



## Early View

Research letter

### **High-flow nasal oxygen: a safe, efficient treatment for COVID-19 patients not in an ICU**

Tiphaine Guy, Audrey Créac'hcadec, Charles Ricordel, Alexandre Salé, Baptiste Arnouat, Jean-Louis Bizec, Marie Langelot, Christine Lineau, David Marquette, Françoise Martin, Mathieu Lederlin, Stéphane Jouneau

Please cite this article as: Guy T, Créac'hcadec A, Ricordel C, *et al.* High-flow nasal oxygen: a safe, efficient treatment for COVID-19 patients not in an ICU. *Eur Respir J* 2020; in press (<https://doi.org/10.1183/13993003.01154-2020>).

This manuscript has recently been accepted for publication in the *European Respiratory Journal*. It is published here in its accepted form prior to copyediting and typesetting by our production team. After these production processes are complete and the authors have approved the resulting proofs, the article will move to the latest issue of the ERJ online.

Copyright ©ERS 2020. This article is open access and distributed under the terms of the Creative Commons Attribution Non-Commercial Licence 4.0.

**R1-ERJ-01154-2020**

**High-flow nasal oxygen: a safe, efficient treatment for COVID-19 patients not in an ICU**

Tiphaine Guy<sup>1\*</sup>, Audrey Créac'hcadec<sup>1\*</sup>, Charles Ricordel<sup>2,3</sup>, Alexandre Salé<sup>2</sup>, Baptiste Arnouat<sup>1</sup>, Jean-Louis Bizec<sup>1</sup>, Marie Langelot<sup>1</sup>, Christine Lineau<sup>1</sup>, David Marquette<sup>1</sup>, Françoise Martin<sup>1</sup>, Mathieu Lederlin<sup>4,5</sup>, Stéphane Jouneau<sup>2,6</sup>.

\*Both authors equally contributed

<sup>1</sup>Department of Respiratory Medicine, Centre Hospitalier Bretagne Atlantique, Vannes, France

<sup>2</sup>Department of Respiratory Medicine, Competence Centre for Rare Pulmonary Diseases, CHU Rennes, University of Rennes, Rennes, France

<sup>3</sup>INSERM U1242, Chemistry Oncogenesis Stress and Signalling, CLCC Eugène Marquis, 35033 Rennes, France.

<sup>4</sup>Department of Radiology, CHU Rennes, University of Rennes, Rennes, France

<sup>5</sup>LTSI, INSERM U1099, University of Rennes, Rennes, France

<sup>6</sup>University of Rennes, CHU Rennes, INSERM, EHESP, IRSET (Institut de recherche en santé, environnement et travail) - UMR\_S 1085, F-35000 Rennes, France.

## **Introduction**

The new severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that causes coronavirus disease (COVID-19), now recognized by the WHO as a pandemic, emerged in late 2019 in China (1). Patients infected with SARS-CoV-2 can develop severe pneumonia and respiratory failure, which often require treatment in intensive care units (ICU) in Western European countries (2). Oxygen therapy and supportive care are still the main forms of therapy for SARS-CoV-2 pneumonia until suitable anti-infective therapies become available.

Three large clusters of SARS-CoV-2 infected patients were detected in France at the end of February 2020, in the East (Mulhouse, Strasbourg), around Paris (Creil, Compiègne), and in the West (Auray and Crac'h, near Vannes in Brittany). High-flow nasal oxygen (HFNO, Airvo2<sup>TM</sup>, Fisher and Paykel Healthcare) has been a standard therapy for non-hypercapnic acute hypoxemic respiratory failure in Vannes hospital since the publication of the FLORALI

trial in 2015 (3). This report describes the use of HFNO to manage SARS-CoV-2 infected patients with respiratory failure on the pulmonology ward rather than in an ICU.

## Cases

A total of 34 consecutive patients who tested positive for COVID-19 by RT-PCR were admitted to the Respiratory Department. HFNO was systematically initiated when the oxygen flow exceeded 5L/min, then 14 single rooms dedicated to HFNO were rapidly set up (“HFNO unit”) with continuous monitoring of pulsed oxygen saturation. HFNO was required by 27 of the 34 patients, therefore this report will focus on them.

