Impact of an Improvised System on Preserving Oxygen Supplies in Patients With COVID-19

Impacto de un sistema improvisado para conservar los suministros de oxígeno en pacientes con la COVID-19

Dear Editor,

Hypoxaemia is a typical feature of the coronavirus disease 2019 (COVID-19). The rapid rise in the number of patients requiring oxygen therapy during the pandemic may cause a sharp increase in oxygen demands and potential threats of supply disruption, particularly in developing countries[1] or nursing homes. Moreover, the use of elevated oxygen flows via nasal cannula raises concerns about exhaled air dispersion distance and the potential risk of generating aerosols.[2–6]

The Double-Trunk Mask (DTM) (image and description in supplement) is a patent-free handmade system which, when placed over nasal cannula, increases the PaO_2 by 50% in patients with acute respiratory failure without clinical impact on $PaCO_2$.[7] From another perspective, the DTM may reduce the oxygen flow required to correct hypoxaemia which, in addition to reducing side-effects of prolonged dry oxygen administration,[8–10] could have crucial implications in situations where medical gases are a rare commodity. The study's objective was to assess the efficacy of the DTM in preserving oxygen consumption in patients with COVID-19.

All adult patients with laboratory-confirmed COVID-19 and hypoxaemia requiring low-flow oxygen therapy (LFOT) $\leq$15 L/min to maintain SpO_2 between 92 and 96%, who were consecutively hospitalized between April and May 2020 in our hospital, were asked to participate in the study.

This ClinicalTrials.gov registered study (NCT04346420) was conducted with the approval of the local ethics committee. All subjects signed informed consent. Exclusion criteria were chronic respiratory diseases, language barriers, confusion, altered consciousness (Glasgow Coma Scale $\leq$12), hypoxaemia corrected with oxygen flow $\leq$3 L/min and any contra-indication to arterial puncture.

Patients were in a semi-recumbent position and received LFOT through their standard oxygen delivery method. The initial oxygen flow and delivery system were determined in accordance with our standard practice. The baseline oxygen flow was titrated to achieve a target SpO_2 value of 94% at the lowest output. Oxygen flow requirements determined the baseline oxygen delivery system (supplements). The baseline delivery system was then replaced by the DTM covering nasal cannula for 30 min. Oxygen output (primary outcome) was adjusted to achieve the same SpO_2 target as at baseline. After this period, the DTM was withdrawn and the standard oxygen delivery system was reinstated for 30 min. Oxygen output was readjusted to achieve the baseline SpO_2 value. Patients received no instructions regarding nasal or mouth breathing during the whole process. Arterial blood gases, vital parameters and oxygen output were measured at baseline (T_0) and at the end of the 30-min DTM period (T_{30}). Vital parameters and oxygen output were measured again 30 minutes after the DTM was withdrawn (T_{60}). Comfort-discomfort level with each system was assessed at T_{30} and T_{60} (supplements).

Eleven subjects were needed to detect a mean difference of 2 L/min[11] (SD, 1.8 L/min) in oxygen output (α-risk, 0.05; power, 90%). Because SpO_2 may inaccurately reflect arterial oxygen saturation (SaO_2) and therefore interfere with our design, patients were retrospectively excluded from the analysis if SpO_2-SaO_2 mismatch exceeded the expected error of 4%.[12,13] Data are presented as mean $\pm$ SD or median [interquartile range (IQR)] as appropriate. Pairwise comparisons were tested with paired *t*-test or Wilcoxon test. Ordinal paired data were compared with Wilcoxon test. *P*-values < 0.5 were considered statistically significant.

