Who Can Make Sense of the WHO Guidelines to Prevent Surgical Site Infection?

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RECENTLY, the WHO (World Health Organization) published guidelines regarding measures to reduce surgical site infection.[1] The guidelines, based on a meta-analysis of the literature, conclude that any patient being anesthetized, intubated, and mechanically ventilated for surgery should receive 80% oxygen (O_2) during anesthesia and, if feasible, for 2 to 6 h after surgery. The recommendations do not include pediatric patients and anesthesia administered without tracheal intubation, and note that uncertainties still remain and further research is needed. Despite these limitations, the recommendations are still surprising because they are not well founded, make a superficial analysis of potential negative effects of breathing 80% O_2, and suggest that oxygen should be produced in-hospital without analyzing the costs, risks, and priorities this would entail in both developed and developing countries. These concerns will be briefly discussed in the following paragraphs.

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No Proof of Reduced Surgical Site Infection in Patients Receiving 80% O_2

The primary result of the WHO meta-analysis is the absence of a significant difference in surgical site infection between patients randomized to receive either 80% or 30 to 35% O_2 during and for a few hours after surgery. The conclusions of the recommendation are, however, based solely on a subgroup of intubated and mechanically ventilated patients, even though this subgroup does not appear to have been defined before the study. The subgroup result may have been enough to stimulate a prospective study but not to serve as a basis for guidelines. Moreover, the WHO guidelines do not include the most recent study,[2] which if included would turn the findings even less robust. The meta-analysis furthermore carries a high risk of overestimating the effects of 80% O_2 due to the lack of solid and large trials on the subject.[3] The strength of this subgroup finding is also limited by the fact that it is not statistically significant among trials with an overall low risk of bias.[4] Another concern is that the research group that was the first to report on a positive effect of 80% O_2 in 2000[5] is basically the same group that published this most recent article,[2] in which they, in contrast to their initial results, found no beneficial effect of a high oxygen fraction. During the 16 yr that have passed since the first study on hyperoxia and surgical site infection,[5] a number of studies have been published, but no consensus has been reached. A meta-analysis published in 2013 concluded that a high oxygen concentration presented an advantage with regard to preventing surgical site infection.[6] However, it included studies that had other focuses than oxygen, *e.g.*, a study that tested the effect of inhaled nitrous oxide by comparing one group receiving 30% O_2 plus 70% N_2O with another group receiving 80% O_2 but no nitrous oxide.[7] If this study is excluded from the meta-analysis, then the positive effect of hyperoxia in the subgroup of intubated, mechanically ventilated patients is no longer statistically significant.

Image: J. P. Rathmell.

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Potentially Negative Effects of High Oxygen

A high concentration of inspired oxygen during anesthesia promotes atelectasis formation that will impair oxygenation during anesthesia and during the postoperative period for as long as the atelectasis persists.[8] Thus, hyperoxia may not be as successful in increasing arterial oxygen tension as might be expected. The observation that atelectasis is as extensive with low as well as with high inspired oxygen during anesthesia[9] cannot be used to claim that the inspired oxygen concentration is of no importance. Atelectasis is produced already during the induction of anesthesia with standard preoxygenation, and there is little or no change thereafter irrespective of oxygen concentration.[8] Ventilation with a low concentration of oxygen, 30 to 40%, after recruitment maneuvers to reopen a collapsed lung, as suggested in protective ventilation strategies,[10,11] will prevent the recurrence of atelectasis, whereas a high oxygen concentration will not. Atelectasis may persist after surgery for some time, even days, impairing oxygenation.[8]

The use of a high concentration of oxygen promotes production of free radicals that can harm tissue.[12] Since the lungs are exposed to the highest oxygen concentrations, the lungs are the primary targets of oxygen toxicity. In fact, 70% O_2 injures isolated rat lungs due to the production of reactive oxygen species within 1 h,[13] and lung injury can be detected in live mice breathing 100% O_2 within 24 h. Moreover, baboons show endothelial cell injury and neutrophil accumulation in the lungs within 3 days of breathing 100% O_2.[13,14] In addition, an experimental model to produce acute respiratory distress syndrome involves letting animals breathe gas with a high concentration of oxygen.[15] The WHO document dismisses the notion that perioperative hyperoxia may have increased long-term mortality after abdominal surgery in cancer patients because it was a subgroup analysis.[16] The WHO guidelines are also based on a subgroup analysis, but in this case, it is apparently acceptable. Moreover, the WHO document concludes that the negative effect of perioperative hyperoxia in cancer patients is biologically implausible. How that can be concluded is difficult to understand. Importantly, a recent randomized study on low *versus* high arterial oxygen tension (median Pa_{O_2} 87 *vs.* 102 mmHg) in mechanically ventilated patients with acute respiratory failure showed a much higher mortality in the high Pa_{O_2} group (44 *vs.* 25%).[17] In another recent observational cohort study in critically ill patients, severe hyperoxia (Pa_{O_2} > 200 mmHg) was accompanied by higher mortality (17%) than normoxia or mild hyperoxia (Pa_{O_2} < 200 mmHg; 11%).[18] The results relate to another category of patients, but, if anything, they do not speak in favor of hyperoxia.

Administration, Risks, and Cost of High Oxygen in the Perioperative Period

The authors of the WHO guidelines admit that there may be some difficulties in providing a high concentration of oxygen postoperatively because it would require a face mask that can make breathing uncomfortable. The technique of high-flow nasal oxygen[19] may circumvent this, making it technically possible to provide a high concentration of oxygen, but this requires an even higher oxygen supply (30 to 60 l/min). The authors also point out the increased cost of administering a higher concentration of oxygen in the perioperative period and suggest that there should be an in-hospital oxygen production. However, the feasibility, possible risk of contamination, and the efficiency remain to be analyzed. The cost may not appear overwhelming for the individual patient, but for a given budget, this cost has to compete with other costs. It is almost surprising that the WHO suggests in its guidelines that a high concentration of oxygen should be given priority without analyzing what must then be eliminated or reduced. If this is difficult in developed countries, it surely will not be less difficult in developing countries.

In summary, the WHO guidelines on using high oxygen concentration during and after surgery in intubated and mechanically ventilated patients can be questioned and may in fact be more harmful than useful.

Competing Interests

The authors are not supported by, nor maintain any financial interest in, any commercial activity that may be associated with the topic of this article.

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