The median (IQR<sub>25-75</sub>) age of patients on HFNO was 77 years (77-79), 81% (22/27) were men, and their median body mass index (BMI) was 25.9 kg/m<sup>2</sup> (23.3-29.4). They were admitted within a median of 7 days (3-8) after the first SARS-CoV2 symptoms appeared.

The median PaO<sub>2</sub>/FiO<sub>2</sub> ratio was 203 (198-286) at admission, and 124 (120/158) immediately prior to HFNO initiation. The median time from admission to HFNO initiation was 2 days (1-3) and the median duration of HFNO was 6 days (2-10). The median Airvo2<sup>TM</sup> total flow was 55L/min (50-60) and the median FiO<sub>2</sub> was 65% (60-70). We used « targeted » oxygen therapy to avoid over oxygenation, and our targeted SpO<sub>2</sub> was between 92 and 94%.

As of March 31, 19 patients (70%) were weaned from HFNO, 4 (15%) were still on HFNO, and 4 (15%) had died (Figure 1). Of the 19 patients weaned from HFNO, 9 had returned home after a median hospital stay of 17 days (14-22), 6 were transferred to a rehabilitation unit, and 4 remained on the ward with reduced oxygen (less than 3L/min). Of the 4 unweaned patients, 2 remained on HFNO unit and 2 were transferred to the ICU. Of the 4 deceased patients, 1 died after 6 days of mechanical ventilation (decision to limit life sustaining therapy in ICU), while the other 3 were not transferred to ICU due to severe comorbidities. Altogether, 7 out of 27 patients (26%) had their respiratory status deteriorated on HFNO and were transferred to ICU where they were mechanically ventilated for a median of 7 days (5-12).

As HFNO can generate infectious aerosols, all health care workers (HCWs) in contact with patients treated with HFNO were taught airborne precautions. The personal protection equipment (PPE) was composed of FFP2 masks (reference M52010-WH, KOLMI<sup>®</sup>, St Barthélemy d’Anjou France), hospital suits (fabric pajamas changed every day), disposable gowns with waterproof aprons, gloves, overshoes, and eye and head protections. The patients themselves also wore surgical masks when an HCW entered their room. Surgical masks have been mandatory for all HCWs while they were on the Vannes hospital site since March 2, 2020. Only one of the 44 HCWs (7 pulmonologists, 20 nurses, 12 caregivers, 3 physiotherapists, 1 dietitian, and 1 psychologist), a nurse, had become infected by April 5, 2020. However, domestic contamination is suspected since this nurse was living with his parents, who had previously been infected via the Eastern France cluster. All three of them tested positive for SARS-CoV-2. No other HCW was absent from work or presented any symptoms of COVID-19.

## **Discussion**

The use of HFNO in COVID-19 raises two issues: its safety and its effectiveness. The theoretical risk of virus aerosolization resulted in early published reports of critically ill SARS-CoV-2-infected patients in China not recommending the use of HFNO or non-invasive ventilation until the patient had been cleared of COVID-19 (4). However, clinical evidence is scarce. Recent guidelines for the clinical management of severe pneumonia following a SARS-CoV-2 infection do not exclude the use of HFNO with maximal precautions to exclude airborne transmission (weak recommendation) (5). And a 2012 meta-analysis found no increased risk of HCWs being infected with SARS when using HFNO (6). In fact, HFNO seemed to have a protective effect, suggesting that avoiding intubation reduced the risk of transmission. More recently, some have recommended using HFNO for patients with moderately severe hypoxaemia, which might make intubation unnecessary, or at least delay it (7).

