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Short report

Comparison of high-flow nasal cannula versus oxygen face mask for environmental bacterial contamination in critically ill pneumonia patients: a randomized controlled crossover trial

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SUMMARY

Whereas high-flow nasal cannula use is gaining prevalence, its high gas flow raises concerns about aerosolization of infectious particles and spread of infection. This randomized controlled crossover non-inferiority trial ($N = 20$) evaluated the degree of environmental contamination by viable bacteria associated with the use of high-flow nasal cannula compared with conventional oxygen mask for critically ill patients with Gram-negative pneumonia. The results show that high-flow nasal cannula use was not associated with increased air or contact surface contamination by either Gram-negative bacteria or total bacteria, suggesting that additional infection control measures are not required.

Introduction

High-flow nasal cannulae (HFNC) are a useful method of oxygen delivery for patients with acute respiratory failure, including pneumonia [1]. However, high gas flows (up to 60 L/min) raise concerns about aerosolization of infectious particles and spread of infection, particularly with the increasing prevalence of multidrug-resistant Gram-negatives [2].

A randomized controlled crossover non-inferiority study was conducted, comparing bacterial airborne and contact surface contamination during use of HFNC to use of a simple oxygen mask in patients with Gram-negative bacterial (GNB) pneumonia. The primary outcome was GNB count. The secondary outcome was total bacterial count (TBC).

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Methods

The study was conducted in a multi-disciplinary intensive care unit (ICU) from October 2015 to April 2017. Respiratory specimens (e.g. sputum, bronchoalveolar lavage, tracheal aspirates) from ICU were screened and those patients with GNB (labelled as 'index bacteria') in their specimens were assessed for eligibility. Where sample plates were contaminated by hands touching the Petri dish or if culture showed ≥100 colony-forming units (cfu) of single GNB strain suggestive of contamination, the results were excluded from analysis.

The study was conducted in accordance with the Declaration of Helsinki. Ethical, chemical, and biological safety approvals were obtained from the Chinese University of Hong Kong, CREC reference number 2015.236-T, and informed consent from patients or their relatives.

Inclusion criteria

Consecutive adult ICU patients with GNB pneumonia (based on clinical, radiological and microbiological criteria) requiring oxygen support (via nasal prongs or face mask) were recruited during office hours.

Exclusion criteria

Mentally incapacitated, imprisoned, pregnant or clinically unstable patients; or those with co-infection with respiratory viruses or *Mycobacterium tuberculosis*.

Intervention

The study was carried out in single-occupancy rooms. Clinical researchers performed sampling and patient care to limit the number of room entries and maintain typical room traffic. Otherwise standard care was provided.

Four experimental conditions were created by delivering oxygen through HFNC (Optiflow™ and AIRVO™, Fisher & Paykel Healthcare Ltd, Auckland, New Zealand) or simple oxygen mask (OM) (Soundway®, Ningbo Shengyurui Medical Appliances Co. Ltd, Ningbo, China) with room ventilation of six or 12 air changes per hour (ACH). Samples were obtained in all four conditions with each patient in a crossover design. The order in which the oxygen delivery devices were applied was randomized using a computer-generated randomization sequence concealed in sealed envelopes. For HFNC, 60 L/min gas flow was applied. Inspiratory fraction of oxygen (FiO_2) for HFNC and the oxygen flow for OM were adjusted to maintain oxygen saturation ≥92%. There was a washout period at 12 ACH between testing the two devices. Six ACH and 12 ACH were chosen based on common Intensive Care Unit and Airborne Infection Isolation room standards [3].

Sampling

Airborne organisms were actively sampled using an Andersen-type impactor air sampler (6-Stage Viable System, Thermo Fisher Scientific, Waltham, MA, USA) [4,5]. Three sets of air samples were collected per sampling condition, at three locations around the room at ≥1 m from patients. Approximately 1 m^3/min of air was sampled per location for 10 min.

Surface contamination was passively sampled by settle plates (Figure 1). Petri dishes placed approximately 0.4 m and 1.5 m from the patient's nose were uncovered at the beginning of each sampling condition and exposed to the environment for 1 h. These distances fell within and beyond the commonly presumed 1 m limit of droplet sedimentation respectively. The 0.4 m corresponded to bedside rails position and 1.5 m was the longest distance consistently achievable in our rooms. At each distance, settle plates were placed on right, anterior, and left of patients.

Microbiology

Tryptic Soy Agar plates were used for air sampling and settle plates. Collected samples were immediately transported for culture and aerobic incubation at 37°C for a maximum of five days, during which the results were read at three time-points on days 1, 2, and 5. The bacterial count and identity of colonies were determined using standard microbiological techniques. Nucleic acid sequencing was employed in a further attempt at identification when necessary.

Statistical analysis

Demographic and baseline physiological data are presented as frequencies (categorical data) and mean with standard deviation (SD) (continuous data) as appropriate.