Of 12 patients who completed the entire study procedure, one was excluded from the analysis because SpO_2-SaO_2 difference at T_0 was 4.3%. Final analyses were performed on 11 patients (61 $\pm$ 14 years; 27% female). E-Table 1 details baseline characteristics. Compared with standard delivery systems, the oxygen output was significantly reduced with the DTM (median [IQR], 5 [4–8] L/min vs 1.5 [1.5–4] L/min; $p = 0.003$) when oxygen saturation and PaO_2 remained stable. The DTM was also associated with a significant but slight increase in $PaCO_2$ (median, 36 vs 37 mmHg, $p = 0.006$), a decrease in pH (median, 7.48 vs 7.45, $p = 0.009$) and an increase in respiratory rate (mean, 26 vs 30 breaths/min, $p = 0.05$), Fig. 1, e-Table 2. Other parameters were unaltered. The DTM was generally considered less comfortable than the baseline oxygen delivery system, especially in patients requiring low oxygen flow at baseline (e-Fig. 2). There were no differences between T_0 and T_{60} for any outcomes (e-Table 2), indicating that all values were reset when the standard delivery system was reinstated.

Treating hypoxaemia is the cornerstone of COVID-19 patient management and this pre-post intervention trial shows that the DTM enables clinicians to safely treat severe hypoxaemia while reducing the oxygen flow by more than half that required with conventional delivery systems. Therefore, settings in which oxygen supplies are limited (e.g. nursing homes, healthcare centres in deprived medical areas, during patient transport) may benefit most from the DTM. Although evaluation of its place relative to the non-rebreathing mask, high-flow oxygen therapy or non-invasive ventilation was not within the scope of this study, we believe the DTM could also be considered when SpO_2 falls below the target value with standard LFOT systems.[7,11] Consequently, the need for non-invasive respiratory support, which increases risks of generating aerosols,[6] may possibly be avoided.

The DTM was considered less comfortable than LFOT delivered through nasal cannulas, yet patients who initially required high oxygen flow considered the DTM as equally comfortable. This might be explained by using a facemask at baseline or the large absolute oxygen flow reduction with the DTM. However, the low number of patients wearing oxygen facemasks at baseline precludes generalization of our conclusions with these systems.

The importance of our findings is emphasized by the large oxygen flow reduction under the DTM (56%) and the high proportion of hospitalized patients who met the inclusion criteria at some point of their stay (266/412). The main limitation was the pre-post intervention design of short duration. Moreover, the investigator who readjusted oxygen flow was not blinded in order to limit prolonged and multiple exposures of healthcare workers. Randomized controlled trials of longer duration involving a broader range of oxygen flows are required.

In conclusion, our study showed that the DTM is a useful oxygen delivery system that enables a safe reduction in oxygen output without hampering patient oxygenation. This finding is of particular interest in the current context of high and potentially overwhelming oxygen demand.

