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Risk of aerosol formation by high flow nasal cannula treatment in critically-ill patients

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ABSTRACT

Background: There is a persistent concern over the risk of respiratory pathogen transmission, including SARS-CoV-2, by formation of aerosols (a suspension of microdroplets and residual microparticles after evaporation) generated by high flow nasal cannula (HFNC) oxygen therapy in critically-ill patients. This concern is fueled by limited available studies on this subject. In the present study, we test our hypothesis that HFNC treatment is not associated with increased aerosol formation as compared to conventional oxygen.

Methods: We used laser light scattering and a handheld particle counter to detect and quantitate aerosols in both healthy subjects, as well as adults with acute respiratory disease, including COVID-19, receiving HFNC versus conventional oxygen therapy.

Results: The use of HFNC was not associated with increased formation of aerosols as compared to conventional oxygen therapy in both healthy subjects (n=3) and subjects with acute respiratory disease, including COVID-19 (n=17).

Conclusion: In line with scarce previous clinical and experimental findings, this study indicates that HFNC itself does not result in overall increased aerosol formation as compared to conventional oxygen therapy. This suggests there is no increased risk of respiratory pathogen transmission by HFNC to health care workers.

Key words: high flow nasal cannula, oxygen therapy, aerosol, respiratory virus, pneumonia, acute respiratory distress syndrome, COVID-19

BACKGROUND

Health care workers are at increased risk for infectious respiratory diseases, including COVID-19, by working in close contact with infected patients. It has been well established that respiratory pathogen transmission occurs through large exhaled respiratory droplets, as produced for example during coughing. However, aerosols, a continuum of microdroplets and residual microparticles after evaporation (size <5μm), which have a much longer airborne time,[1,2] may under specific circumstances also form an important mode of spread of respiratory microbes and viruses.[3,4] Not surprisingly, during the current COVID-19-related global health care crisis, concerns over the ability of certain respiratory medical interventions and procedures to generate aerosols carrying SARS-CoV-2 (bio-aerosols) has spiked.[5-7]

One of the respiratory interventions that remains a topic of active discussion in the clinical field regarding risk for bio-aerosol formation is oxygen therapy by high flow nasal cannula (HFNC), a potentially beneficial respiratory support modality in critically-ill patients in the intensive care unit (ICU).[6,8,9] It has been suggested that the high flow (up to 60L/min in adults) of warmed, humidified oxygen during HFNC treatment forced over respiratory mucosa generates aerosols. However, it is important to realize that expiratory flows during normal coughing or labored breathing without any respiratory support are much higher, which somewhat questions the relative importance and physiological basis for the view of HFNC as an aerosol-generating procedure.[7] In fact, recent observational and experimental findings suggest that HFNC does not generate higher numbers of aerosols as compared to conventional oxygen therapy modalities.[10-13] Likewise, clinical studies do not show evidence of increased risk of transmission of SARS-CoV-1 and SARS-CoV-2 from patients receiving HFNC to health care workers,[14,15] and also do not show increased surface or air dispersion of viral and bacterial pathogens.[13,16]

Although the above data together provides re-assuring data on the safety of HFNC regarding pathogen transmission during the COVID-19 crisis, the sample sizes of the individual studies so far, in particular involving actual patients with acute (infectious) respiratory disease, are small.[13] This may

importantly fuel the hesitant approach or even avoidance of HFNC treatment in COVID-19 patients by health care professionals.[6,8,17] Therefore, to gain further evidence on this subject, in the present study we test our hypothesis that HFNC treatment is not associated with increased aerosol formation as compared to conventional oxygen therapy in patients with acute respiratory diseases, including COVID-19.

METHODS

This study was approved by the local medical ethical committee at the Amsterdam UMC, location AMC (2020_098/NL73585.018.20 and W20_321#20.353).