GNB count and TBC were found to be non-normal using the Kolmogorov and Shapiro tests. Wilcoxon signed rank test was used to compare the medians of bacterial count in different conditions (SPSS Statistics 24, IBM Corp., Armonk, NY, USA). $P < 0.05$ was considered significant. A sample size of 20 patients was required to achieve 90% power to detect non-inferiority using one-sided *t*-test with margin of non-inferiority 0.200, true mean difference 0, significance level 0.05, and square root of the within-mean square error 0.2. A 2×2 crossover design with equal number in each sequence was used (PASS14 Power analysis and sample size software 2015; NCSS, LLC, Kaysville, UT, USA).

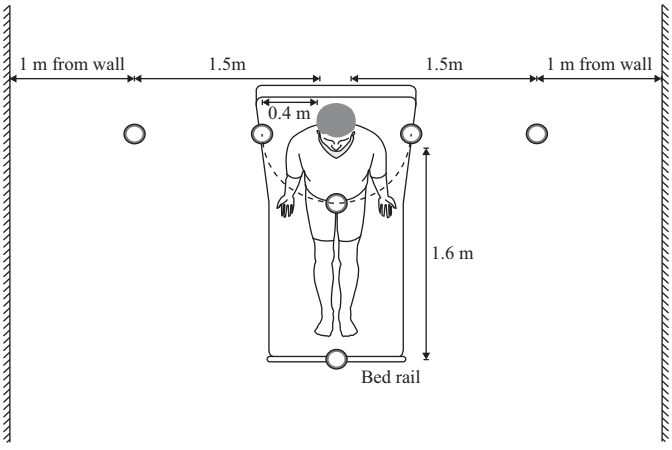

Figure 1. Placement of settle plates around patients. At each sampling condition, Petri dishes are placed 0.4 m and 1.5 m from the patient's nose at the right, centre, and left positions to evaluate the environmental surface bacterial load.

Results

Respiratory specimens from 196 patients were positive for GNB. Reasons for exclusion were mechanical ventilation ($N = 170$), influenza co-infection ($N = 4$), persistent hypoxia ($N = 1$) and ICU discharge ($N = 1$). One of 20 eligible recruited patients dropped out due to nasal discomfort from HFNC. Sensitivity analysis was performed for this patient's missing data by imputing the median from other patients under the same sampling conditions. GNB and TBC analysis results remained unchanged. The results from 19 patients with full data sets are presented. The mean (SD) age was 59 (14) years. Eight patients were female. Pneumonia was community-acquired in one patient and hospital-acquired in 18. The mean (SD) Acute Physiology and Chronic Health Evaluation II score was 20.1 (4.1), sequential organ failure assessment score 3.4 (2.1) and PaO_2/FiO_2 ratio 276.7 (114.1) mmHg [6,7]. Mean (SD) oxygen flow rate while using OM was 8.6 (2.2) L/min and the FiO_2 while using HFNC was 0.5 (0.1).

Primary outcome

Table I shows no difference in GNB count between the HFNC and OM use for air samples, settle plates at 0.4 or 1.5 m, and at six or at 12 ACH ($P = 0.119–0.500$).

At least one organism matching the index bacteria was found in 28% (18/65) of samples showing GNB. Gram-negatives identified included *Pseudomonas aeruginosa* and other species, *Acinetobacter baumannii* complex, and other species, *Stenotrophomonas maltophilia*, *Klebsiella pneumoniae*, *Escherichia coli*, *Enterobacter aerogenes*. Less common were *Brevundimonas* spp., *Empedobacter brevis*, and *Sphingomonas* spp.

Secondary outcome

At six air changes per hour, the total bacterial count on plates placed at 1.5 m while the patients were using HFNC was statistically significantly higher than when using an oxygen mask, after one and two days of incubation. Otherwise, no difference in TBC was detected between HFNC and OM use (Table I).

Post-hoc analysis

The TBC on settle plates placed at 0.4 m was higher than at 1.5 m with either device ($P = 0.002–0.037$) and higher at six ACH than at 12 ACH with either device ($P = 0.000–0.002$).

Discussion

Use of HFNC compared with an oxygen mask in patients with GNB pneumonia was not associated with greater bacterial airborne or contact surface contamination with viable GNB at oxygen flow rates normally used in clinical practice. This suggests that, when HFNC is used in this setting, no additional infection control precautions are required over and above those applied to patients receiving oxygen by face mask.

Our results are consistent with previous data demonstrating that droplet spread is no greater in patients using HFNC than following forceful exhalation, but that study did not assess the potential for infectious spread by aerosolization [8]. Passing high gas flows through respiratory devices is considered an aerosol-generating procedure. However, for an organism to cause airborne infection it must survive a process of desiccation and rehydration. This study demonstrates that the number of viable airborne GNB is not increased by HFNC.

