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WHAT'S NEW IN INTENSIVE CARE

Airborne spread of SARS-CoV-2 while using high-flow nasal cannula oxygen therapy: myth or reality?

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In 2020, a new pandemic caused by SARS-CoV-2 was declared [1], and since the first cases of coronavirus disease 2019 (COVID-19), clinicians had to apply different modes of respiratory support, previously used on patients with severe respiratory failure from other etiologies. In particular, high-flow nasal cannulae (HFNC) and non-invasive ventilation (NIV) were variably applied in early reports from China [2] and Europe [3]. Yet, the extent of airborne contamination of clinical areas during the use of HFNC has sparked intense debate and highlighted the need for inclusive investigation in this area.

SARS-CoV-2 may be spread by direct or indirect contact with infected individuals through respiratory secretions or droplet transmission, as well as through fomites [4]. Once airborne, the half-life of SARS-CoV-2 is approximately one hour [95% credible interval, 0.64 to 2.64] [5]. Airborne transmission was initially underestimated; indeed in one analysis in February 2020 of 75,465 cases in China, airborne transmission was not reported [6]. A later study by Liu et al. from Wuhan analyzed aerosol samples using droplet digital polymerase chain reaction, and concluded that virus aerosol deposition on protective apparel or floor surface and their subsequent re-suspension was a conceivable transmission pathway [7]. These findings were further corroborated by Santarpia et al. on 13 isolated patients, who concluded that transmission may occur via contaminated objects and airborne transmission, as well as direct transmission via droplets [8]. Several other factors modulate the specific risk of healthcare workers (HCW) of being infected with SARS-CoV-2 and could be grouped into patient-related and HCW-related risk factors. Patient-related risks are associated with the volume and distance of respiratory particles generated and mobilized from the patient, the viral titre and long-term viability within the aerosolized particles, and finally the ability of the virus to penetrate innate host defenses. In contrast, HCW-related factors are associated to the HCW's health status, comorbidities and immunocompetency, the length of time of exposure and adequacy of worn personal protective equipment (PPE). Patients with COVID-19 often present to the emergency department with substantial respiratory drive and persistent dry cough. Thus, based on the aforementioned evidence, viral transmission from respiratory particles and droplet dispersion may theoretically pose a significant risk to HCW, specifically in patients who are undergoing means of ventilatory support without shielding their mouths, and during the early days of hospital admission, when the viral load is the highest [9].

Unfortunately, to date, the literature describing risks of airborne contamination by HFNC versus other means of support, i.e. NIV via face mask or helmet or nose mask, is heavily reliant on preclinical data, not specifically focused on SARS-CoV-2, and thus is inducing rather than answering controversy in the field (Table 1). In an important preclinical study by Gaeckle and collaborators [10], particle concentration and size from the respiratory tract of 10 healthy individuals receiving oxygen with various modes of delivery were measured through an aerodynamic particle spectrometer. Importantly, no increase in the concentration of aerosols generated was found with the use of HFNC or NIV when compared with breathing room air or non-humidified oxygen modalities. However,

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Table 1 Studies of risk of airborne contamination from HFNC versus other forms of ventilatory support, in settings both directly and not directly related to SARS-CoV-2

