Effects of Lower vs Higher Oxygenation Targets on CO_2, pH Levels, and Mortality in ICU Patients with COPD and Acute Hypoxemic Respiratory Failure

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Background

Treatment with supplemental oxygen is lifesaving for patients admitted to an intensive care unit (ICU) with chronic obstructive pulmonary disease (COPD) and acute hypoxemic respiratory failure. While guidelines generally recommends to target a relatively low peripheral oxygen saturation at 88-92% in COPD patients, no guidelines currently exist on oxygenation strategies for COPD patients admitted to an ICU.[1–3] We present the analysis of a pre-planned subgroup of all patients with known COPD in the Handling Oxygenation Targets in the ICU (HOT-ICU) trial demanding the presence of acute hypoxemic respiratory failure at enrollment.[4] The aim was to assess if a lower partial pressure of arterial oxygen (PaO_2) target of 8 kPa reduced 90-day all-cause mortality compared to a higher PaO_2 target of 12 kPa.

Methods

Allocation in the HOT-ICU trial was stratified for COPD at enrolment, which was diagnosed based on either a spirometry in stable phase or a medical history indicative of COPD. The primary outcome of the present study was 90-day all-cause mortality, while secondary outcomes were serious adverse events (SAEs) in the ICU at 90 days, days alive without life-support at 90 days, days alive out of hospital at 90 days, and one-year all-cause mortality. We described and compared oxygenation parameters for all COPD patients during the intervention period, supplemented with weighted averages of the arterial partial pressure of carbon dioxide ($PaCO_2$), pH and standard bicarbonate (SBC) for the Danish COPD patients in the trial.

Results

In the HOT-ICU trial 563 patients had COPD: 277 and 286 in the lower- and higher-oxygenation group, respectively. Baseline characteristics were similar between groups. During the 90-day intervention period, median PaO_2 and arterial oxygen saturation (SaO_2) were 9.1 kPa (IQR: 8.7 – 9.9 kPa) and 92% (91–93%) in the lower-oxygenation group, and 12.1 kPa (11.2 – 12.9) and 96% (94–97%) in the higher-oxygenation group.

The 497 Danish patients had a median baseline $PaCO_2$ of 6.3 kPa (5.4 – 8.4 kPa), pH of 7.31 (7.24 – 7.38), and SBC of 22.7 mmol/L (19.7-26.0 mmol/L) in the lower group and $PaCO_2$ of 6.5 kPa (5.4 – 8.1 kPa), pH of 7.31 (7.24 – 7.36), and SBC of 22.3 mmol/L (19.7-25.7 mmol/L) in the higher group. Based on 27,045 arterial blood gases, time-weighted averages of $PaCO_2$, pH, and SBC spanning the entire intervention period did not differ significantly between the oxygenation groups.

We observed no statistically significant differences between oxygenation groups in the primary outcome of 90-day all-cause mortality (adjusted relative risk 0.98; 95% CI 0.82–1.17; P=0.67) and in all secondary outcomes.

Discussion and Conclusions

These data represent the first large randomised clinical trial comparing targeted oxygen therapy for COPD patients in an ICU setting, but it is important to note that the inclusion criteria were based on the need for supplemental oxygen therapy due to hypoxemic respiratory failure and not hypercapnia, which entails that not all patients necessarily suffered from a COPD exacerbation at randomisation. No difference was found in 90-day all-cause mortality when comparing a lower versus a higher oxygenation strategy in this preplanned study of COPD patients enrolled in the HOT-ICU trial. Time-weighted averages of $PaCO_2$, pH, and SBE seemed unaffected by oxygenation strategies despite clear separation for both PaO_2 and SaO_2 during the intervention period. Based on the results it is not evident that a higher oxygenation target entails an increased risk of hypercapnia or worse clinical outcome for ICU patients with COPD and acute hypoxemic respiratory failure.

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