In only 28% of positive samples did at least one of the environmental isolates match the index bacteria. Whereas it is possible that detected bacteria did not originate from the patient, the higher number of cfu on plates placed at 0.4 m compared with those at 1.5 m suggests that most bacteria did. We believe the low concordance with the index infecting bacteria reflects a mainly upper respiratory tract origin, as production of droplets and aerosols containing lower

Table I
Gram-negative bacterial count and total bacterial count by device (air sampling and settle plate), air changes per hour, and days of incubation ($N = 19$)

Sample	ACH	1-day incubation			2-day incubation			5-day incubation		
		HFNC	OM	*P*-value	HFNC	OM	*P*-value	HFNC	OM	*P*-value
Gram-negative bacteria										
Air (cfu/m^3)	6	0 (0–0)	0 (0–0.1)	0.770	0 (0–0)	0 (0–0)	0.208	0 (0–0.1)	0 (0–0.05)	0.250
	12	0 (0–0)	0 (0–0)	0.167	0 (0–0)	0 (0–0)	0.902	0 (0–0)	0 (0–0)	0.416
0.4 m settle plate	6	0 (0–0)	0 (0–0)	0.862	0 (0–0)	0 (0–0.2)	0.568	0 (0–0)	0 (0–0)	0.250
(cfu/plate)	12	0 (0–0)	0 (0–0)	0.3925	0 (0–0)	0 (0–0)	0.500	0 (0–0.3)	0 (0–0)	0.119
1.5 m settle plate	6	0 (0–0)	0 (0–0)	0.207	0 (0–0)	0 (0–0)	0.573	0 (0–0)	0 (0–0)	0.207
(cfu/plate)	12	0 (0–0)	0 (0–0)	0.500	0 (0–0)	0 (0–0)	0.500	0 (0–0)	0 (0–0)	0.500
Total bacterial count										
Air (cfu/m^3)	6	1.7 (1.0–4.3)	2.4 (1.1–4.2)	0.707	3.6 (2–6.9)	3.8 (1.9–5.5)	0.700	5.2 (2.2–8.7)	4.5 (1.7–9.6)	0.105
	12	1 (0.5–1.7)	1.3 (0.5–2.0)	0.915	1.6 (1.0–2.7)	1.9 (1.1–3.1)	0.776	2.1 (1.0–4.2)	2.3 (0.9–3.5)	0.205
0.4 m settle plate	6	1.7 (0.7–4.5)	1.3 (0.7–2.0)	0.428	3.7 (0.8–7.2)	2 (0.7–2.8)	0.287	4.3 (1.3–6.0)	2.0 (1.0–5.0)	0.175
(cfu/plate)	12	0.7 (0.2–1.8)	1 (0.3–2.2)	0.175	1 (0.8–1.5)	2 (0.7–3.2)	0.987	1.7 (0.7–3.3)	2.0 (1.0–3.3)	0.186
1.5 m settle plate	6	1.0 (0.5–1.8)	0.3 (0.3–0.8)	0.0385	1.3 (1–2.7)	0.7 (0.3–1.3)	0.010	1.7 (1.3–3.0)	1.3 (0.3–2.3)	0.091
(cfu/plate)	12	0.7 (0.2–0.8)	0.3 (0–1)	0.387	0.7 (0.3–1.2)	1 (0.3–1.3)	0.786	0.7 (0.3–1.7)	1.0 (0.3–2.7)	0.187

ACH, air changes per hour; HFNC, high-flow nasal cannulae; OM, oxygen mask; cfu, colony-forming units.
Values for HFNC and OM are median (interquartile range).
All statistical tests one-tailed.

respiratory tract organisms is predominantly due to coughing, and cough frequency during the sampling period was simply a matter of chance [9]. It may also reflect antibiotic therapy in the period between respiratory sampling and carrying out the experiment. Most importantly, the risk of infection is more likely to be related to the extent of bacterial contamination (which was not higher with HFNC), than the exact origin of the organisms.

This finding of a difference between HFNC and oxygen masks on 1.5 m settle plates at six ACH is of doubtful clinical significance. The difference was small and there were no differences in bacterial count in air samples (or 0.4 m plates) under the same conditions.

We acknowledge several limitations. First, we measured bacterial count and did not distinguish between pathogenic and non-pathogenic bacteria. Even with the use of advanced microbiological techniques such as nucleic acid sequencing it was not possible to identify every organism cultured. However, it seems unlikely that HFNC would have a differential effect on spread of pathogenic and non-pathogenic bacteria. Second, our findings do not apply to bacteria that require special media or prolonged culture. In particular, they do not apply to *M. tuberculosis*. Third, we studied bacteria only and can draw no conclusions about the spread of viruses or fungi. Fourth, the gas flow rate used with the OM was relatively high, although much lower than with HFNC.

HFNC use in patients with Gram-negative pneumonia did not increase airborne and surface GNB contamination compared to an oxygen mask, suggesting that additional infection control measures are not required when using HFNC in patients with GNB pneumonia without co-infection. However, this is a pilot study from one centre with set protocols, and a larger multicentre trial is indicated before definitive recommendations can be made.

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Conflict of interest statement

The BASIC Collaboration, which is administratively and logistically based at the Department of Anaesthesia and Intensive Care, The Chinese University of Hong Kong, has received unrestricted educational grants from Fisher & Paykel Healthcare Limited. C. Gomersall is the chair and G. Joynt is a member of the BASIC steering committee. C. Gomersall, G. Joynt, and C. Leung have received travel grants from the BASIC Collaboration for teaching. The remaining authors declare no conflicts of interests.

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