High-Flow Nasal Cannula Oxygen in Critically Ill Adults: Do the Nose or Lungs Know There's a Difference?

Intra-nasal oxygen was introduced by Arbuthnot Lane in 1907, using rubber nasal catheters. This approach was advocated by Adrian Stokes for use in critically ill victims of phosgene gas warfare during World War I.[1] However, placement of rubber catheters into the nasal cavity (and often removal) was quite uncomfortable and required some skill (it makes our eyes water just thinking about the procedure). Nasal catheter use was gradually abandoned and replaced by the minimally invasive nasal cannula, as it was simple to apply and better tolerated. By 1929, Dr Alvan Barach had developed a bifurcated malleable-metal cannula that was held in position by a cloth headband.[2] Today's nasal cannula has evolved to be the most common appliance for oxygen therapy; modern plastics now provide soft intra-nasal prongs. Its low cost and simple technology support administration with minimal training by healthcare providers and patients and their family members. The basic cannula system includes an oxygen flow meter, small-bore connecting tubing attached to either a blind-ended tube with elastic headband or an over-the-ear lariat with under-the-chin adjustment. Permutations of the standard device include:

- Models sized for perinatal and pediatric patients[3]
- Incorporation with eye glasses
- A single prong for sidestream sensing of exhaled carbon dioxide[4]
- Reservoir systems (moustache and pendant) (used primarily in long-term ambulatory care)[5,6]
- A sensor to allow flow only on inspiratory demand (also used primarily in long-term ambulatory care)[7]
- High-flow designs for adult and perinatal/pediatric patients[8-10]

Nasal masks have also been applied to the nose specifically for oxygen delivery.[11] Humidification of oxygen to cannulas, for non-ambulatory low-flow applications, has traditionally been accomplished using unheated low-flow ($\leq$ 6 L/min) diffuser humidifiers ("bubblers") despite lack of efficiency and evidence of benefit.[12] There are some unheated humidifiers available with adequate humidity characteristics for use with a larger-bore cannula for flows in the 6–15 L/min range (Salter Labs, Arvin, California). Heated water systems capable of providing 100% body humidity have recently been incorporated into high-flow nasal cannulas (HFNCs) to preserve nasal mucosa and improve comfort. The Vapotherm 2000i (Vapotherm, Stevensville, Maryland) uses a heater and single-use cartridge in line with an air-oxygen blender. The mixed gas flow is independently controlled (range 1–40 L/min). The down side of such systems is that they add substantial cost and technology to the basic cannula system.

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In this issue of Respiratory Care, Parke and colleagues present original research on an HFNC in an intensive care unit setting to provide supplemental oxygen to patients with mild to moderate hypoxemic respiratory failure.[13] Sixty patients were enrolled, and data were analyzed from 56 patients. The patients were randomized to either HFNC or high-flow oxygen via aerosol-type face mask (HFFM), which had been their institution's standard therapy. The HFNC group used an Optiflow cannula with humidification by an MR880 heated humidifier (both from Fisher & Paykel Healthcare, Auckland, New Zealand). Although it was not explicitly described, we presume that an oxygen-air blender delivered the blended source gases to the cannula. They used a face mask designed for high-flow aerosol applications (Hudson RCI, Research Triangle Park, North Carolina). Oxygen from a flow meter was mixed using a "venturi" air entrainer and they used a humidifier system similar to that used with the HFNC (MR850, Fisher & Paykel Healthcare, Auckland, New Zealand). Both humidifiers were equipped with similar heated-wire corrugated tubing devices.

The study objective was to determine if HFNC would be better tolerated and/or result in fewer treatment failures than HFFM. Treatment failure was defined as worsening respiratory failure that required a change in the device providing respiratory support within 24 hours of study enrollment.[13]

Respiratory therapists and physicians have benefited from a growing collection of medical literature supporting evidence-based guidelines and decision-making pathways for medical gas therapy. Guidelines are currently available for patients in general wards, emergency departments, and inten-

sive care units.[14,15] Parke and colleagues are to be congratulated for a lucid evaluation of an alternative oxygen-delivery device compared to previous standard therapy for patients with mild to moderate hypoxemia. All too frequently, application of new therapy is based on administrative decisions, without using research to guide clinical practice.

