closing volume [2, 3]. CPAP can be delivered via nasopharyngeal tube or face mask and generated by a water column (bubble CPAP) or a dedicated CPAP driver [4, 5]. Recently high-flow nasal prong (HFNP) therapy has been introduced to provide respiratory support in preterm and term infants [6–8]. HFNP therapy has many possible advantages over other forms of oxygen therapy: the inspired gas mixture can be heated and humidified to reduce damage to the upper airway mucosa; the inspired oxygen concentration can be titrated to the patient’s need; mechanically, it is better tolerated by the patient; and potentially, CPAP can be delivered [9–12]. Studies in neonates have shown that the amount of CPAP delivered by HFNP depends on the flow

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(relative to the size of the patient) and on the leak around the nasal cannula [13]. Most studies of HFNP therapy have been performed in neonates, and little clinical experience is reported in older children [6].

HFNP therapy was introduced in our paediatric intensive care unit (PICU) in 2005 and a subsequent significant change has been observed in the care of infants with respiratory distress with a suspected reduction in invasive ventilation. This retrospective analysis aimed to describe; our 5-year institutional experience of HFNP therapy in infants <24 months of age; the subgroups of patients requiring HFNP; the need for escalation of respiratory support from HFNP to other forms of non-invasive or invasive ventilation; the incidence of complications associated with HFNP therapy; our ventilatory practice in comparison with the subgroup of infants with bronchiolitis in all other PICUs in Australia and New Zealand.

Methods

Study design

The study was a retrospective analysis of all infants admitted to the PICU and treated with HFNP therapy between 2005 and 2009. Demographic and physiological real-time data were extracted from the unit's clinical information system (CIS). Informed consent from parents or guardians was waived by the local ethics committee.

Setting

The PICU is a 19-bed tertiary mixed surgical/cardiac/medical unit with approximately 1,100 admissions per year.

Definition of patient disease groups

The database was queried for all infants <24 months of age who were treated with HFNP therapy within their first 24 h of admission to the PICU. These infants were allocated to six disease groups using the Australian New Zealand Paediatric Intensive Care (ANZPIC) registry coding criteria [14]: clinically defined viral bronchiolitis with or without a positive test for respiratory syncytial virus (RSV), adenovirus, metapneumovirus or influenza (BRONCH); lung disease without peripheral airway obstruction (LDO); upper airway obstruction (UAO); neuromuscular conditions (NM); cardiac conditions (CARDIAC); and other (OTHER). Within the BRONCH disease group, preexisting risk factors such as prematurity, or underlying cardiac or neurological disorders were also identified. Criteria for admission to the PICU for respiratory distress is an oxygen requirement of more than 2 l/min and the need for respiratory support additional to supplemental oxygen.

Definition of respiratory support subgroups

Infants within each disease group were then divided into respiratory support subgroups, as follows: HFNP only (HF), HFNP followed by other non-invasive ventilation (HF + N), HFNP followed by other non-invasive, followed by invasive ventilation (HF + N + I), or HFNP followed by invasive ventilation (HF + I).

HFNP system

A humidified high-flow system was used with a low-resistance paediatric nasal cannula (BC3780 and RT3229, Fisher & Paykel Healthcare, Auckland, New Zealand). The inspired oxygen concentration was titrated to achieve pulse oximeter oxygen saturations (SpO₂) of >94%. The flow rate used was generally set at 6 l/min at the beginning of the HFNP treatment and then weaned at the discretion of the attending consultant, most commonly down to 4 l/min. Failure of HFNP therapy was defined as the need for escalation of therapy to either non-invasive ventilation with a face mask, or invasive ventilation with an endotracheal tube delivered by the ventilator (Evita XL; Draeger, Lubeck, Germany). Discontinuation of HFNP therapy was based on reduced oxygen requirement (generally inspired oxygen fraction <0.4), and clinical improvement in the work of breathing, respiratory rate (RR) and heart rate (HR).

Patient parameters

Body weight, age at admission, length of stay (LOS), and paediatric index of mortality risk of death (PIM2 ROD) score were recorded [15]. Additionally, LOS and intubation rate of all infants with viral bronchiolitis admitted to all PICUs in Australia and New Zealand were extracted from the most recent ANZPIC data registry and compared to our dataset [16].

