Serious Air Leak Syndrome Complicating High-Flow Nasal Cannula Therapy: A Report of 3 Cases

abstract

Despite the absence of clinical safety data, heated, humidified high-flow nasal cannula (HHFNC) therapy is increasingly being used as an alternative to positive-pressure ventilation in pediatrics. This use of HHFNC is “off label” because the US Food and Drug Administration’s approval for these devices was only for air humidification and not as a modality to provide positive distending pressure. For the first time we describe 3 cases who developed serious air leaks related to HHFNC therapy. The first child was a previously healthy 2-month-old male infant with respiratory syncytial virus bronchiolitis who developed a right pneumothorax on day 5 of his illness at 8 liters per minute (lpm). He subsequently required intubation and ventilation for 14 days. The second case involved an otherwise healthy 16-year-old boy with cerebral palsy who developed pneumomediastinum and died of its complications. He was receiving 20 lpm HHFNC therapy when he developed pneumomediastinum. The third case involved a 22-month-old, previously healthy boy who developed subdural hematoma secondary to abuse. He developed a right pneumothorax while receiving HHFNC at a flow of 6 lpm, requiring chest tube placement. These cases emphasize the need for extreme caution while using HHFNC for the off-label indication of providing positive distending pressure in children, especially at flows higher than the patient’s minute ventilation. A more detailed study to specifically look at the serious adverse events related to HHFNC is urgently needed. Pediatrics 2013;131:e1–e6

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KEY WORDS
respiration, artificial, ventilators, mechanical, pneumothorax, adverse effects, oxygen inhalation therapy, high-flow nasal cannula, child

ABBREVIATIONS
CPAP—continuous positive airway pressure
HFNC—high-flow nasal cannula
HHFNC—heated, humidified high-flow nasal cannula
ICP—intracranial pressure
PPV—positive-pressure ventilation

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High-flow therapy is defined as oxygen therapy at flow rates greater than patient inspiratory flows at various minute volumes. The terms high-flow nasal cannula (HFNC), heated, humidified high-flow nasal cannula (HHFNC), and high-flow therapy are often interchangeably used. High flow without heated humidification is uncomfortable and poorly tolerated. The introduction of HHFNC in the early 1990s allowed optimal humidification of inspired gas at high flows, which was not possible before. Since then, different versions of HHFNC devices have become commercially available, and HHFNC is increasingly being used as a substitute for continuous positive airway pressure (CPAP) or positive-pressure ventilation (PPV) across all ages. This use is occurring despite the knowledge that the US Food and Drug Administration’s approval of these devices is only for optimal humidification of oxygen therapy and not as a modality of providing positive distending pressure. There are 6 published randomized controlled trials on HFNC. Of these, only 2 studies compared HFNC with CPAP in neonates only. Only 1 study among the 2 used HHFNC that is currently used in most NICUs.

Air leak syndrome is a well-known complication of PPV. Recent evidence suggests that HHFNC provides increased pressure within airways, and this pressure being delivered is not predictable or sustained. Such an unpredictable rise in pressure may potentially cause air leak syndromes in patients. Despite an acknowledgment of the scant amount of clinical data on safety and efficacy, HHFNC is increasingly being used in neonates as a means of providing positive airway pressure. Similarly, in older children and adults HHFNC is increasingly being used without extensive clinical data supporting its use to provide positive airway pressure. In this novel report, we describe a case series in which HHFNC may have contributed to the development of air leak syndrome.

**CASES**

**Case 1**

A 2-month-old previously healthy infant with respiratory syncytial virus bronchiolitis was transferred on day 5 of his illness from another hospital due to worsening respiratory status. In the referring facility he was medically managed with nasal cannula oxygen at a flow of 2 lpm, nasogastric feedings, and intermittent albuterol. On admission to a tertiary hospital, he was noted to be tachypneic with a respiratory rate in the 60-65 per minute, with moderate retractions (Table 1). Multiple chest radiographs, including one just before transfer, revealed no air leaks within the chest. Soon after transfer, he was placed on HHFNC (Fisher Paykel, Auckland, New Zealand) initially at 6 lpm with a fractional inspired oxygen concentration of 0.4, which was increased to 8 lpm within 1 hour of admission. A chest radiograph taken 4 hours after starting HHFNC therapy showed a right pneumothorax (Fig 1 A–C), which necessitated emergency transfer to the PICU. The patient subsequently required airway intubation and mechanical ventilator support due to worsening respiratory distress. He required mechanical ventilator support for 14 days and was discharged from the hospital after full clinical recovery on hospital day 29.