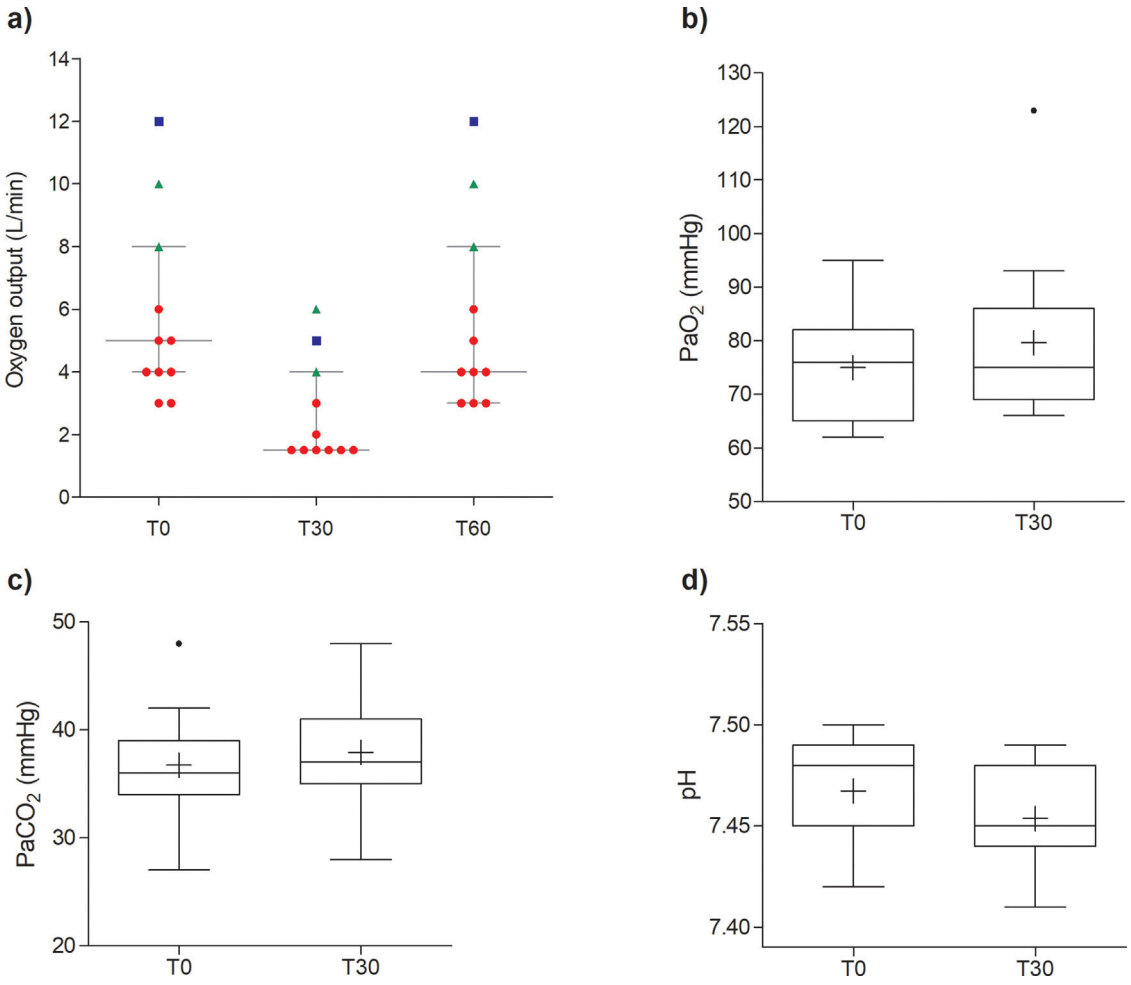

Fig. 1. Change of oxygen output and blood gas outcomes. (a) Panel shows raw values of oxygen flow before (T_0) and after (T_{30}) wearing the double-trunk mask, as well as after reinstating the baseline oxygen delivery system (T_{60}). Horizontal lines indicate median, 25th and 75th percentiles. The shape of each data point represents the baseline oxygen supply system: circles for nasal cannula, triangles for oronasal mask and square for the non-rebreathing mask. (b–d) Panels show respectively PaO_2, $PaCO_2$ and pH outcomes before (T_0) and after (T_{30}) wearing the double-trunk mask. The boxes indicate 25th and 75th percentiles; horizontal lines and "+" within boxes indicate median and mean, respectively; whiskers indicate the highest and lowest values within 1.5× interquartile range; and points beyond the whiskers indicate outliers.

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Conflict of interest

None.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.arbres.2020.07.019.

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The Value of C-Reactive Protein-to-Lymphocyte Ratio in Predicting the Severity of SARS-CoV-2 Pneumonia

Valor del ratio proteína C-reactiva-linfocitos para predecir la gravedad de la neumonía causada por SARS-CoV-2

Dear Editor,

Clinical severity of COVID-19 infections ranges widely, from asymptomatic or mild disease of the upper airways to pneumonia and acute respiratory distress syndrome (ARDS).[1–3] We aim to describe biological features and outcomes of 240 patients admitted for SARS-CoV-2 pneumonia, as well as identify predictors of intensive care unit (ICU) admission (either direct admission or transfer to ICU within 96 h of admission from emergency department), need for invasive mechanical ventilation (IMV) and in-hospital mortality.