Continuous physiological variables

Ventilatory parameters and physiological variables, such as HR, RR, SpO₂, inspired oxygen fraction (FiO₂, value when initially started on HFNP therapy) and SpO₂/FiO₂ ratio were downloaded every 30 min. Data were extracted from 4 h prior to initiation of HFNP therapy and continued for 24 h. All data were extracted from the unit's CIS (Critical Care Manager; PICIS, Wakefield, MA). Data were either automatically downloaded from monitors and validated or manually entered by the bedside nurse.
Table 1  Disease groups and respiratory support mode

<table>
<thead>
<tr>
<th>Group</th>
<th>HF</th>
<th>HF + N</th>
<th>HF + N + I</th>
<th>HF + I</th>
<th>All HF</th>
</tr>
</thead>
<tbody>
<tr>
<td>BRONCH</td>
<td>129</td>
<td>41</td>
<td>4</td>
<td>2</td>
<td>167</td>
</tr>
<tr>
<td>LD</td>
<td>55</td>
<td>9</td>
<td>4</td>
<td>4</td>
<td>72</td>
</tr>
<tr>
<td>UAO</td>
<td>6</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>8</td>
</tr>
<tr>
<td>NM</td>
<td>8</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>10</td>
</tr>
<tr>
<td>CARDIAC</td>
<td>11</td>
<td>1</td>
<td>0</td>
<td>12</td>
<td>24</td>
</tr>
<tr>
<td>OTHER</td>
<td>6</td>
<td>4</td>
<td>1</td>
<td>6</td>
<td>17</td>
</tr>
<tr>
<td>Total</td>
<td>206</td>
<td>56</td>
<td>10</td>
<td>26</td>
<td>298</td>
</tr>
</tbody>
</table>

Adverse outcomes

A system for prospectively coding complications is included in the CIS. These fields and the clinical notes were screened for adverse events such as cardiac and respiratory arrest, pneumothorax, gastric distension and mucosal injury due to cannula position. The number of failed HFNP treatments in respect of the need for other non-invasive and invasive ventilation was recorded.

Comparison with ANZPIC registry

To investigate the change in ventilator practice over time in our unit, case records were extracted from the local ICU database for all children admitted during the study period with bronchiolitis. In addition, case records were extracted from the ANZPIC Registry [14] for patients with bronchiolitis admitted during 2008. Intubation rate and LOS in our unit in 2009 were compared to the ANZPIC Registry patients in 2008.

Statistical analysis

Study groups, including the ANZPIC dataset, were compared using Fisher’s exact test for categorical variables and variables presented as percentages. Wilcoxon’s rank-sum test was used to compare admission parameters and LOS. Data are presented as medians and interquartile ranges unless otherwise stated. To determine whether there was an impact of underlying disease or time since initiation of treatment on the change in the physiological variables, a linear mixed model was used. HR, RR, SpO2, and SpO2/FiO2 ratio were used as dependent variables, patient group and HFNP therapy sequence as factors, and time as a covariate.

Results

Between January 2005 and December 2009 a total of 298 infants received HFNP therapy in our PICU. Table 1 presents the distribution by disease group and respiratory support mode. Overall, 36 (19%) infants receiving HFNP therapy needed escalation to other non-invasive and 36 (12%) to invasive ventilation. Of the infants with a primary diagnosis of viral bronchiolitis, only 6 (4%) required escalation to invasive ventilation. There was a significantly greater incidence of invasive ventilation in the CARDIAC (n = 12, 50%) and OTHER (n = 7, 41%) groups compared with the BRONCH (n = 6, 45%) and LD (n = 8, 12%) groups (p < 0.05). Most of the cardiac infants needed intubation for a cardiac surgical procedure or cardiac failure.

Table 2 shows the admission parameters and LOS of infants with viral bronchiolitis only. Significant differences were found between the HF group and the infants requiring escalation to other non-invasive ventilation for PIM2 ROD score, admission FiO2 and LOS (p < 0.01). There were no differences found between the therapy groups in terms of age. Although PIM2 ROD score and LOS were higher in the HF + N + I and HF + I groups compared to the HF group, statistical comparison was not applicable due to the low number of infants in each group.

