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Hyperoxemia and excessive oxygen use in COVID-19-related ARDS: preliminary results of a prospective cohort study

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TO THE EDITOR:

Patients with severe COVID-19 pneumonia commonly fulfill the ARDS Berlin definition[1,2] and must be ventilated using protective parameters to avoid ventilator-induced lung injury.[3,4] A target SaO_2 of 92-96% is recommended,[5] because an SaO_2 < 92% or > 96% might be harmful.[6,7]

Experimental studies have demonstrated that exposure to high FiO_2 can induce pulmonary inflammation due to excessive production of reactive oxygen species.[8] Moreover, hyperoxemia (i.e., increased PaO_2) has deleterious systemic effects, such as reduced cardiac output and vasoconstriction in cerebral and coronary circulation.[9] Despite such risks, hyperoxemia and excessive oxygen use are common in patients with ARDS.[10]

During the COVID-19 pandemic, excessive oxygen use causes an additional problem: oxygen shortage. The great number of patients requiring ventilatory support simultaneously may compromise oxygen stocks. In this scenario, avoiding hyperoxemia and excessive oxygen use become an important strategy to spare oxygen. We hypothesized that hyperoxemia and excessive oxygen use might be common events in intubated COVID-19 patients. Therefore, our objective was to determine the frequency of such events during the first two days of mechanical ventilation (MV) in patients with COVID-19.

This is a preliminary analysis from a prospective cohort study that has been conducted in two dedicated COVID-19 ICUs (at the University Hospital of the Federal University of Juiz de Fora and at Hospital Regional Doutor João Penido, both located in the city of Juiz de Fora, Brazil) since 2020, March 1st. The objective of the main study is to describe MV parameter settings in COVID-19 patients. The study was approved by the research ethics committees of the two institutions, and written informed consent was obtained from the next of kin or guardian of the patient.

Consecutive patients ≥ 18 years of age, infected with SARS-CoV-2 (confirmed by RT-PCR), and receiving invasive MV for at least 48 h were eligible for participating in the study. We excluded patients transferred from another hospital who had been on invasive MV, patients for whom life-sustaining treatments were withheld, and patients with hypoxemia (PaO_2 < 55 mmHg regardless of the FiO_2) on day 1 of MV. Ventilatory parameters were set by the attending physician.

Clinical and laboratorial parameters were obtained on the day of admission to the ICU. On day 1 and day 2 of MV (at 8 a.m.), MV parameter settings and arterial blood gas measurements, were recorded. We defined hyperoxemia as a PaO_2 > 100 mmHg and excessive oxygen use as an FiO_2 > 60% in patients with hyperoxemia. Sustained hyperoxemia was defined as the presence of hyperoxemia on days 1 and 2 of MV.

Results are reported as medians and interquartile ranges or absolute and relative frequencies. Differences between patients with normoxemia and those with hyperoxemia were tested using the Wilcoxon test or the chi-square test, as appropriate.

During the study period, 239 patients with confirmed COVID-19 were admitted to one of the ICUs. Of those, 122 were excluded: 82 patients did not receive invasive MV, 24 received invasive MV for less than 48 h, 14 had life-sustaining treatments withheld, and 2 were hypoxemic on day 1. Therefore, 117 patients were included in the study. The median age of the patients was 66 (58-75) years, and 61 (52.1%) were male. On admission, the median Simplified Acute Physiology Score 3 was 48 (41-57), and the median Charlson comorbidity index was 3 (2-5). On day 1 of MV, the medians of the following parameters were: PaO_2/FiO_2 = 191 (142-248) mmHg; plateau pressure = 24 (22-28) cmH_2O; driving pressure = 14 (11-16) cmH_2O; PEEP = 10 (10-12) cmH_2O; and respiratory system compliance = 29.3 (24.7-35.6) mL/cmH_2O. During the period on MV, 72 patients (62%) were placed in the prone position, and 40 patients (34%) needed hemodialysis. All-cause hospital mortality was 63.0%, and ICU mortality was 59.3%.

Hyperoxemia was present in 80 (68.4%) and 74 (63.2%) of the patients on days 1 and 2 of MV, respectively, regardless of FiO_2 ranges. Of the 80 patients with hyperoxemia on day 1, 53 (66.3%) sustained a PaO_2 > 100 mmHg on day 2. Cumulative relative frequency distributions of PaO_2 were similar on days 1 and 2 (Figure 1).

FiO_2 levels decreased on day 2, when compared with those on day 1, in patients with hyperoxemia (Figure 1). There was a reduction in excessive oxygen use on day 2 (28 patients [23.9%]) when compared with that on day 1 (43 patients [36.8%]; p = 0.03; Figure 1). However, there was an increase in the number of patients with hyperoxemia among those with an FiO_2 < 0.6 (46 patients on day 2 vs. 37 on day 1; Figure 1). Together, these findings suggest that intensivists neglected to decrease FiO_2 when gas exchange improved.