Detection of aerosols in healthy subjects

We visually detected and quantified both large respiratory droplets and aerosols in three healthy volunteer adults, similar to our previous descriptions.[1,4] Particles/droplets were detected in complete darkness with a SprayScan® (Spraying Systems, Glendale Heights, IL, USA) laser sheet during normal, unsupported breathing or breathing during treatment with either a non-rebreather mask (NRM, Salter Labs, Lake Forest, IL, USA) at 15L/min or HFNC (Fisher&Paykel Healthcare Limited, Auckland, New Zealand) at 34-37^{0}C and 60L/min. As a positive control, these subjects were also asked to cough in order to generate both large respiratory droplets and aerosols,[1,4] and they received normal saline (NaCl 0.9%) nebulization through the HFNC system to generate aerosolized microparticles. Quantification (light pixels) with ImageJ software was performed as described before.[4,18] All subjects received the different treatments in cross-over and measurements were caried out after approximately 5 minutes per experimental condition. The experimental lab space (normal atmospheric pressure) in which the measurements took place is a dust-free room (in order to minimize serious background signals), kept at a constant temperature of 20.5 +/- 0.5 ^{o}C, with a measured relative humidity of 45 +/- 3%. Laser diffraction measurement using a spray particle/droplet measurement system with wavelength 0.6µm

(Malvern Spraytech, Malvern, UK) was used to determine size distribution of the positive aerosolized microparticle control using normal saline nebulization via the HFNC system.[4,18]

Detection of aerosols in patients

For this part, we prospectively included adult subjects receiving conventional oxygen therapy, by a NRM or low flow nasal cannula (LFNC), versus HFNC for various acute respiratory diseases in the ICU or specialized COVID-19 ward. Subjects were treated inside negative pressure rooms up to -7.5 kPa. As direct visualization of aerosols with a laser sheet in the dark obviously is not possible in these subjects, we used a particle counter (Royco HH200, PACSCI EMC, Hollister, CA) to detect 0.5µm and 5µm microparticles during 15 seconds of air sampling at two distances (30cm and 1m) in four positions around the head of the patient (left, right, rear, front) to assess for dispersion in all directions. Previously, we validated the technique of handheld particle counting to detect aerosol formation as described elsewhere.[18] In addition, we separately measured aerosolized microparticles generated by normal saline nebulization through a HFNC system as a positive control for detection of aerosols by the hand held particle counter.

Statistical analysis

Data from the healthy adults are derived from two separate experiments per condition per subject and presented in means ± SEM, and analyzed with repeated measures ANOVA with post hoc LSD test. Data from measurements in the subjects are presented in proportions and medians (IQR), and analyzed with by Fisher exact test or Mann-Whitney U test. A p value of < 0.05 was considered statistically significant. Data analysis was performed with IBM SPSS Statistics 26 software.

RESULTS

First, to have a more general estimation of the ability of HFNC to generate aerosols, we visualized and quantitated particles/droplets in healthy adults breathing either unsupported or while receiving oxygen through a NRM or HFNC. To have the highest chance to detect particle emission, we compared these conditions while subjects were breathing with their mouth open. As compared to unsupported breathing or a NRM, HFNC treatment was not associated with increased aerosol formation (Figure 1). Normal saline nebulization through the HFNC system to generate aerosolized microparticles as a positive control, indeed resulted in much higher numbers of aerosols (Figure 1). By laser diffraction we showed that the size of these nebulized normal saline particles was well below 10µm, confirming the size range of aerosols (Figure 2). Similarly, no increased HFNC-mediated aerosols during other conditions, e.g. closed mouth breathing, differential flow speeds (10-60L/min) or upon intranasal inhalation of normal saline to mimic rhinitis were found in a set of separate experiments (data not shown). In addition, upon visualization of aerosols detected during HFNC treatment, these numbers were neglectable when we compared this to the cloud of both large respiratory droplets and aerosols generated during a normal cough of a so-called 'high emitter' (Figure 3).[4] However, as the expiratory flow generated during coughing maneuvers is highly variable in both rate and direction, we did not directly compare this further.