Reference	Ventilation techniques investigated	Study design and size	Relevant results
Studies directly related to SARS-COV-2			
Guy T et al. (2020) High-flow nasal oxygen: a safe, efficient treatment for COVID-19 patients not in an ICU. *Eur Respir J:* 2,001,154	HFNC	Clinical study ($N=27$). Patients with RT-PCR-confirmed COVID-19 infection placed on HFNC for non-hypercapnic acute hypoxemic respiratory failure	After a 30-day follow-up, only one nurse was infected with SARS-CoV-2 during the study period, potentially by domestic contact
Ahn JY et al. (2020) Environmental contamination in the isolation rooms of COVID-19 patients with severe pneumonia requiring mechanical ventilation or high-flow oxygen therapy. *J Hosp Infect.* S0195-6701(20)30,401–1	HFNC, NIV	Clinical case series ($N=3$). 3 patients with COVID-19 pneumonia (two mechanically ventilated, and one on HFNC/NIV)	13 of the 28 environmental samples in a room of a patient receiving HFNC/NIV showed positive results and viable virus. Air samples were negative for SARS-CoV-2
Studies not directly related to SARS-COV-2, testing various types of ventilatory support and interfaces: corroboration of risk			
Leonard S et al. (2020) Reducing aerosol dispersion by high-flow therapy in COVID-19: High resolution computational fluid dynamics simulations of particle behavior during high velocity nasal insufflation with a simple surgical mask. *J Am Coll Emerg Physicians Open*. 1(4):578–591	HVNI, LFO_2, and tidal breathing	In silico computational fluid dynamics simulation evaluating particle and droplet behavior with use of Type 1 surgical masks	Exhaled particulate mass capture by the mask was 88.8% (HVNI at 40L/min) vs 77.4% (LFO_2 at 6 L/min). Particle distribution escaping to the room, (> 1 m from face) was 8.23% for HVNI + mask versus 17.2% for LFO_2 + mask
Leung CCH et al. (2019) Comparison of high-flow nasal cannula versus oxygen face mask for environmental bacterial contamination in critically ill pneumonia patients: a randomized controlled crossover trial. *J Hosp Infect* 101(1):84–87	HFNC at 60L/min, and OM at 8.6 ± 2.2 L/min	Randomized controlled crossover trial ($N=20$). Environmental contamination by viable bacteria in critically ill patients with Gram-negative pneumonia receiving HFNC or OM	There were marginal differences in bacterial contamination between the HFNC and OM used
Hui DS, (2015) Exhaled air dispersion during non-invasive ventilation via helmets and a total facemask. *Chest*. 147: 1336–1343	NIV via two different helmets via a ventilator and total facemask via a bilevel positive airway pressure device	Preclinical study using human patient simulator	During NIV via a helmet with the lung simulator programmed in mild lung injury, exhaled air leaked through the neck-helmet interface with a radial distance of 150 to 230 mm when inspiratory positive airway pressure was increased from 12 to 20 cmH_20. During NIV via a helmet with air cushion around the neck, there was negligible air leakage. During NIV via a total facemask for mild lung injury, air leaked through the exhalation port to 618 and 812 mm when inspiratory pressure was increased from 10 to 18 cmH_2O, respectively, with the expiratory pressure at 5 cm H_2O.
Tran K, (2012) Aerosol Generating Procedures and Risk of Transmission of Acute Respiratory Infections to Healthcare Workers: A Systematic Review. *PloS one*. 7: e35797	HFNC, NIV, BiPAP	Systematic review; Ten non-randomized studies included (Five relevant case–control studies and five retrospective cohort studies)	NIV was reported to present an increased risk of transmission of SARS to HCWs [$n=2$ cohort; OR 3.1(1.4, 6.8)]. HFNC and manipulation of oxygen or BiPAP masks were not found to be significant in terms of risk to HCWs

Table 1 (continued)

Reference	Ventilation techniques investigated	Study design and size	Relevant results
Studies not directly related to COVID-19, testing various types of ventilatory support and interfaces: corroboration of safety			
Gaeckle NT, (2020) Aerosol Generation from the Respiratory Tract with Various Modes of Oxygen Delivery. *Am J Respir Crit Care Med*. 202: 1115–1124	Non-humidified NC, face mask, heated and humidified HFNC, and NIPPV, in a negative pressure room	Clinical study ($N = 10$). Aerosol generation was measured from healthy participants with each oxygen mode during maneuvers of normal breathing, talking, deep breathing, and coughing	Oxygen delivery modalities of humidified HFNC and NIPPV did not increase aerosol generation from the respiratory tract
Studies not directly related to SARS-COV-2, with equivocal findings regarding risks			
Agarwal A, (2020) High-flow nasal cannula for acute hypoxemic respiratory failure in patients with COVID-19: systematic reviews of effectiveness and its risks of aerosolization, dispersion, and infection transmission *Can J Anaesth*. 67(9):1217–1248	HFNC	Systematic review; seven studies included (six simulation studies, one crossover study)	Included studies did not provide data that can be extrapolated to the risk of airborne transmission of SARS-CoV-2