An evidence-based and comprehensive approach for recommending supplemental oxygen and then (if needed) to initially select a specific oxygen-delivery appliance can be complex. The determination requires evaluation of the patient scenario, age, preexisting medical conditions, treatment setting, technical limitations, cost constraints, and issues related to convenience. Often, institutional tradition or protocols are imposed. Assessment of hypoxemic respiratory failure is often complicated by cardiovascular disease or neuromuscular disorders, either or both of which may cause hypercapnic failure that requires mechanical ventilatory support. In addition, treatment also necessitates elucidating the pathophysiologic cause of the hypoxemia, which is often only determined by response to initial therapy. Hypoxemia from pulmonary pathology with predominant right-to-left pulmonary shunting tends to respond poorly to only increasing the F_{IO_2}. Noninvasive continuous positive airway pressure (CPAP) (during spontaneous breathing) or applied PEEP (during mechanical ventilation) may be needed to elevate P_{aO_2} and saturation. As the Parke study notes in the discussion section, changing the oxygen-therapy device from a protocol or escalating therapy is tempered by both clinical judgment of objective patient data and subjective decision making.

After reading the Parke paper, the following question should be reviewed as clinicians put the study into perspective and for further consideration when incorporating HFNC into their armamentarium of oxygen-delivery appliances: did the study attend to the hypotheses that HFNC would be better tolerated and result in fewer treatment failures than HFFM?

Treatment failure was defined as worsening respiratory failure necessitating changing either device within 24 hours of initiating oxygen therapy. Parke et al acknowledge that the clinicians were not held to strict criteria for identifying worsening respiratory failure. A combination of clinical findings, in no particular order, made up the clinicians' decision tree: dyspnea; fatigue; worsening gas exchange; and intolerance of the oxygen-delivery appliance.

An independent analysis of patient tolerance is a difficult task. It is dependent on a patient's perception of comfort in wearing a medical device. There may be individual bias in wearing a nasal versus facial appliance that may have nothing to do with their sensation of dyspnea but relate to problems in claustrophobia, communication, or oral access. A study by Roca and colleagues analyzed *tolerability* based on patient perceptions of comfort, mucosal drying ("dry mouth"), and dyspnea during a comparison of HFNC versus oxygen mask.[16] No numerical comfort scale survey was performed as part of the Parke et al study, similar to patients' subjective perception of pain on a visual analog 0–10 scale.

It would appear that the 60 subjects in the study by Parke et al[13] were selected randomly from a cardiothoracic and vascular intensive care unit. Their Table 1 suggests that the patients were tachypneic and required more than 4 L/min via cannula or 6 L/min via oxygen mask. For the purposes of the study design, the randomization was to either HFNC or HFFM, although neither of the devices may have been able to meet the F_{IO_2} and/or inspiratory flow requirements.

The ranges of hypoxemia and respiratory breathing frequency were substantial. Based on one standard deviation, the room air P_{aO_2} range was 56–88 mm Hg in the HFNC group and 62–92 mm Hg in the HFFM group. Of interest is the lack of significant difference between the 2 groups in their P_{aO_2}/F_{IO_2} ratios during the first 4 hours of oxygen administration. Although the mean respiratory rates were similar, the upper level of one standard deviation for both groups exceeded 25 breaths/min.

One of the most interesting findings in the Parke et al study was the frequency of desaturation events among patients in the 2 treatment groups. Although not specifically defined, they were far more common in the HFFM group: a mean of 1.86 desaturations/patient, compared to 0.79 desaturations/patient in the HFNC group. The first consideration would be to determine if these events were related to technical differences in the systems' ability to deliver the expected F_{IO_2} at flows adequate for the patients' often increasing flow demand. The Methods section and Figures 1 and 2 shed some light on this issue. The HFNC had an initial flow of 35 L/min and F_{IO_2} titrated as necessary to attain $S_{pO_2} \geq 95\%$. Unfortunately, Figure 1 does not identify the means by which the air/O_2 mixtures were provided and independently adjusted. We must presume that an air/O_2 blender with independent flow control was used. (To allow other clinicians to reproduce the research, more detailed equipment specifications are recommended.) Gas flow to the HFFM was generated from a flow meter; a diluter device provided the means to adjust F_{IO_2}. However, with a diluter there is potential for the total flow of mixed gas to decrease as F_{IO_2} is increased. This is especially critical with a face mask with an open design, no gas reservoir, and outlet holes, through which room air can easily be secondarily entrained.[17-19] We have observed this problem in recently extubated patients who were placed on similar masks with standard large-volume aerosol nebulizers. Failure of the system to meet patient inspiratory flow demand and allow secondary room air entrainment at the mask has been interpreted as patient deterioration. Often this occurs as the respiratory rate exceeds approximately 25 breaths/min. The spiral of worsening hypox-

