Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Journal of Hospital Infection 116 (2021) 103—105

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevier.com/locate/jhin

Letter to the Editor

Nasal high-flow oxygen therapy in COVID-19 patients does not cause environmental surface contamination

Sir,

Nasal high-flow oxygen therapy (NHF) may spread the severe acute respiratory syndrome coronavirus (SARS-CoV-2) through respiratory droplets and contact with fomites. This concern leads to significant controversies regarding recommendations for its use in different evidence-based guidelines of therapy in coronavirus infectious disease 2019 (COVID-19) patients [1]. We, therefore, aimed to determine whether NHF use for COVID-19 patients was associated with higher environmental surface SARS-CoV-2 contamination compared with those who were intubated and mechanically ventilated (MV).

We performed an observational, single-centre study initially including 10 consecutive critically ill COVID-19 patients who required intensive care unit (ICU) admission (five NHF and five MV). All patients were admitted to ICU negative-pressure single rooms with 12 air changes per hour. Closed-aspiration systems were used in mechanically ventilated patients. Patients with NHF only wore surgical masks above the NHF cannula when healthcare personnel were inside the room. The Ethics Committee of Vall d'Hebron University Hospital approved this study (PR(AG)225/2020), and the need for informed consent was waived due to the observational nature of the study.

Confirmation of SARS-CoV-2 persistence on environmental surfaces was based on the detection of viral genome by reverse-transcription quantitative polymerase chain reaction (RT-qPCR). Sample collection was performed within the first 24 h of admission and after three days, before the daily room cleaning, from the following sites: bedside monitor, mechanical ventilator screen, computer keyboard, nurse medication trolley, infusion pumps, patient sheet, bed handle, personnel protective equipment (gloves, coat, protection glasses, hat), stethoscope, room floor at 1.5 m distance from the patient, and a filter paper placed immediately before the room high-efficiency particulate air (HEPA) filter. Environmental and equipment surfaces (approximately 5 × 5 cm) were sampled using moistened sterile swabs.

If all samples were negative, inclusion of two additional patients (one of each group (NHF and MV)) was planned. Two more samples were collected for these two additional patients. First, air sampling of room air was performed using a Sartorius MD8 microbiological sampler, containing a gelatine membrane filter for a fixed given sample volume of 1000 L by placing the sampler near the patient (50 cm). After sampling, the filter was immediately sent to the lab where 3 mL of Dulbecco's modified Eagle medium (DMEM; Lonza, Allendale, NJ, USA) was added and frozen at -80°C until the analysis was performed. A second additional sample from the NHF cannula of the non-intubated patient was also obtained. The swabs were transferred immediately into 3 mL of DMEM, sent out to the microbiology laboratory and frozen at -80°C until RT-qPCR analyses were perfiormed. Total nucleic acids were extracted using NucliSENS EasyMAG (BioMérieux, Marcy l'Etoile, France) according to the manufacturer's instructions. Detection of SARS-CoV-2 genome was carried out by a commercial multiplex RT-qPCR assay (TaqMan™ 2019-nCoV Assay Kit v2, Thermofisher, USA).

SARS-CoV-2 samples containing viral RNA, as determined by RT-qPCR, were assessed for the presence of infectious virus by titration in Vero E6 cells (ATCC® CRL384 1586™), as previously reported [2,3]. Vero E6 cells were cultured in DMEM (Lonza) supplemented with 2% foetal calf serum (FCS; EuroClone), 100 U/mL penicillin (ThermoFisher Scientific, Life Technologies), 100 μg/mL streptomycin (ThermoFisher Scientific, Life Technologies), and 2 mM glutamine (ThermoFisher Scientific, Life Technologies).

Direct samples and serial 10-fold dilutions in supplemented DMEM were transferred to Vero E6 monolayers. Plates were monitored daily under a light microscope and wells were evaluated for the presence of cytopathic effect (CPE) at 6 days after infection. Results are expressed as median (25^{th}—75^{th} percentile).