**Case 2**

A 16-year-old boy with severe developmental delay and well-controlled epilepsy was hospitalized for elective gastrostomy surgery for failure to thrive. His previous hospitalization in the past 7 years occurred 6 months previously for a medication-related adverse effect. He underwent an uneventful percutaneous endoscopic gastrostomy placement under general anesthesia (fentanyl, propofol, nitrous oxide). Post-surgery, he developed severe laryngospasm requiring brief reintubation. An hour later, he was extubated and transferred to the general pediatric floor. Four hours post-surgery, he was found to be hypoxemic (arterial oxygen saturation in the low 80% range) and was placed on 4 L/minute of HHFNC (Fisher Paykel) with a fractional inspired oxygen concentration of 1.0 and transferred to high-dependency unit. A chest and abdominal radiograph performed at this stage showed right lower lobe pneumonia without any pneumothorax, and HHFNC flow was increased to 8 lpm via a nasopharyngeal airway due to worsening respiratory distress. Four hours later, his respiratory status further worsened (Table 2), which necessitated transfer to the PICU. In the PICU, HHFNC flow was increased.

**TABLE 1** Vital Signs of Case 1

<table>
<thead>
<tr>
<th>Hours From the Event *</th>
<th>−2.5</th>
<th>−1</th>
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<th>5</th>
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<tr>
<td>RR, breaths per min</td>
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<tr>
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<tr>
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<td>78</td>
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<td>87</td>
<td>82</td>
<td>68</td>
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<tr>
<td>SatO2</td>
<td>100</td>
<td>97</td>
<td>100</td>
<td>94</td>
<td>100</td>
<td>100</td>
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<tr>
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<td>8</td>
<td>8</td>
<td>8</td>
<td>8</td>
<td>Intubated</td>
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<tr>
<td>FiO2</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>Intubated</td>
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</tr>
</tbody>
</table>

*Table 1: Vital Signs of Case 1*

**Footnotes:** DBP: diastolic blood pressure; FiO2: fraction of inspired oxygen concentration; HR: heart rate; MAP: mean blood pressure; RR: respiratory rate; SatO2: oxygen saturation by pulse oximetry; SBP: systolic blood pressure.

*Event* means air leak syndrome (pneumothorax or pneumomediastinum).
increased to 15 lpm and then to 20 lpm to optimize respiratory support. In-exsufflator therapy with the use of an Emerson Coughassist (Philips Healthcare, Andover, MA) device was also started. A chest radiograph performed ~24 hours after starting HHFNC showed extensive pneumomediastinum, subcutaneous emphysema, and intraperitoneal free air (Fig 1 D–F). In-exsufflation was discontinued after pneumomediastinum was discovered. His condition deteriorated, and after consultation with the family, the family opted to place him on comfort care, which was followed by his death 2 days later.

**Case 3**

A 22-month-old boy was admitted for suspected physical abuse when he was found to be lethargic followed by generalized tonic-clonic seizure in day care. After a visit to a local hospital’s emergency department, he was airlifted to a PICU in a tertiary facility. A computed tomographic scan of the head showed a large left subdural hematoma with no skull fracture or cerebral edema. He had a brief episode of focal seizure involving his head and right arm, which was easily controlled with medications. He was transferred to the regular ward after 2 days of observation in the PICU. On day 5 of his hospitalization he developed an episode of generalized tonic-clonic seizure, which necessitated airway intubation, and he was admitted to the PICU for ventilatory support (Table 3). A repeat head computed tomographic scan showed increased subdural hematoma with increased cerebral edema, midline shift, and signs of raised intracranial pressure (ICP). The patient’s elevated ICP responded well to medical management. With gradual resolution of his subdural hematoma and elevated ICP, he was successfully extubated after 14 days of ventilatory support and was placed on 6 lpm of HHFNC (Fisher Paykel). All previous chest radiographs while the patient was mechanically ventilated did not show any evidence of air leak syndrome. While receiving 6 lpm of HHFNC, an abdominal radiograph performed 5 hours postextubation to check placement of the feeding tube showed a large right pneumothorax with complete collapse of the right lung (Fig 1 G–I). After confirmation with a chest radiograph, a chest tube...
was immediately inserted and maintained on low intermittent suction as the patient continued to receive 6 lpm of HHFNC. His collapsed lung immediately reexpanded, and the chest tube was removed 3 days later. The boy made a full recovery and was discharged from the hospital.