emia is accelerated if the F_{IO_2} of the nebulizer is mistakenly increased, further decreasing total flow. We have been able to simulate this phenomenon in the lab, using an intubation manikin attached to a mechanical double-lung analog with one side being driven by a mechanical ventilator, causing the adjacent lung to ventilate the manikin. An oxygen analyzer placed in the trachea documented declining F_{IO_2} with tachypnea and/or increasing the F_{IO_2} from the nebulizer. An air/O_2 blender or high-flow large-volume nebulizer may remedy the clinical problem.[20,21]

The HFNC design has the potential to allow inboard leaks through the mouth, but at the same time may set up the nasal cavity and pharynx as an oxygen reservoir. There are no data to help determine if the increased number of desaturation events in the HFFM group could be directly correlated with the patient's tachypnea. If that were the case, failure of the system's inherent design (mask dilution and/or flow limitation) could be implicated as the cause of desaturation events and identify the advantage of the blender-driven HFNC.

A potential major feature that may also identify the technical advantage of the HFNC is its ability to generate CPAP. Parke and colleagues demonstrated this effect with their HFNC system in a previous publication.[22] The HFNC used in this study is an example of using an adjustable flow of humidified gas to create CPAP as it meets resistance in the anatomical upper airways. This approach has been documented for use in both perinatal/pediatric and adult patients.[23-26] The attributed mechanism of the action of positive pressure is multifaceted: improved work of breathing by the mechanical effect on respiratory musculature; improved gas exchange by decreasing low ventilation-perfusion in the lung; and purging the anatomical airways of carbon dioxide while using them as an oxygen reservoir.[27] Unlike the tighter-sealing nasal CPAP masks or nasal pillows, the HFNC used in the Parke et al study is not well suited for obstructive sleep apnea or noninvasive ventilation, and not requiring a tight seal may prevent some discomfort. However, both mask designs are dependent upon a level of seal by the oropharynx and mouth to maintain CPAP in the major airways and lung.

The lessons provided by the Parke et al study[13] may be more valuable than its objective of demonstrating superiority of one oxygen-delivery device over another for patients with moderate hypoxemia. The study illustrates that the challenges of clinical research when matching a device to a patient problem are based on "hard science," critical thinking, and the art of responding to often subtle clues. Parke et al note the study's limitations and the difficulty of performing detailed, real-time analysis of factors that prompted oxygen desaturation episodes and treatment failure. A number of factors may have introduced bias into the findings. Besides knowing the oxygen-delivery apparatus to elevate F_{IO_2} and meet flow demand, a few other factors may have included air dilution systems, mask design, and potential deteriorating cardiopulmonary disease states.

This randomized controlled study by Parke and colleagues has advanced the evidence for clinical use of the high-flow cannula beyond the bench or case series. It has modeled an approach for respiratory care clinicians to thoughtfully review new equipment as it is made available from manufacturers. The study does appear to uncover both the benefits and limitations of HFNC. Although HFNC may not be needed for many patients with mild hypoxemia and moderate respiratory rate, it does appear to be ideal for some patient problems. HFNC probably requires greater caution when applied to patients with pathophysiologies that induce intrinsic PEEP, such as unstable COPD or asthma, as its role remains controversial. A low level of extrinsic CPAP may not be effective in counteracting PEEPi and could lead to unintended increase in lung volume.[28,29] These insights should allow further investigations to better select specific patient problems for which it is best suited, including patients with moderate hypoxemia who initially do not respond well to low-flow cannula, do not tolerate face mask, or have pathophysiology that would benefit from a low level of CPAP. In retrospect, it would appear that the nasal catheter might have been well suited to treat World War I victims of gas exposure.[30]

Bryan A Wattier RRT
Jeffrey J Ward MEd RRT FAARC
Respiratory Care Program
University of Minnesota
Mayo Clinic
Rochester, Minnesota

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The authors have disclosed no conflicts of interest.

Correspondence: Bryan Wattier RRT, Respiratory Care Program, University of Minnesota, Mayo Clinic, 200 First Street SW, Siebens 10-12C, Rochester MN 55905.

DOI: 10.4187/respcare.01250