Hyperoxia

Definitions

Multiple – between papers, using different endpoints (SpO_2 vs FiO_2 vs PaO_2). Is Oxygen or saturated Hb the problem?

- PaO2 > 13.3 kPa – only achievable with supplemental Oxygen
- SpO_2 97-100%
- Moderate 101-299 mmHg / Severe $\geq$ 300 mmHg

Endpoints of mortality (overall, in-hospital, 30-day), ventilator free days

Harms

Preclinical studies demonstrate

- Free radical generation
- Inflammation
- Cycle of inflammation / Oxygen utilisation

Studies

Helmershorst (2015); Large meta-analysis and systematic review of observational studies across disciplines (sepsis, ICU, cardiac arrest, TBI, trauma). Observational studies – not possible to infer causation. OR 1.21 in favour of normoxia. Studies used their own definitions.

OXYGEN-ICU (2016); Large RCT, ICU population. Single site, stopped early. Compared conservative (target SpO_2 94-98%) with conventional (SpO_2>97%). Heavily criticised, showed significant improvement in mortality with conservative Oxygen.

IOTA (2018); Meta-analysis of RCTs – 25 included across disciplines. Criticised because of weighting towards flawed OXYGEN-ICU trial. Compared "liberal" vs "conservative" (used study's own definitions). Small trend favours normoxia.

The Association between Supraphysiologic Arterial Oxygen Levels and Mortality in Critically Ill Patients (2019); Multi-centre RCT. Intended to examine relationship between hyperoxia and mortality. Compared Oxygen dose (time weighted PaO_{2AUC}/Time) over 1/3/5 days with mortality. Dose dependent increase in mortality for time >13.3kPa ("oxygen dose").

ICU-ROX (2019); Large multi-centred RCT comparing conservative vs usual. Strict "as low as possible" protocol to achieve SpO_2 > 90%. Subgroups (underpowered) suggest conservative may be of benefit in HIE, sepsis – but not overall. Outcomes were ventilator free days. True difference between group's FiO_2 administered.

High intraoperative inspiratory oxygen fraction and risk of major respiratory complications (2017); Large observational study of noncardiac surgery. Used median FiO2 to remove "ceiling effect" of

preoxygenation. Stratified by median FiO_2. Suggest worsening mortality, respiratory complications and ventilator time with higher median FiO_2.

UHL data

107 patients, March 2017, covering 6750 patient hours, 5318 Oxygen / 1432 room air

Mean initial PaO2 17.3 kPa

62.6 % normoxic within 6 hours of ABG

Median time to normoxia 4.8 hrs

References

Helmershorst 2015 http://dx.doi.org/10.1097/CCM.0000000000000998

OXYGEN-ICU http://dx.doi.org/10.1001/jama.2016.11993

ICU-ROX http://dx.doi.org/10.1056/NEJMoa1903297

IOTA http://dx.doi.org/10.1016/S0140-6736(18)30479-3

Staehr-Rye 2017 http://dx.doi.org/10.1093/bja/aex128