**DISCUSSION**

In this report we discuss 3 cases of air leak syndrome associated with HHFNC therapy. Over the past decade, HHFNC is increasingly being used in lieu of PPV in neonates, older children, and adults. However, the evidence supporting this practice change is scant. Furthermore, accumulating evidence in recent years raises concerns about the efficacy and safety of HHFNC.

Both in vitro and in vivo studies have revealed that HHFNC therapy generates positive pressures in the nasopharynx. Artificial lung model studies have shown dangerously high airway pressures with minimal leaks in HHFNC. Chang et al. studied the relationship between flow and pressure using HHFNC device. At all flows ranging from 1 to 8 lpm HHFNC generated much higher pressures compared with a CPAP device. At 8 lpm CPAP generated a pressure of ~30 cm H2O compared with HHFNC, which generated a pressure of >120 cm H2O measured at the nasal prongs. However, in contrast, other studies in simulated infant models have shown that the pressure generated in the nasopharynx was similar to or less than that of CPAP.

**Definition of HFT**

Any delivered flow in excess of subject’s intrinsic inspiratory flow is called “high flow.”

Because inspiratory flow is dependent on several factors (see below) that, in turn, are dependent on the subject’s weight and age, no single flow rate can be given for the pediatric age group that could be called high flow. In general, flows in excess of 2–8 L/min in neonates are considered high flows. The terms HFT, HFNC, and HHFNC are often used interchangeably. HHFNC is a form of HFT. HFT if delivered via nasal cannula (as opposed to a mask interphase) is called HFNC.

HFNC devices to deliver up to 8 L/min in neonates and 40 L/min have been approved. Calculation of inspiratory flow

**TABLE 2** Vital Signs of Case 2

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DBP, diastolic blood pressure; FIO2, fraction of inspired oxygen concentration; HR, heart rate; MAP, mean blood pressure; RR, respiratory rate; SaO2, oxygen saturation by pulse oximetry; SBP, systolic blood pressure.

**TABLE 3** Vital Signs of Case 3

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DBP, diastolic blood pressure; FIO2, fraction of inspired oxygen concentration; HR, heart rate; MAP, mean blood pressure; RR, respiratory rate; SaO2, oxygen saturation by pulse oximetry; SBP, systolic blood pressure.

**TABLE 4** HFT, HFNC, and HHFNC: Terminology and Definitions

**Definition of HFT**

Any delivered flow in excess of subject’s intrinsic inspiratory flow is called “high flow.”

Because inspiratory flow is dependent on several factors (see below) that, in turn, are dependent on the subject’s weight and age, no single flow rate can be given for the pediatric age group that could be called high flow. In general, flows in excess of 2–8 L/min in neonates are considered high flows. The terms HFT, HFNC, and HHFNC are often used interchangeably. HHFNC is a form of HFT. HFT if delivered via nasal cannula (as opposed to a mask interphase) is called HFNC.

HFNC devices to deliver up to 8 L/min in neonates and 40 L/min have been approved. Calculation of inspiratory flow

**Inspiratory flow**

Minute ventilation (minute vol)/inspiratory time fraction

Minute ventilation = tidal volume (VT) × respiratory rate

Inspiratory time fraction = inspiratory time (Ti)/total respiratory cycle (Ttot)

Example: If respiratory rate is 60 breaths per min, Ttot would be 1 s. If inspiratory time is 0.5 s, then inspiratory time fraction would be 0.5. There are normal predicted values for VT and respiratory rate for children of different ages. Inspiratory time fraction varies according to disease process. In general, it is <0.5 in normal health.
pneumothorax, supporting this notion.

Although the pressure and flow relationship has been studied both in vitro and in vivo, the relationship between flow and delivered minute ventilation has not been studied. The flow driver in a traditional CPAP setup delivers flows only during child’s inspiration through the nasal cannula in preterm infants is associated with prolonged oxygen requirement; a randomized controlled trial. Early Hum Dev. 2011;87(3):205–208


23. Miller MP, Sagy M. Pressure characteristics of mechanical ventilation and incidence of pneumothorax before and after the implementation of protective lung strategies in the management of pediatric patients with severe ARDS. *Chest*. 2008;134(5):969–973


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