Table 3 shows the increased use of HFNP therapy in our PICU for viral bronchiolitis over the study period. In comparison to Table 1, all patients intubated at admission were included. In 2005, 52 infants were admitted with only 7 infants receiving HFNP therapy, whereas in 2009, 44 of 67 infants with bronchiolitis were started on HFNP therapy.
Table 3: Infants with viral bronchiolitis listed by year

<table>
<thead>
<tr>
<th>Year</th>
<th>Total BRONCHI</th>
<th>HF and HF + N</th>
<th>Total intubated</th>
</tr>
</thead>
<tbody>
<tr>
<td>2005</td>
<td>52</td>
<td>7 (13%)</td>
<td>19 (37%)</td>
</tr>
<tr>
<td>2006</td>
<td>72</td>
<td>32 (44%)</td>
<td>21 (29%)</td>
</tr>
<tr>
<td>2007</td>
<td>49</td>
<td>23 (46%)</td>
<td>15 (31%)</td>
</tr>
<tr>
<td>2008</td>
<td>90</td>
<td>56 (62%)</td>
<td>12 (13%)</td>
</tr>
<tr>
<td>2009</td>
<td>67</td>
<td>44 (66%)</td>
<td>5 (7%)</td>
</tr>
<tr>
<td>Total</td>
<td>330</td>
<td>161 (49%)</td>
<td>72 (22%)</td>
</tr>
</tbody>
</table>

therapy and only 5 (7%) required intubation and ventilation. The overall intubation rate in our unit dropped from 37% in 2005 to 7% in 2009 whereas, in 2008, the ANZPIC data registry reported an overall intubation rate of 28%.

The median LOS in the 2008 ANZPIC registry for bronchiolitis infants was 2.42 days compared with 2.53 in our study ($p = ns$).

Table 4 shows admission parameters for infants with LD. There were significant differences between the HF and HF + N groups with lower PIM2 ROD score and FiO₂ and shorter LOS ($p < 0.001$) in the HF group. Statistical comparison for the HF + N and HF + N + I groups was not applicable due to low numbers.

Analysis of continuous physiological variables

In all infants there was a significant reduction in RR and HR after initiation of HFNP therapy ($p < 0.001$). There was a significant interaction between disease group and HR and RR as well as between HFNP therapy and HR and RR (mixed linear model, $p < 0.001$). The patients with viral bronchiolitis had the greatest change in HR and RR after initiation of HFNP therapy (Figs. 1 and 2). After 90 min the mean RR and mean HR had both decreased by more than 20% of the baseline (mean decrease in RR was 7.0 breaths/min, 95% CI 4.2–9.8, $p < 0.05$, and mean decrease in HR was 13 beats/min, 95% CI 9.25–16.75, $p < 0.05$) in the HF group whereas in the HF + N group similar rapid decreases in RR and HR could not be demonstrated (mean decrease in RR was 5.0 breaths/min, 95% CI 0–10, and mean decrease in HR was 6 beats/min, 95% CI 0.6–11.4). There was no significant interaction between HFNP therapy and SpO₂ or SpO₂/FiO₂ ratio.

Adverse effects

There were two in-hospital respiratory arrests and one in-hospital cardiac arrest identified in the database. All three of which occurred before admission to the PICU and before start of HFNP. No pneumothorax, gastric or abdominal distension or mucosal injuries were identified.

Table 4: Admission parameters for infants with lung disease (medians and interquartile ranges)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HF (n = 55)</th>
<th>HF + N (n = 9)</th>
<th>HF + N + I (n = 4)</th>
<th>HF + I (n = 4)</th>
<th>All HF (n = 72)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PIM2 ROD score (%)</td>
<td>0.83</td>
<td>3.61</td>
<td>3.23</td>
<td>1.77</td>
<td>0.81</td>
</tr>
<tr>
<td>FiO₂</td>
<td>0.39–1.06*</td>
<td>1.14–4.42*</td>
<td>2.41–7.34</td>
<td>0.61–6.58</td>
<td>0.75–1.22</td>
</tr>
<tr>
<td>LOS (days)</td>
<td>0.5</td>
<td>0.6</td>
<td>0.55</td>
<td>0.55</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>0.4–0.6*</td>
<td>0.6–0.8*</td>
<td>0.51–0.60</td>
<td>0.50–0.63</td>
<td>0.4–0.6</td>
</tr>
<tr>
<td></td>
<td>1.42</td>
<td>7.83</td>
<td>25.56</td>
<td>11.46</td>
<td>1.83</td>
</tr>
<tr>
<td></td>
<td>0.88–2.69*</td>
<td>5.42–16.46*</td>
<td>20.09–42.02</td>
<td>9.68–14.88</td>
<td>0.69–4.31</td>
</tr>
</tbody>
</table>

