Oxygen can be a double edged sword

Michele Samaja, 1 Davide Chiumello 2

Oxygen is routinely administered to almost all patients undergoing general anaesthesia,1 to ensure adequate oxygenation from intubation until awakening—the period when complications due to hypoxaemia are most likely to occur.2 Currently, the optimal target for oxygen administration is not yet clear and varies from normal arterial oxygen saturation to hyperoxaemia (usually defined as >97-98% arterial oxygen saturation). The hyperoxaemia strategy has been widely used since a seminal study highlighted the benefits of liberal (80%) compared with restrictive (30-35%) inspired oxygen to reduce the risk of postoperative infection.3 Accordingly, the 2016 World Health Organization guidelines recommend that patients receive a liberal fraction of inspired oxygen during general anaesthesia and in the immediate postoperative period.4 5

Basic research, however, shows that oxygen can be a double edged sword.6 It is a fundamental substrate for the oxidative phosphorylation that feeds biological energy to every aerobic cell. But in certain circumstances, oxygen may give rise to highly reactive compounds that cause damage and functional impairment to vital tissues such as the brain, disrupting the redox balance, weakening the antioxidant barrier, and increasing the vulnerability of tissues to oxidative injury during periods of both hypoxaemia and hyperoxaemia.7

In a clinical context, one large cross sectional study performed during general anaesthesia in Japan reported that 83% of the participants had a “preventable hyperoxaemia,” defined as >98% arterial oxygen saturation.8 Subsequent studies showed no substantial benefit associated with 80% inspired oxygen (compared with 30%) in reducing the risk of infection,9 10 and others showed that supraphysiological oxygen administration may be associated with worse outcomes than restrictive strategies.11 12 13 Accordingly, the current British Thoracic Society guidelines recommend keeping arterial oxygen saturation in the 94-98% range to avoid harm from both hypoxaemia and hyperoxaemia.14

In a linked paper, McIlroy and colleagues used an algorithm to calculate the area under the curve plotting administered oxygen >21% against the time spent with oxygen saturation >92%. Their study included 350 647 adults from 42 centres in the United States and documented postoperative organ injury in 6.5% (kidneys), 2.8% (myocardium), and 4.4% (lungs) of participants. The median area under the curve quantifying supraphysiological inspired oxygen was equivalent, for example, to a patient receiving 80% inspired oxygen throughout a 135 minute procedure, or 60% oxygen throughout a 204 minute procedure.

Supraphysiological oxygen administration was associated with a higher risk of organ injury: Patients at the 75th centile of area under the curve had 26% greater odds of acute kidney injury (95% confidence interval 22% to 30%), 12% greater odds of myocardial injury (7% to 17%), and 14% greater odds of lung injury (12% to 16%) than those at the 25th centile. In addition, it was also associated with 30 day mortality (odds ratio 1.06, 0.98 to 1.15).

Unlike previous studies, this new investigation leaves little room for uncertainty: supraphysiological oxygen administration and saturation are associated with a higher risk of organ damage, although the absolute risk remains low.

Future research on this topic could deal with some of the study’s acknowledged limitations. Firstly, not all participants were screened for kidney and heart injury after their surgery (postoperative serum creatinine and troponin levels were measured in 58% and 16%, respectively). Secondly, it is unclear how the findings would change if the threshold definition for supraphysiological oxygen was increased. Thirdly, the authors were unable to consider confounders such as diet, lifestyle, and drug use, which can influence the strength of the antioxidant barrier and hence susceptibility to organ injury.

Future researchers could also consider the oxygen carrying capacity of blood (haematocrit, haemoglobin concentration) and include an outcome measuring cognitive impairment because experimental evidence suggests that brain tissue is particularly vulnerable to redox imbalance.18 Finally, observational analyses such as this cannot be used to infer a causal link between supraphysiological oxygen and organ injury. Experimental studies may be more suitable to help establish cause and effect.

Despite such limitations, McIlroy and colleagues’ study suggests it is time to reconsider the liberal use of oxygen during general anaesthesia.17 The study also highlights the role of basic research in paving the road to clinical research, following the paradigm...
“from bench to bedside—and back.” Research collaborations between biochemists and anaesthesiologists should be encouraged, especially to identify cause-effect relationships between supraphysiological oxygen administration and organ injury.

Competing interests: The BMJ has judged that there are no disqualifying financial ties to commercial companies. The authors declare the following other interests: None.

Provenance and peer review: Commissioned; not externally peer reviewed.