The only nurse infected with SARS-CoV-2 in the present study was probably contaminated by his parents. If so, none of the HCWs on this 14-bed unit were infected with HFNO after a 30-day follow-up. As the median incubation time is 5 days (8), it seems likely that using HFNO to treat COVID-19 patients requiring oxygen (> 5L/min) was safe for HCWs at our institution. However, there is still a risk of aerosolization and all HCWs were required to wear personal protective equipment, not just FFP2 masks, when using HFNO. Hydro-alcohol handwash and “social distancing” are also major tools for avoiding infection. Above all, the experience of HCWs with HFNO management and continued training in anti-airborne precautions undoubtedly help minimize the risk of contamination in the respiratory unit.

The results of this monocentric study (23/27 patients recovered, 19/27 weaned from HFNO, including 9 discharged) suggest that HFNO is effective. However, further confirmatory studies at other centres are urgently needed. Our 15% in-hospital mortality rate is similar to the 14% recently published from a French 3-year multicenter prospective study which included adults admitted with influenza and influenza-like illness (9). Managing infected patients with HFNO could save critical ICU resources, including access to mechanical ventilation, in the context of a large-scale COVID-19 outbreak. HFNO allows patients to feed more easily than when on other forms of oxygen supplementation, particularly mechanical ventilation, and facilitates respiratory/bronchial physiotherapy and muscle rehabilitation. Mechanical ventilation may require curarization and thus induce additional muscle loss. Another positive feature of HFNO is that patients can continue talking and interacting with their family and HCWs. This is psychologically very important for everyone involved.

## **Conclusion**

While these results should be confirmed in larger studies, we believe that our data strongly suggest that SARS-CoV2 infected patients with non-hypercapnic acute hypoxemic respiratory failure can benefit from HFNO outside an ICU. The technique appears to be safe for HCWs and could well liberate critical ICU resources.

## References

1. WHO Director-General's opening remarks at the media briefing on COVID-19 - 18 March 2020 2020 [Available from: <https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---18-march-2020>].
2. Grasselli G, Zangrillo A, Zanella A, Antonelli M, Cabrini L, Castelli A, et al. Baseline Characteristics and Outcomes of 1591 Patients Infected With SARS-CoV-2 Admitted to ICUs of the Lombardy Region, Italy. *JAMA*. 2020.
3. Frat JP, Thille AW, Mercat A, Girault C, Ragot S, Perbet S, et al. High-flow oxygen through nasal cannula in acute hypoxemic respiratory failure. *N Engl J Med*. 2015;372(23):2185-96.
4. Cheung JC, Ho LT, Cheng JV, Cham EYK, Lam KN. Staff safety during emergency airway management for COVID-19 in Hong Kong. *Lancet Respir Med*. 2020;8(4):e19.
5. Alhazzani W, Moller MH, Arabi YM, Loeb M, Gong MN, Fan E, et al. Surviving Sepsis Campaign: guidelines on the management of critically ill adults with Coronavirus Disease 2019 (COVID-19). *Intensive Care Med*. 2020.
6. Tran K, Cimon K, Severn M, Pessoa-Silva CL, Conly J. Aerosol generating procedures and risk of transmission of acute respiratory infections to healthcare workers: a systematic review. *PLoS One*. 2012;7(4):e35797.
7. Matthay MA, Aldrich JM, Gotts JE. Treatment for severe acute respiratory distress syndrome from COVID-19. *Lancet Respir Med*. 2020.
8. Lauer SA, Grantz KH, Bi Q, Jones FK, Zheng Q, Meredith HR, et al. The Incubation Period of Coronavirus Disease 2019 (COVID-19) From Publicly Reported Confirmed Cases: Estimation and Application. *Ann Intern Med*. 2020.
9. Benezit F, Loubet P, Galtier F, Pronier C, Lenzi N, Lesieur Z, et al. Non-influenza respiratory viruses in adult patients admitted with influenza-like illness: a 3-year prospective multicenter study. *Infection*. 2020.

## Figure Legends

**Figure 1:** Graphic representation of the 27 COVID-19 patients treated with high-flow nasal oxygen (HFNO) in pulmonology department of Vannes hospital, France. Main outcomes are reported such as intensive care unit (ICU) admission, orotracheal intubation (OTI), or death.