For this retrospective, observational study, all consecutive patients with laboratory-confirmed SARS-CoV-2 infection and pneumonia (positive result by real-time polymerase chain reaction testing of a oropharyngeal plus nasopharyngeal sample[4]), who visited the emergency department and were subsequently admitted to the hospital between February 28th and April 21st, 2020, were included. Patients without pneumonia were excluded. The Institutional Ethics Board approved this study and due to its nature, waived the need for informed consent. Clinical outcomes were monitored until May 15th, 2020. Patients were divided into two groups: non-ICU and ICU-admitted (either direct admission or transfer to ICU within 96 h of admission from emergency department).

Descriptive statistics were used for basic features of study data; appropriate statistical tests were performed to compare both groups. Univariate and multivariable binary logistic regression,[5] multinomial logistic regression[5] and Cox regression[6] analyses were performed to identify variables associated with ICU admission, mechanical ventilation and in-hospital mortality, respectively.

Among the 800 patients admitted during the observation period for SARS-CoV-2, 465 (58%) patients had pneumonia. Of these patients, 225 were excluded from analysis due to outpatient care, inter-hospital transfer or unavailable data. The population therefore comprised 240 patients (115 non-ICU and 125 ICU-admitted [65% direct admission to ICU and 35% transfer to ICU within 96 h of admission from emergency department]). The mean age was 57.7 ([standard deviation] [17.8]) years and 67% of all patients were male. The median (interquartile range [IQR]) duration of onset of symptoms to hospital admission was 7 (4; 8) days (Table 1 Panel A).

When compared to non-ICU patients, ICU-admitted patients were more likely to be men and have higher body mass index (BMI). ICU-admitted patients also showed higher levels of creatinine, C-reactive protein, neutrophils, lactate dehydrogenase (LDH), white blood cell count, troponin, D-dimer, ferritin, and troponin. Similarly, we observed elevated C-reactive protein-to-lymphocyte, neutrophil-to-lymphocyte ratio and lower lymphocyte count and oxygen saturation upon admission (first 24 h) in ICU-admitted patients. During hospitalization (days 3–5), those admitted to the ICU developed severe lymphopenia more frequently (0.6 vs. 1.1; $P < .001$) than non-ICU patients. Levels of C-reactive protein, neutrophils, white blood cell count, alanine aminotransferase (ALT) and LDH, D-dimer and ferritin were higher in ICU-admitted patients over time (day 3–5) (Table 1-Panel A).

No significant differences were observed in therapies administered to ICU-admitted and non-ICU patients. Most patients received lopinavir/ritonavir plus hydroxychloroquine plus azithromycin upon hospital admission (92% vs. 94%, $P = .558$).

BMI, ferritin levels and the C-reactive protein-to-lymphocyte ratio upon admission were independently associated with ICU admission (either, direct ICU admission and transfer to ICU in the first 96 h of admission) in the multivariable analysis (Table 1-Panel B). For patients who were direct to ICU admission, BMI (overweight or obese: odds ratio [OR] 2.13 [95% confidence interval [CI] 0.94–4.85]), ferritin levels (+100 ng/ml: OR 1.06 [95% CI 1.02–1.09]), the C-reactive protein-to-lymphocyte ratio (+10 units: OR 1.05 [95% CI 1.03–1.07]) and platelets levels ($+10 \times 10^9$/L: OR 1.05 [95% CI 1.00–1.09]) were independently associated with ICU admission (AUC = 0.78 [95% CI 0.72–0.84]), whereas for patients transferred to ICU within 96 h of admission from emergency department, BMI (overweight or obese: OR 3.33 [95% CI 1.28–8.67]), ferritin levels (+100 ng/ml: OR 1.04 [95% CI 1.00–1.08]), the C-reactive protein-to-lymphocyte ratio (+10 units: OR 1.04 [95% CI 1.01–1.06]) and platelets levels ($+10 \times 10^9$/L: OR 0.94 [95% CI 0.88–0.99]) were