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High-flow oxygen therapy in elderly patients infected with SARS-CoV2 with a contraindication for transfer to an intensive care unit: A preliminary report

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ABSTRACT

Objectives: In a conventional hospital ward, we used high-flow nasal oxygen (HFNO) to treat elderly COVID-19 patients noneligible for intensive care unit transfer.

Methods: This study was conducted in the Institut Hospitalo-Universitaire Méditerranéenne Infection, Assistance Publique-Hôpitaux de Marseille (AP-HM), France. We used high-flow nasal oxygen (HFNO) in our conventional infectious disease ward from 15 September 2020 for elderly patients noneligible for intensive care unit transfer.

Results: Of the 44 patients (median age 83 years [57–94], mean: 80.25), 61.4% (27/44) were men. The median Charlson score was 7 (1–15). The median of the NEWS-2 score upon admission was 8 (3–11) and was 10 at the time of initiation of HFNO. The median PaO2/FiO2 ratio was 103 (71–151) prior to HFNO initiation. Among the 44 patients, 16 patients (36.4%) had been weaned from HFNO, and 28 patients had died (63.6%).

Conclusions: In this preliminary report, we observed that HFNO saved the lives of one-third of elderly COVID-19 patients who would have systematically died.

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Introduction

COVID-19 has emerged as a world pandemic that has caused more than 2.7 million deaths and has infected 124 million people worldwide (Johns Hopkins University, 2021). Severe infections occur in patients over 65 years of age who are suffering from comorbidities and most deaths have occurred in patients over 80 years of age (Lagier et al., 2020). The most common complication is severe pneumonia with acute respiratory distress syndrome requiring admission to intensive care units, which have limited availability in a pandemic context.

There is uncertainty in the management of COVID-19 between the need to conduct therapeutic trials and the need to focus on the quality of care. A considerable difference has emerged in the way in which Asian and Western countries have managed the pandemic, resulting in a conflict between a pragmatic approach and an almost virtual approach to a previously unknown disease. This may largely explain the higher mortality from COVID-19 in Western countries such as France at the beginning of the outbreak, where some patients were unfortunately offered either a therapeutic trial or the prospect of doing nothing and staying at home, to await the onset of dyspnoea (Lagier et al., 2020). However, patient management was considerably improved by the quality of care when an early diagnosis was reached (Risch, 2020), when we evaluated “happy hypoxemia” and observed lesions by performing low-dose CT (Lagier et al., 2020; Brouqui et al., 2020), and when we detected coagulation disorders by measuring D-dimers independently of any antiviral treatment, regardless of whether they were evaluated by a randomised clinical trial (Lagier et al., 2020). This pragmatic approach allowed us to maintain very low mortality in our institute (Lagier et al., 2020), as well as in our intensive care facility (<15%, personal data) (Lagier et al., 2020).

Nevertheless, one weak point remained the management of patients with comorbidities and/or those who were of an age that did not allow them to be transferred to intensive care. For these

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patients noneligible for an ICU but who presented with refractory hypoxemia not responding to conventional oxygen support, we used high-flow nasal oxygen (HFNO) in our conventional infectious disease ward from 15 September 2020. Here, we report the use of HFNO to manage these SARS-CoV2 patients.

Material and methods

Patients

This study was conducted in the Institut Hospitalo-Universitaire Méditerranée Infection, Assistance Publique-Hôpitaux de Marseille (AP-HM). As previously described, we proposed early massive screening and standardised management of the patients in the day-care hospital or in one of the infectious diseases wards of our hospital (75 beds). From 15 September 2020, we were equipped with HFNO (Airvo2®, Fisher and Paykel Healthcare, Villebon sur Yvette, France) which became a standard therapy for acute hypoxemic non-hypercapnic respiratory insufficiency. Data were retrospectively collected and analysed from 15 September to 1 December 2020. Severity was assessed using the National Early Warning Score adapted to COVID-19 patients (NEWS-2) as well as the Charlson score, as previously described (Liao et al., 2020; Charlson et al., 1987).