* $p < 0.001$ & $p < 0.01$

Discussion

In this retrospective analysis we showed that since the introduction of HFNP therapy in our PICU, the need for intubation and mechanical ventilation in infants with viral bronchiolitis decreased significantly over the 5-year period, from 37% in 2005 to 7% in 2009. A similar reduction in intubation rate for bronchiolitis patients has also been reported in a retrospective study by McKiernan et al. [6]. They reported a reduction from 23% to 6%, but did not report whether non-invasive ventilation with a face mask was used in their unit. This reduction reported in our unit is unlikely to be explained by an overall improved standard of care across time, as the ANZPIC registry data for 2008 still reported a comparatively higher ventilation rate for infants with bronchiolitis in a PICU [16]. As with any retrospective analysis, it is always difficult to demonstrate a cause and effect relationship, but there are some important findings in our retrospective analysis that may have been related to the reduced intubation rate.

The most common reason for non-elective admission to a PICU in Australia is viral bronchiolitis which imposes a significant financial burden on the hospital [16]. In our retrospective analysis, infants with viral bronchiolitis comprised the largest proportion of infants receiving HFNP therapy, followed by infants with lung disease. Similar to respiratory care of the preterm infant in the NICU [8], there has been an increasing trend toward the use of non-invasive ventilation in the PICU in order to reduce the risks associated with invasive ventilation. In our 5-year observation period, the proportion of infants...
Fig. 1 HR in infants with viral bronchiolitis 90 min before and 6 h after the start of HFNP therapy. HR decreased significantly in the HF group (linear mixed model, \( p < 0.001 \)). Successfully treated infants in the HF group showed a significantly lower HR 90 min after the start of HFNP therapy than those in the HF + N group (\( p < 0.05 \)). The data are presented as means and 95% CI.

Fig. 2 RR of infants with viral bronchiolitis 90 min before and 6 h after the start of HFNP therapy. RR decreased significantly in the HF group (linear mixed model, \( p < 0.001 \)). Successfully treated infants in the HF group showed a significantly lower RR 90 min after start of HFNP therapy than those of the HF + N group (\( p < 0.05 \)). The data are presented as means and 95% CI.

with viral bronchiolitis treated with HFNP increased from 13% to 66%, while those requiring intubation decreased proportionately. The admission criteria did not change during this observational study. Our standard admission practice was that infants with respiratory distress and an increased oxygen requirement of >2 L/min were reviewed by a PICU consultant or senior registrar either in the emergency department, paediatric ward or during retrieval from a referring hospital. Infants were only admitted to the PICU if respiratory support additional to supplemental oxygen was considered necessary.

Escalation of therapy to other non-invasive ventilation occurred in one-quarter of infants with bronchiolitis as the first 24 h of admission. The mean HR and mean RR discriminated between responders and non-responders to HFNP therapy. Responders showed a 20% decrease in RR and HR within 90 min of the start of HFNP therapy, whereas non-responders showed little change in RR and HR. Infants who required escalation of treatment to other non-invasive ventilation had a higher PIM2 ROD score and \( \text{FiO}_2 \) when HFNP therapy was started on admission.

Did the introduction of HFNP lead to longer LOS? The median LOS for all infants with bronchiolitis in our unit was no different from that reported in the ANZPIC registry data for 2008 [16]. With the increased experience, indications for HFNP were broadened and HFNP therapy was initiated in infants with causes of respiratory distress other than viral bronchiolitis. Infants with LD who needed escalation to other non-invasive ventilation were generally sicker on admission, demonstrating a higher PIM2 ROD score and \( \text{FiO}_2 \) and had a longer LOS. In infants with cardiac disease the intubation rate was 50% within the first 24 h of admission suggesting that HFNP therapy was not as effective in this population of infants. This was due to the fact that these infants were intubated for a cardiac procedure or severe cardiac failure.

This study was limited to a single institution without a control group, and clinical practice changed over the study period. A multicentre randomized controlled trial comparing HFNP therapy with standard care is needed to assess and prove the efficacy of HFNP therapy.

In conclusion, HFNP therapy provided efficient respiratory support and oxygen delivery in infants with respiratory distress in our PICU, and its introduction coincided with a significant reduction in the need for intubation of infants with viral bronchiolitis. Further research is required to establish safety and efficacy of HFNP definitively.

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References