Second, as healthy volunteers obviously lack mucus hypersecretion associated with infectious respiratory diseases and may thus introduce a type II error, we measured aerosol formation in subjects receiving conventional oxygen therapy, by a NRM or low flow nasal cannula (LFNC), versus HFNC. A total of 17 subjects with acute respiratory diseases receiving either conventional oxygen or HFNC treatment admitted to the ICU (n=13) or a specialized COVID-19 ward unit (n=4) were included in the study (Table 1). In 9 (53%) of the subjects the underlying disease was COVID-19. As expected, subjects on HFNC received higher flow rates as compared to the conventional group (p=0.001) (Table 1). However, both groups had similar median counts for both the 0.5µm and 5µm aerosol sizes as sampled at 30cm and 1m distance from the patient (Table 2). No differences between the number of aerosols

and the level of pressure inside the rooms was found. As a positive control for the handheld particle counter, normal saline nebulization through a HFNC system results in aerosolized microparticle counts that are of several orders of magnitude higher: 224.6 x 10^3 [180.3-311.7 x 10^3] and 2.2 x 10^3 [1.3-6.8 x 10^3] for 0.5µm and 5µm particle sizes respectively.

DISCUSSION

The main finding of this study of aerosol dynamics is that HFNC treatment itself is not associated with increased aerosol formation, as determined in both healthy subjects and critically-ill subjects (N=17) with acute respiratory disease, including COVID-19.

Our findings are in line with a very recent study among nine patients with COVID-19,[13] as well as recent experimental observations in ten healthy subjects.[10] Importantly, it provides further scientific basis for studies that have failed to detect increased dispersion of bacteria or viruses, such as SARS-CoV-1, SARS-CoV-2, to surrounding surfaces or air by HFNC.[13,16] In contrast, Ahn et al. detected viable SARS-CoV-2 particles in environmental swabs, but in this case-study the only patient that received HFNC was also subsequently treated with non-invasive mechanical ventilation.[19] Recently, Vianello et al. reported a case series of 28 patients with COVID-19 treated with HFNC.[14] They showed that none of the staff (wearing FFP2 masks) working in close contact with these patients had a positive SARS-CoV-2 PCR test within a 14-day time frame. Such studies underline prior views of the safety of HFNC during this current COVID-19 health crisis.[9,12]

By the combined effort from these studies derived from different investigator groups and patient cohorts, using various aerosol and pathogen detection methods, the risk of bio-aerosol generation by HFNC may appear to be low. However, a clear limitation to studying aerosol dynamics in relation to transmission of novel pathogens such as SARS-CoV-2, is our current lack of understanding of virion stability as well as infectivity (number of virions needed to produce an active infection).[4,20] It should thus be noted that aerosol detection findings in the setting of HFNC, such as in the current study, without measurements of virus particles or transmission to health care workers must be cautiously interpretated.[17] Nevertheless, the stark contrast between our findings of low aerosol formation during HFNC treatment and the very high numbers of both large respiratory droplets as well as aerosols that can be produced by a normal single cough or sneeze, as clearly demonstrated in various studies,[2,4] at the least suggests that we should to our best effort protect health care workers

from this type of transmission risk while they work in close contact with patients, regardless of whether they receive any form of respiratory support or not.

In conclusion, our study among healthy subjects and critically-ill adult patients, including with COVID-19, provides additional evidence to scarce, previous findings that HFNC is not associated with increased aerosol formation. Further research investigating modes and risk of pathogen (SARS-CoV-2) transmission to health care workers is urgently needed.

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FIGURE LEGENDS

Figure 1. Aerosol detection

Detected particles/droplets (quantified by maximum light pixels/mm^2) during open mouth breathing during no oxygen support (none), non-rebreathing mask (NRM, 15L/min), HFNC (60L/min) and HFNC with normal saline nebulization (positive control for generating aerosolized microparticles). *p =0.032 by repeated measures ANOVA with post hoc LSD analysis, as compared to all other groups. Data (mean ± SEM) from N = 3 subjects measured twice in separate experiments.

Figure 2. Aerosol size range from normal saline nebulization

Microparticle size distribution detected by laser diffraction during normal saline nebulization via HFNC treatment (positive control for generating aerosolized microparticles).

