When Less Is More: Why Extubation With Less Than Routine 100% Oxygen May Be a Reasonable Strategy

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GLOSSARY

Cao_2 = arterial oxygen content; **DO_2** = oxygen delivery; **Fio_2** = inspiratory fraction of oxygen; **Hb** = hemoglobin; **HFNOT** = high-flow nasal oxygen therapy; **IOTA** = Improving Oxygen Therapy in Acute illness, systematic review and meta-analysis; **LAD** = left anterior descending artery; **MBF** = organ blood flow; **MVO_2** = myocardial oxygen demand; **O_2** = oxygen; **OS-CMR** = oxygenation-sensitive cardiovascular magnetic resonance; **Pao_2** = arterial pressure of oxygen; **PEEP** = positive end-expiratory pressure; **PROXI trial** = PeRioperative OXygen Fraction, effect on surgical site Infection and pulmonary complications after abdominal surgery multicenter trial; **Sao_2** = arterial oxygen saturation; **SSI** = surgical site infections

The high-pitched beep of the plethysmograph—announcing 100% oxygen (O_2) saturation—is well recognized by anesthesiologists. For this, however, a supraphysiological inspiratory fraction of oxygen (Fio_2) is frequently applied, exposing the patient to an excess of O_2. There is growing evidence that an exaggerated arterial partial pressure of oxygen (Pao_2), also called "hyperoxia," may not be as benign as it was previously thought to be.

Clearly, in acute hypoxemia due to impaired gas exchange in the lungs, application of high Fio_2 may increase Pao_2. If the Pao_2 is increased excessively, however, it can lead to hyperoxia-mediated vasoconstriction in almost all vascular beds, particularly in the coronary arteries. Breathing an Fio_2 of 100% leads to a relative increase in coronary resistance of 40% compared to breathing air.[1] In animal studies, Guensch et al[2] showed that hyperoxia resulted in a significant decrease of myocardial signal intensity in oxygenation-sensitive cardiovascular magnetic resonance (OS-CMR) imaging in the perfusion territory of a stenotic coronary artery. This was accompanied by a colocalized attenuation in peak circumferential strain. A decrease in left ventricular ejection fraction, cardiac output, and O_2 extraction ratio was also noted in stenosed animals under hyperoxia compared to healthy control animals.[2]

Another side effect of O_2 is caused by gas absorption, which is a known mechanism of atelectasis formation. Calculations show that after tracheal intubation, alveolar collapse can be expected after 6 minutes of breathing pure O_2, compared to 30 minutes when breathing ambient air. It has been demonstrated that the amount of pulmonary atelectasis after induction of anesthesia is related to the level of Fio_2 used and the preoxygenation period. The amount of O_2 used during preoxygenation and induction is such a strong determinant of atelectasis formation that variations in inspiratory O_2 concentration during anesthesia do not seem to yield differences in the amount of atelectasis at the end of anesthesia; this is because most atelectases already occur during the first minutes of breathing 100% O_2.[3]

Physiological considerations make it plausible that absorption atelectases can be reduced by positive end-expiratory pressure (PEEP).[4] This principle was used, for example, in a landmark study of lower tidal volumes in acute respiratory distress patients with the use of Fio_2/PEEP tables.[5] PEEP values as suggested by the table in Brower et al[5] (eg, 14 cm H_2O for an Fio_2 of 80%) may lead to negative hemodynamic consequences.

While using a high Fio_2 has been proposed to reduce surgical site infections (SSIs) in the past, a recent systematic review and meta-analysis did not show a convincing beneficial effect. Moreover, it questioned the strength of the related recommendation.[6] The Danish PeRioperative OXygen Fraction, effect on surgical site Infection and pulmonary complications after abdominal surgery multicenter trial (PROXI trial) compared an Fio_2 of 80% with 30% during emergency or elective laparotomy and found no difference in the rate of SSI or in mortality.[7] A comparison between near-physiological O_2 targets (Pao_2, 130–150 mm Hg) and moderate hyperoxic O_2 targets (Pao_2, 200–300 mm Hg) in cardiac surgery with cardiopulmonary bypass showed no difference in myocardial injury, lactate levels, or hypoxic events.[8]

There are situations in which the benefits of a high Fio_2 may outweigh the potential harm of hyperoxia. Intubation is the best example, as hyperoxia prolongs apnea tolerance, which results in invaluable extra time to manage the airway. This is also reflected by current guidelines for intubation,

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in which preoxygenation with F_{IO_2} of 100% is one of the mainstays.[9]