The main characteristics of the patients included in this study are summarized in Table I. Two of the patients were initially included as MV patients (only had samples at day 1 of MV) and subsequent samples were collected when they were supported with NHF after extubation (Cases 1 and 2 among MV patients that correspond to Cases 6 and 8 among NHF patients, respectively). A total of 252 environmental samples were collected from the first 10 patients. No differences between the time of positive nasopharyngeal swab collection and time of environmental sample collection were observed (median of three days (one to five) in NHF and four (three to nine) in MV patients; P=0.222). At the time of first collection, patients with NHF were supported with a median flow of 55 Lpm (50—60) and had a median respiratory rate of 23 (22—24) bpm and a SpO_2/F_IO_2 ratio of 154 (145—192). The RT-qPCR reactions were negative for all the tested surfaces.

An additional 29 samples were obtained from two more patients. Only the sample collected from the NHF cannula was positive for SARS-CoV-2 RNA. This NHF cannula positive sample

https://doi.org/10.1016/j.jhin.2021.04.034

Table I
General characteristics of the population included

Case	Age	SAPS III	APACHE II	No. of quadrants in chest X-ray	D-dimer (ng/mL)	IL-6 (mg/dL)	Type of room	Type of respiratory support	Days from positive RT-qPCR to first sample collection
1	37	23	19	4	171	100	ICU single-room with negative pressure	MV	3
2	56	49	18	2	6329	2359	ICU single-room with negative pressure	MV	3
3	49	13	22	4	221	195	ICU single-room with negative pressure	MV	9
4	55	30	22	4	3177	53	ICU single-room with negative pressure	MV	3
5	71	67	31	4	953	103	ICU single-room with negative pressure	MV	10
6	37	23	20	4	171	100	ICU single-room with negative pressure	NHF	1
7	44	32	21	2	225	108	ICU single-room with negative pressure	NHF	6
8	56	49	18	2	6329	2359	ICU single-room with negative pressure	NHF	5
9	54	25	22	4	1321	4541	ICU single-room with negative pressure	NHF	4
10	69	30	31	4	456	365	ICU single-room with negative pressure	NHF	1
11	72	23	26	2	170	22	Intermediate care, double-room	NHF	1
12	39	38	19	4	3319	2656	ICU single-room with negative pressure	MV	5

APACHE II, Acute Physiology and Chronic Health disease Classification System; IL, interleukin; MV, mechanical ventilation; NHF, nasal high flow; RT-qPCR, real-time reverse-transcription polymerase chain reaction; SAPS III, Simplified Acute Physiology Score.

was inoculated to susceptible Vero E6 cells, but no CPE was observed after a six-day observation period. Therefore, no infectious SARS-CoV-2 was found in any of the environmental samples collected in this study. However, the degree of surface and air contamination from SARS-CoV-2 in a previous study was highly heterogeneous [4]. The singularity of the present study is that it includes the largest data on the environmental persistence of SARS-CoV-2 in the rooms of COVID-19 patients being treated with NHF. Moreover, we compared the environmental contamination associated with NHF use to MV. Lack of environmental contamination in an ICU environment with negative-pressure rooms was observed in both groups. Indeed, it has recently been shown that NHF by itself may not increase aerosol generation in healthy volunteers in a negative-pressure room [5]. Interestingly, despite it being impossible to place living SARS-CoV-2 on a surface to obtain a positive control for obvious safety reasons, we could obtain one positive RT-qPCR from the nasal cannula of one of the non-intubated patients suggesting that the sample collection and PCR technique was correctly performed. These results were similar to the previous results reported by Colaneri *et al.* [6], who obtained a unique positive PCR sample from inside the helmet of one non-intubated patient.

The limitations of this study are that, firstly, air sampling was performed in only two patients and we cannot exclude that with increasing the litres of air sampling, we could probably obtain a positive sample. Secondly, the study was performed in ICU rooms with negative pressure and use of closed-aspiration systems in intubated patients and therefore its results may not be generalizable to other hospital environments.

Despite these limitations, our results suggest that, with adequate infrastructure, NHF does not increase environmental surface contamination in critically ill patients with COVID-19.