Figure 3. Aerosol visualization patterns

Particle/droplet visualization by laser light scattering from a healthy adult (with the face orientated sideward from the left side, y/x-axis mm distance) receiving high flow nasal cannula (HFNC) at 60L/min (left panel), during a single cough without respiratory support (middle panel), and during HFNC with normal saline nebulization for positive control of visualization of aerosolized microparticles (right panel).

QUICK LOOK

Current Knowledge

Aerosols may play a role in pathogen transmission, including SARS-CoV-2. Respiratory care therapies that generate aerosols may increase this risk to health care workers who come in close contact to infected patients. Currently, there is an ongoing debate on whether oxygen therapy by high flow nasal cannula (HFNC) leads to increased risk of aerosol formation.

What This Paper Contributes To Our Knowledge

In both healthy adult, as well as subjects with acute respiratory diseases, including COVID-19, the use of HFNC was not associated with increased aerosol formation as compared to conventional oxygen therapy by a non-rebreather mask or low flow nasal cannula.

Table 1. Patient characteristics

	Conventional oxygen treatment (n=7)[a]	HFNC oxygen treatment (n=10)	p-value[b]
Male – n (%)	5 (71.4)	5 (50.0)	0.622
Age (yr)– median [IQR]	52.0 [47.5-63.0]	70.0 [61.8-73.0]	**0.040**
Respiratory illness – n			
Pneumonia	7	7	
COVID-19	5	4	
Pleural effusion	0	2	
(Mucus) airway obstruction, unspecified	0	1	
Flow (L/min) – median [IQR]	7.00 [2.50-13.5]	50.0 [45.5-52.2][c]	**0.001**

[a] conventional oxygen treatment: low flow nasal cannula (LFNC, n=4) or non-rebreathing mask (NRM, n=3). [b] by Fisher exact test or Mann-Whitney U test. [c] flow humidified and set at 37^0C temperature

HFNC: high flow nasal cannula

Table 2. Aerosol detection

Particle size (µm)	Distance from the patient (cm)*	Median particle count [IQR]*		p-value[a]
		Conventional (n=7)	HFNC (n=10)	
0.5	30	103.8 [100.8-107.5]	93.4 [59.8-130.4]	0.669
5	30	6.0 [4.5-12.1]	6.8 [3.1-11.8]	0.625
0.5	100	107.3 [92.9-117.7]	67.6 [53.1-122.0]	0.187
5	100	8.7 [6.3-9.9]	6.4 [2.3-9.9]	0.407

[a] by Mann-Whitney U test. HFNC: high flow nasal cannula

Figure 1

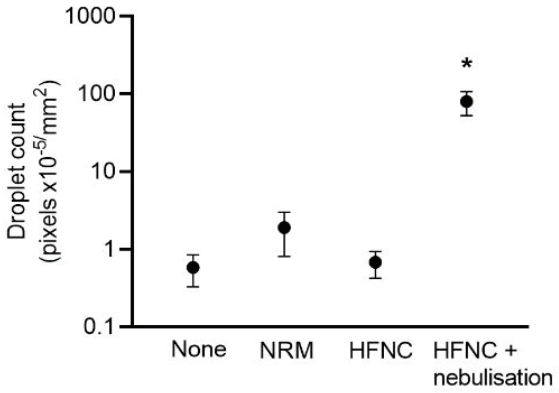

Figure 2

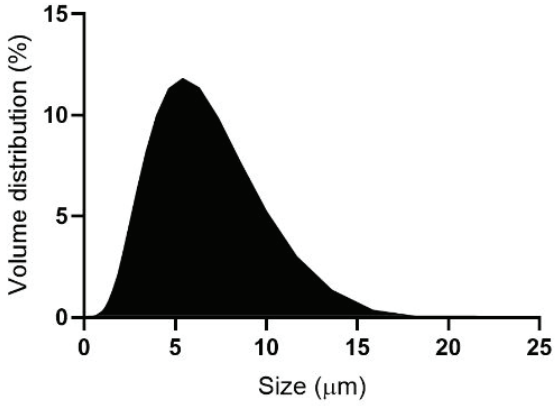

Figure 3