The proportion of patients with hyperoxemia in our cohort was higher than that found in a similar study

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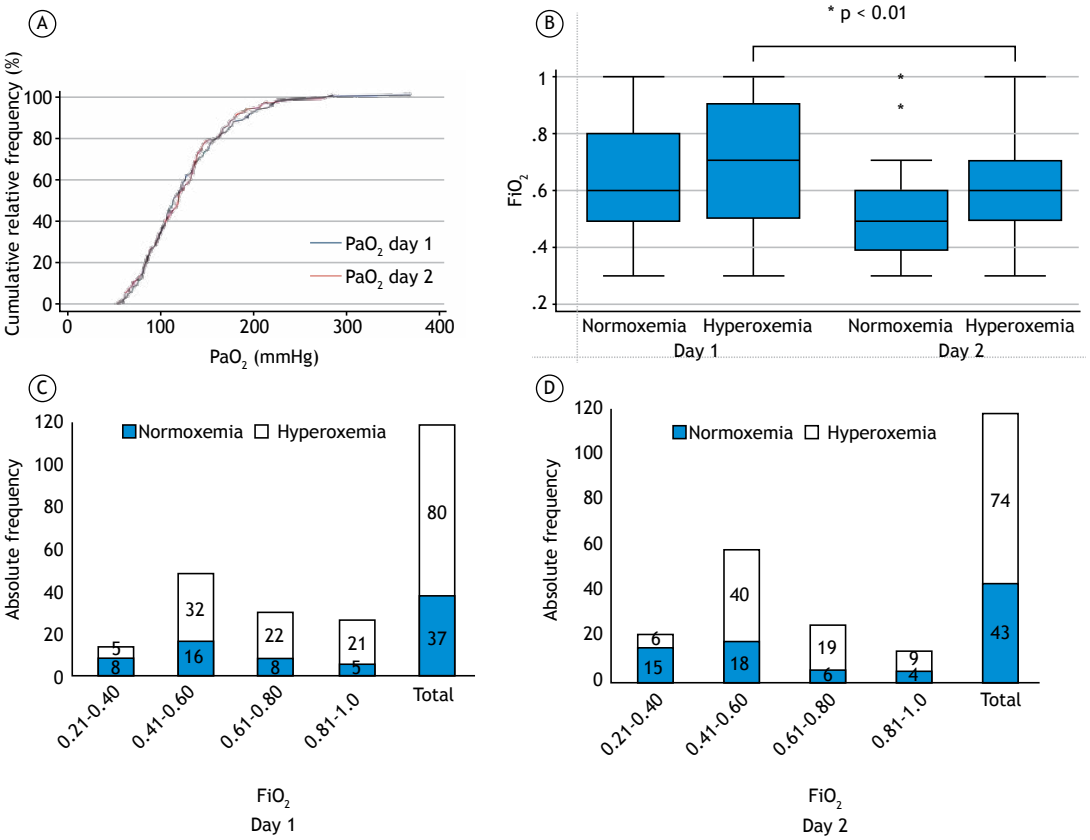

Figure 1. In A, a graph showing that cumulative relative frequency distributions of PaO_2 were similar on day 1 (blue line) and day 2 (red line) of mechanical ventilation (MV). In B, box plot showing FiO_2 levels on days 1 and 2 of MV and classified by the presence of normoxemia or hyperoxemia. There was a significant decrease in FiO_2 on day 2, when compared with that on day 1, among patients with hyperoxemia ($p < 0.01$). In C and D, histograms showing absolute frequencies of normoxemia or hyperoxemia in different ranges of FiO_2 on days 1 (in C) and 2 (in D) of MV.

including patients with ARDS due to other causes.[10] In that study,[10] 30% of the patients presented with hyperoxemia on day 1 of MV; among those, FiO_2 was high in 66%. The great number of patients admitted to ICUs during the COVID-19 pandemic, resulting in work overload of health care professionals, might explain that difference. Moreover, the necessity of using personal protective equipment may reduce the frequency at which COVID-19 patients are seen by physicians, nurses, and respiratory physical therapists, as well as the frequency at which mechanical ventilator settings are adjusted.

During the COVID-19 pandemic, some hospitals have run out of oxygen in Brazil. Our results show the importance of optimizing PaO_2 and FiO_2 levels during the ventilatory support of COVID-19 patients. That can be a useful strategy to minimize the shortage of oxygen.

The present study has limitations. Our analyses were based on arterial blood gas analysis and FiO_2 that were determined at a specific time each day; therefore, they might not reflect the spectrum of values that occurred throughout that day. In addition, we evaluated hyperoxemia and high FiO_2 only in the first two days of MV, and we cannot rule out the possibility that settings after day 2 of MV might have interfered on final outcomes.

In conclusion, hyperoxemia and excessive oxygen use are events that might be common during the first days of MV in COVID-19 patients. Avoiding the occurrence of these events should be used as a strategy to reduce oxygen shortage.

AUTHOR CONTRIBUTIONS

EPG: study conception and design; data acquisition, analysis, and interpretation; drafting and revision of preliminary versions; and approval of the final version. MMR: data analysis and interpretation; drafting and revision of preliminary versions; and approval of the final version. GBC: data acquisition, analysis, and interpretation; revision of preliminary versions, providing intellectual content of critical importance; and approval of the final version. EVC: study conception and design; data acquisition; revision of preliminary versions, providing intellectual content of critical importance; and approval of the final version. BVP: study conception and design; data analysis and interpretation; drafting and revision of preliminary versions; and approval of the final version.

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