Reducing the F_{IO_2} after intubation often leads to safety concerns among anesthesia caregivers. This might not be reflected by physiological evidence. While the high O_2 concentration in the functional residual capacity is a relevant O_2 reserve in case of airway problems (eg, 2.5–3 L of O_2), the amount of physically dissolved O_2 in the blood is minimal. Oxygen delivery (DO_2) to the heart calculates from the organ blood flow (MBF) multiplied by the arterial oxygen content (Cao_2): $DO_2 = MBF \times Cao_2$. Cao_2 can be derived from the hemoglobin (Hb) concentration, arterial oxygen saturation (Sao_2) of Hb, and the Pao_2: $Cao_2 = (1.34 \times Hb \times Sao_2) + (0.0031 \times Pao_2)$. Assuming a Pao_2 of 100 mm Hg, a consecutive Sao_2 of 100%, and an Hb of 100 g/L, the resulting Cao_2 is 134 mL O_2/100 mL blood. Importantly, as Sao_2 is already maximal, O_2 can only be physically dissolved in the plasma, represented by the second term of the equation. At a Pao_2 of 100 mm Hg, this physically dissolved portion of Cao_2 is 0.31 mL O_2/100 mL plasma. Increasing the Pao_2 to 300 mm Hg will increase this physically dissolved portion to 0.93 mL O_2/100 mL plasma, thus increasing Cao_2 effectively from 134.0 to 134.1 mL O_2/100 mL blood. This is an increase in DO_2 by 0.075% given that Sao_2 and Hb remained unchanged. In the publication Guensch et al,[2] the authors note a hyperoxia triggered decrease in left anterior descending artery (LAD) blood flow of −12.7% ± 2.3% in healthy animals and −14.8% ± 2.0% in animals with a significant LAD stenosis, respectively. Of note, drops in myocardial blood flow of up to 30% have also been recorded in humans during inhalation of O_2.[1] Thus, it is clear that the resulting decrease in blood flow (up to 30%) cannot be outweighed by the 0.075% increase in Cao_2, inadvertently leading to a decrease in DO_2. Increasing the F_{IO_2} does only increase DO_2 by an irrelevant amount, which may be even compromised by a reduction in blood flow. This may lead to changes in the myocardial oxygenation balance but does not lead to tissue ischemia as long as myocardial oxygen demand (MVO_2) is matched by DO_2. However, in scenarios where MVO_2 is just matched by DO_2 with little reserve or with factors decreasing Cao_2 (eg, anemia) or MBF (eg, drop in blood pressure), despite high Pao_2, ischemia may be the consequence.

Thus, when speaking of safety attained through high inspired O_2 concentrations, this is true for loss of airway and hypoventilation problems only (eg, cannot intubate/cannot ventilate situations), but not for the surgical period (given the fact that the airway is secured) or as a preventive maneuver in the case of hemodynamic instability. There is growing evidence that not only is there no benefit to high inspired O_2 concentrations, but there may even be possible harm as pointed out in the Improving Oxygen Therapy in Acute illness (IOTA) systematic review and meta-analysis showing an increased mortality with liberal O_2 use for over 15,000 acutely ill adults.[10]

For the extubation phase, there is even less published evidence regarding optimal O_2 concentrations. While an F_{IO_2} of 100% is often applied, there are important caveats worth mentioning in relation to this practice. Based on our clinical experience, and in line with the published literature, we believe that emergence from anesthesia and the subsequent extubation is potentially a highly stressful period for the patient.[11,12] Tracheal irritation, cough, strain, pain and the decreasing level of sedatives expose the patient to hemodynamic stress, which is clinically detectable as hypertension and tachycardia, also causing an imbalance in myocardial O_2 demand and supply.[11–13]

High F_{IO_2} favors atelectasis formation, which increases the respiratory work of the recovering patient. The combination of high F_{IO_2} with simultaneously performed airway suctioning consistently leads to atelectasis formation before extubation. Benoît et al[14] showed reduced postoperative atelectasis using an F_{IO_2} of 40% compared to 100%. In spite of this, current extubation guidelines still recommend preoxygenation with an F_{IO_2} of 100% before extubation, even in airways deemed to be low risk.[15] The goal is to maximize O_2 stores to provide continued oxygenation in case of unexpected difficult extubation. However, the use of maximal O_2 concentrations during extubation may lead to more problems than benefits. Prolongation of apnea time at extubation comes at the high cost of promoting atelectasis, and perhaps more importantly, reducing coronary blood supply. The latter has been neglected in the current debate over prophylactic hyperoxia during extubation.[16,17] Under many extubation conditions, the patient's airway and respiratory capabilities can be adequately assessed.

Consequently, based on these physiological considerations, we propose a personalized approach to applying hyperoxia that uses a reduced F_{IO_2} before and after extubation for patients who are not at risk of a compromised airway, do not have impaired oxygenation, and have known or suspected coronary artery disease. Because most of the described unwanted O_2 effects occur in a dose-dependent manner, even a small reduction in F_{IO_2} will benefit the patient. We propose using an F_{IO_2} of 60%–80%, based on the individual risk assessment of the responsible clinician. After extubation, O_2 administration should be aimed at providing normoxemia, with a target peripheral O_2 saturation in the range of 94% (or even 92%) to 98%.

Which oxygenation targets are optimal is the subject of ongoing debate, but we believe that, given the potency of the O_2, we should use it with caution—like every other drug—in a targeted, individualized manner. Signs of mismatch between O_2 supply and demand should then trigger an immediate search and appropriate treatment of the underlying pathology (eg, hypoventilation, atelectases, muscle weakness, obstructive sleep apnea syndrome) rather than injudicious installation of a full-facemask with O_2 and dialing up O_2 flow. To avoid atelectases, high O_2 concentrations should only be applied together with maneuvers that prevent atelectases, such as continuous PEEP. While PEEP and other noninvasive ventilation strategies may be difficult to apply in patients emerging from general anesthesia, high-flow nasal oxygen therapy (HFNOT) has been shown to provide PEEP in spontaneously breathing patients.[18] Also here, we would advocate using an O_2/air blender to titrate inspired O_2 according to patient needs.

We believe that future research will further improve our understanding of the effects of O_2 and optimal O_2 targets for our patients. However, already today we can highlight the principle of ensuring an adequate O_2 supply. Because tissue oxygenation is flow dependent, too much O_2 will probably hamper coronary supply via vasoconstriction, but severe

hypoxia will do this for sure via hypoxemia (in spite of the vasodilatory effects of hypoxemia)! Stepping away from established principles and guidelines, such as the Difficult Airway Society Guidelines for the management of tracheal extubation,[15] has to be done deliberately and with careful monitoring, whenever possible in research projects.

While further research is needed to better stratify risks and benefits and to provide the basis for decision-making, choosing the best F_{IO_2} is up to the treating clinician, who should take into account the individual risk factors for each extubation, thereby balancing the benefits and the harms of O_2 therapy.

DISCLOSURES

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