HFNC high-flow nasal cannulae, *NIV* non-invasive ventilation, *HVNI* high velocity nasal insufflation, LFO_2 low flow oxygen therapy, *OM* conventional oxygen mask, *BiPAP* bi-level positive airway pressure, *NC* nasal cannula, *NIPPV* non-invasive positive pressure ventilation, *NRB* non-rebreather mask

it should be noted that this was a small study in healthy participants, without ongoing pulmonary disease, which limits extrapolations to patients infected by SARS-CoV-2. Indeed, these results were also contingent upon the method of sampling aerosolized particles, which in itself carries risk of sampling error. Furthermore, consistent results suggest that fitting of HFNC or NIV interfaces, i.e. nasal pillow/mask or face mask, plays a crucial role in droplet generation. In a study by Hui et al.[11], conducted on a human patient simulator of dispersion of traceable particles, the authors concluded that exhaled air dispersion was higher using NIV and dependent on the applied settings, as corroborated by substantial increases in dispersed air when NIV pressure was increased from 5 to 20 cmH_2O or HFNC flow from 10 to 60 L/min. However, the highest dispersion was found by loosening the HF nasal cannulas or the HF oxygen circuit tube [11]. Tran et al.[12] studied the transmission of SARS from patients undergoing ventilatory support to HCW. They found that the virus could be dispersed through NIV, but not from HFNC or BiPAP mask adjustment. The study was limited by the small population and questionable methodology, and further emphasized the current lack of systematic appraisal of airborne viral transmission from infected patients. Finally, an in silico computational fluid dynamics simulation by Leonard et al. showed that using a simple surgical mask over the HFNC interface is effective in reducing distribution of aerosolized particles [13].

In the setting of SARS-CoV-2, evidence on this subject is highly limited and anecdotal. Various investigators have suggested that HFNC and NIV are associated with proven aerosolization of viable virus particles around the patient bedspace, but failed to establish a clear association with an increased number of HCW infections. To illustrate, one clinical study demonstrated that distribution of viable virus particles throughout the immediate clinical environment occurred with HFNC and NIV [14]. A separate clinical study showed that when staff were fully trained in the use of PPE, the rate of HCW infection whilst being in the immediate vicinity of HFNC was extremely low [15]. More high-quality evidence is clearly needed to better establish the true risk of infection to HCWs from aerosolization. For HFNC, the continued perception of a risk of viral aerosolization remains a significant obstacle to its uptake for management of hypoxemic respiratory failure in COVID-19, as highlighted by discordant recommendations on its use from health organizations and medical societies across the globe. Nevertheless, potential risks should be balanced with the described benefits with the use of HFNC, even in COVID-19 patients in the prone position.

Taken together, airborne contamination via generation of aerosols during HFNC must at this stage be assumed

as conceivable and potentially perilous to the HCW, until proven otherwise. Preclinical data, whilst useful to establish the mechanics of aerosolization, unfortunately do not capture the endpoint of absolute risk, which ultimately depends on the quantity and viability of pathogenic material and specific HCW risks. In the meanwhile, reducing dispersion through simple measures, such as surgical masks and careful fitting of the interfaces and sealing of the circuit on supported patients are strongly recommended. Further clinical research, and particularly systematic human studies, which can correlate the degree of ventilation-dispersed aerosols with the quantity and viability of dispersed virulent particles that are capable of causing infection, are urgently required.

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Compliance with ethical standards

Conflicts of interest
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