Author contributions

O.R., V.R.G. and J.V.A. contributed to the conception and design of the study, the acquisition, analysis and interpretation of the data and drafting the manuscript. A.P. and J.R. contributed to the acquisition, analysis and interpretation of the data and drafting the manuscript. A.A., L.A., M.C., J.S., T.P. and R.F. contributed to the conception and design of the study and interpretation of the data. All authors critically revised and approved the final version of the manuscript.

Conflict of interest statement

O.R. reports speaker fees from Hamilton Medical, Ambu and Aerogen Ltd and a research grant from Hamilton Medical. He also received non-financial research support from Timpel and Masimo Corporation in the last five years all outside the submitted work.

Funding

This study was funded by a grant from Instituto de Salud Carlos III of the Spanish Health Ministry (COV20-01054).

References

[1] Raoof S, Nava S, Carpati C, Hill NS. High-flow, noninvasive ventilation and awake (nonintubation) proning in patients with coronavirus disease 2019 with respiratory failure. Chest 2020;158:1992—2002.

[2] Rodon J, Muñoz-Basagoiti J, Perez-Zsolt D, Noguera-Julian M, Paredes R, Mateu L, et al. Identification of Plitidepsin as potent inhibitor of SARS-CoV-2-induced cytopathic effect after a drug repurposing screen. bioRxiv 2020. https://doi.org/10.1101/2020.04.23.055756. 04.23.055756.

[3] Brustolin M, Rodon J, Rodríguez de la Concepción M, Ávila-Nieto C, Cantero G, Pérez M, et al. Protection against reinfection with D614- or G614-SARS-CoV-2 isolates in hamsters. bioRxiv 2021. https://doi.org/10.1101/2021.01.07.425729. 2021.01.07.425729.

[4] Birgand G, Peiffer-Smadja N, Fournier S, Kerneis S, Lescure FX, Lucet JC. Assessment of air contamination by SARS-CoV-2 in hospital settings. JAMA Open Netw 2020;3:e2033232.

[5] Gaeckle NT, Lee J, Park Y, Kreykes G, Evans MD, Hogan Jr CJ. Aerosol generation from the respiratory tract with various modes of oxygen delivery. Am J Respir Crit Care Med 2020;202:1115—24.

[6] Colaneri M, Seminari E, Novati S, Asperges E, Biscarini S, Piralla A, et al. Severe acute respiratory syndrome coronavirus 2 RNA contamination of inanimate surfaces and virus viability in a health care emergency unit. Clin Microbiol Infect 2020;26:1094.e1—5.

O. Roca[a,b,*]
A. Pacheco[a]
J. Rodon[c]
A. Antón[d]
J. Vergara-Alert[c]
L. Armadans[d]
J. Segalés[e,f]
T. Pumarola[d]
M. Campins[g]
R. Ferrer[a,b]
V. Rodríguez-Garrido[d]

[a]*Servei de Medicina Intensiva, Hospital Universitari Vall d'Hebron, Institut de Recerca Vall d'Hebron, Barcelona, Spain*

[b]*Centro de Investigación Biomédica en Red de Enfermedades Respiratorias (CIBER), Madrid, Spain*

[c]*IRTA, Centre de Recerca en Sanitat Animal (CReSA, IRTA-UAB), Campus de la Universitat Autònoma de Barcelona, Barcelona, Spain*

[d]*Servei de Microbiologia, Hospital Universitari Vall d'Hebron, Institut de Recerca Vall d'Hebron, Barcelona, Spain*

[e]*UAB, Centre de Recerca en Sanitat Animal (CReSA, IRTA-UAB), Campus de la Universitat Autònoma de Barcelona, Barcelona, Spain*

[f]*Departament de Sanitat i Anatomia Animals, Facultat de Veterinària, UAB, Bellaterra (Cerdanyola del Vallès), 08193, Spain*

[g]*Servei de Medicina Preventiva, Hospital Universitari Vall d'Hebron, Barcelona, Spain*

* Corresponding author. Address: Servei de Medicina Intensiva, Hospital Universitari Vall d'Hebron, Passeig de la Vall d'Hebron, 119-129, Barcelona, 08035, Spain.
E-mail address: oroca@vhebron.net (O. Roca)

Available online 31 May 2021