HOT of the Press – The HOT-ICU Study

Key Articles

Schjorring OL, et al. Lower or higher oxygenation targets for acute hypoxemic respiratory failure. NEJM. 2021. Published online January 20, 2021.

Background

- Patients admitted to the ICU with hypoxemic respiratory failure often received supplemental oxygen with a high FiO2.
- High levels of FiO2 (hyperoxia) has been associated with increased mortality in some recent trials and studies.
- There is currently no clinical practice guideline on oxygenation targets for adult patients in the ICU with hypoxemic respiratory failure.
- Recent evidence:
    - *Panwar, et al. Am J Respir Crit Care Med. 2016*
        - Small, multicenter trial in vented ICU patients that found no evidence of harm for patients where SpO2 was targeted to 88%-92% compared with SpO2 target of 96% or higher
    - *Girardis, et al. JAMA. 2016*
        - Single center, randomized trial that demonstrated lower mortality for patients with a PaO2 target of 70-100 mm Hg compared with a higher PaO2 target of 150 mm Hg.
    - *Barrot, et al. NEJM. 2020*
        - LOCO2 trial
        - Stopped prematurely due to higher frequency of mesenteric ischemia and 90-day mortality in the lower oxygenation group.
    - *Mackle, et al. NEJM. 2020*
        - ICU-ROX trial
        - No between-group differences in the number of ventilator-free days or 28-day mortality in patients treated with a lower oxygenation strategy.

Objective

- To test the hypothesis that targeting a PaO2 of 60 mm Hg would reduce 90-day mortality compared to targeting a PaO2 of 90 mm Hg in adult ICU patients with hypoxemic respiratory failure.

Study

- Investigator-initiated, multicenter, stratified, parallel-group trial

- 35 ICUs in Denmark, Switzerland, Finland, Netherlands, Norway, Iceland, and the UK
- Inclusion:
    - Adult greater than or equal to 18 years of age
    - Admitted to the ICU with hypoxemic respiratory failure
    - Receiving at least 10 L of O2 via an open system OR had an FiO2 of at least 50% in a closed system
    - Expected to receive supplemental O2 for at least 24 hours in the ICU
    - (Assumed that the P:F ratio would be below 300 for all patients)
- Exclusion:
    - Patients who could not be randomized within 12 hours of ICU admission
    - Receiving home O2
    - Patients poisoned with CO, cyanide, or paraquat
    - Sickle cell disease
    - Pregnancy
    - Underwent solid-organ transplant
    - Long-term mechanical ventilation
    - Brain death or withdrawal of active therapy
- Intervention
    - Patients randomly assigned in 1:1
    - Lower-Oxygenation Group
        - Received oxygen to target a PaO2 of 60 mm Hg
    - Higher-Oxygenation Group
        - Received oxygen to target a PaO2 of 90 mm Hg
    - Up to 90-days after randomization
    - Investigators recorded the lowest and highest PaO2 in predefined 12-hr intervals, along with the SaO2 and FiO2
    - Supplemental oxygen devices chosen by the clinicians
- Primary Outcome
    - 90-day all-cause mortality
- Secondary Outcomes
    - Serious adverse events
        - New episodes of shock
        - MI
        - Cerebral ischemia
        - Mesenteric ischemia
    - % of days free from MV, RRT, vasopressors

Results

- 2,928 patients
    - 1,462 assigned to the Lower-Oxygenation Group
    - 1,466 assigned to the Higher-Oxygenation Group
    - Similar baseline characteristics
- Oxygenation and ICU Interventions

    - Use of mechanical ventilation, prone positioning, inhaled vasodilators, ECMO, RRT, transfusions, and circulatory support were similar in the 2 groups.
    - As expected, PaO2 values were lower in the Lower-Oxygenation Group compared to the Higher-Oxygenation Group.
- Primary Outcome
    - 90-day all-cause mortality
        - Lower-Oxygenation Group: 42.9%
        - Higher-Oxygenation Group: 42.4%
        - RR 1.02; CI 0.94 to 1.11; p=0.64
- Secondary Outcomes
    - No difference in patients alive without life support, alive after hospital DC, or serious adverse events between the groups.

Limitations

- Oxygenation targets selected in this study may be considered different standard care in other countries.
- Arterial sampling for PaO2 was intermittent and not standardized.
- Used conversion tables for FiO2 in patients receiving supplemental oxygen in an open system and did not have an arterial line for sampling.
- Some potential treatment differences in individual ICUs
- Higher 90-day mortality as initially hypothesized

Authors Take Home Points

- A lower oxygenation target did not reduce 90-day mortality compared to a higher oxygenation target in adult patients admitted to the ICU with acute hypoxemic respiratory failure.
- “Findings lend weight to the utility of conservative oxygen therapy in patients with acute hypoxemic respiratory failure compared with the recent LOCO2 trial”.