Inclusion criteria

Patients had to have been not eligible for an ICU transfer due to their age and/or severe comorbidities but, prior to their infection with COVID-19, had to be living independently at home. The decision for beginning HFNO was systematically taken by both infectious disease and ICU physicians.

Ethics

The study was conducted in the Institut Hospitalo-Universitaire (IHU) Méditerranée Infection (https://www.mediterranee-infection.com/), Assistance Publique-Hôpitaux de Marseille in the south of France. Data were collected retrospectively from the routine care setting using the hospital’s electronic health recording system. According to European General Data Protection Regulation No 2016/679, patients were informed of the potential use of their medical data and that they could refuse that their data be used. The analysis of collected data followed the MR-004 reference methodology registered under No. 2020-152 in the AP-HM register. The noninterventional retrospective nature of the study was approved by our institutional review board committee (Mediterranée Infection No.: 2021-009).

Results

Between 14 September 2020 and 1 December 2020, 44 patients were treated using 24 h a day HFNO. Patients were fed normally. One patient who died had a potential contraindication (hypercapnia) for the use of HFNO, but the indication was decided jointly with ICU specialists because of absence of other therapeutics with the objective of increased comfort of the patient. Of the 44 patients, the median age of patients treated with HFNO was 83 years (57–94, mean: 80.25) and 61.4% (27/44) were men (Table 1). Patients were admitted to our ward within a median of seven days (1–14) after the first COVID-19 symptoms appeared. The median Charlson score was 7 (1–15) and only two patients had a score <4. In the medical history of these two patients, one suffered from Down syndrome with obstructive sleep apnoea and obesity, and the other had polycythaemia complicated by acute pulmonary embolism. The median of the NEWS-2 score [2] upon admission was 8 (3–11) and was 10 at the time of initiation of HFNO. The median time from admission to HFNO initiation was three days (0–9 days). The mean level of oxygen flow before initiation of HFNO was 12.7 L/min (7 L/min to 15 L/min). The median PaO2/FiO2 ratio was 103 (71–151) prior to HFNO initiation. C-reactive protein ranged from 28 to >350 mg/L (mean of 146 mg/L). Among the 44 patients, 16 patients (36.4%) had been weaned from HFNO, and 28 patients had died (63.6%). Of the 16 patients who were weaned, the mean duration of HFNO treatment was 10 days (4–25 days). Ten of these 16 patients were transferred to a rehabilitation unit, three were transferred in other hospitalization wards and three returned home or to their retirement home.

Discussion

Here, we demonstrate that HFNO can be used as oxygen therapy supportive care for COVID-19 infection, outside the ICU, as recently highlighted in another French cohort (Guy et al., 2020). The specificity of our cohort is the severity of our patients noneligible for transfer to the ICU. In contrast to one recent report (Guy et al., 2020), we demonstrated that this technique may be effective in elderly patients and/or in patients with many comorbidities highlighted by an increased Charlson score, and who are contra-indicated for an ICU transfer. Despite this, more than a third of such patients who would die in all cases without HFNO were saved. In addition, patient comfort was optimised, as previously described.

This approach taken was pragmatic, focusing on improving the quality of care and outside of any randomised trial which would have been entirely unethical, given the severity of our patients' conditions and which is not useful in the context of an emerging pandemic, as previously described (Frieden, 2017). We chose a step-by-step implementation of our therapeutic management strategy. From the beginning of the disease, we decided to test patients at an early stage and on a massive basis, using PCR (Lagier et al., 2020). Secondly, we proposed the use of an antiviral treatment, followed by anticoagulation treatment and anti-inflammatory treatment for late stages of COVID-19 infections (Lagier et al., 2020). The use of HFNO is a new step in the care of these patients, further reducing mortality. Regarding the entire management of COVID-19 patients and to avoid the use of such techniques, the earliness of the diagnosis and the management remain key. Some authors have reported that the use of supplemental oxygen in prehospital care can play a role to reduce risk of hospitalization and death (Mc Cullough et al., 2020,2021).

Table 1

| Baseline characteristics of the 44 patients. | N (%) |
|----------------|----------------|
| Age (Mean, Median) | 80.25 y (83 y) |
| <65 y | 3 (6.8%) |
| 65–75 y | 7 (15.9%) |
| 75–85 | 24 (54.6%) |
| >85 y | 10 (22.7%) |
| Charlson score | |
| 1–5 | 9 (20.5%) |
| 6–8 | 32 (72.7%) |
| >9 | 3 (6.8%) |
| NEWS-2 score (admission) | |
| <3 | 4 (9.1%) |
| 4–6 | 8 (18.2%) |
| 7–10 | 27 (61.4%) |
| >10 | 5 (11.3%) |
| NEWS-2 score (at the time of HFNO initiation) | |
| <3 | 0 |
| 4–6 | 1 (2.3%) |
| 7–10 | 22 (50%) |
| >10 | 21 (47.7%) |
Close monitoring is required for these patients (Mc Cullough et al., 2020, 2021). In our experience, we prefer to initiate oxygen supplementation during hospitalization.

This preliminary report demonstrated the contribution of HFNO for the management of elderly patients contraindicated for an ICU transfer. Future studies including a larger number of patients and in depth clinical analysis will be interesting to confirm the contribution of HFNO in elderly COVID-19 patients. Issues to be addressed in the future will include a) optimising patient selection and being able to start HFNO earlier in order to increase the proportion of survivors; b) performing a long-term follow-up of elderly COVID-19 infected patients treated with HFNO.

Conflicts of interest

The authors have no conflicts of interest to declare.

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References

Brouqui P, Amrane S, Million M, Cortaredona S, Parola P, Lagier JC, et al. Asymptomatic hypoxia in COVID-19 is associated with poor outcome. Int J Infect Dis 2020;102 (October)233–8, doi:http://dx.doi.org/10.1016/j.ijid.2020.10.067 Online ahead of print.

Charlson ME, Pompei P, Ales KL, Mackenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis 1987;40:373–83.

Frieden TR. Evidence of health decision making-beyond randomized controlled trials. N Engl J Med 2017;377:465–75.

Guy T, Créachcáide C, Ricordel C, Salé A, Arnoux B, Bizet JL, et al. High-flow nasal oxygen: a safe, efficient treatment for COVID-19 patients not in an ICU. Eur Respir J 2020;September2001154, doi:http://dx.doi.org/10.1183/13993003.01154-2020 Online ahead of print. PMID: 32859678. Free PMC article.

Lagier JC, Million M, Gautret P, Colson P, Cortaredona S, Giraud-Gatineau A, et al. Outcomes of 3,737 COVID-19 patients treated with hydroxychloroquine/ azithromycin and other regimens in Marseille, France: a retrospective analysis. Travel Med Infect Dis 2020;36(July–August):101791, doi:http://dx.doi.org/10.1016/j.tmaid.2020.101791 Epub 25 June 2020.

Liao X, Wang B, Kang Y. Novel coronavirus infection during the 2019–2020 epidemic: preparing intensive care units—the experience in Sichuan Province, China. Intensive Care Med 2020;46:357–60.

McCullough PA, Alexander PE, Armstrong R, Avintz C, Bain AF, Bartlett RP, et al. Multifaceted highly targeted sequential multidrug treatment of early ambulatory high-risk SARS-CoV-2 infection (COVID-19). Rev Cardiovasc Med 2020;21(December (4))517–30, doi:http://dx.doi.org/10.31083/jrcm.2020.04.264 PMID: 33387997.

McCullough PA, Kelly RJ, Ruocco G, Lerna E, Tumlin J, Wheelan KR, et al. Pathophysiologic basis and rationale for early outpatient treatment of SARS-CoV-2 (COVID-19) infection. Am J Med 2021;134(January (1)):16–22. doi: http://dx.doi.org/10.1016/j.amjmed.2020.07.003 Epub 7 August 2020. PMID: 32771461; PMCID: PMC7410805.

Risch HA. Early outpatient treatment of symptomatic, high-risk Covid-19 patients that should be ramped-up immediately as key to the pandemic crisis. Am J Epidemiol 2020;May;kwa093, doi:http://dx.doi.org/10.1093/aje/kwa093 Online ahead of print.