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Editorial

EDITORIAL

Physiologically difficult airway in critically ill patients: winning the race between haemoglobin desaturation and tracheal intubation

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Tracheal intubation in critically ill patients remains high-risk despite advances in equipment, technique, and clinical guidelines.[1] Approximately one in three patients experience moderate complications, and almost one in four experience severe complications.[2,3] Peri-intubation cardiac arrest occurs in 2–4% of cases, and is highly associated with peri-intubation oxygen desaturation and hypotension.[2,4] A 2018 study reported that patients who desaturated or became hypotensive had 3.99 and 3.41 times higher adjusted odds, respectively, of a cardiac arrest compared with those who did not.[2] The difficult airway is even more dire, with 50% of patients experiencing serious life-threatening complications.[5] Contemporary thinking is that safety comes with first pass success.[6,7] Although this may be empirically true, there is still a 15–20% complication rate on first attempt. Moreover, hypoxaemia and haemodynamic instability before intubation are associated with increased adjusted odds of complications, despite first attempt success.[6,7] These physiological derangements increase the risk of peri-intubation decompensation independent of anatomical challenges with laryngoscopy or tube placement.[8] Here I address the most common complication: hypoxaemia.

Physiological aberrations exist on a spectrum, with some more reversible than others. Figure 1 describes the risk of haemoglobin desaturation during tracheal intubation using a bell-shaped curve distribution. Those with the least risk of desaturation are on the left, but represent only a small percentage of the total. Many patients have an increased risk of desaturation during airway management, particularly in the face of difficult preoxygenation.[9] Measures that can reduce the risk of desaturation include flush rate denitrogenation,[10] upright position,[11,12] mask ventilation between induction of anaesthesia and laryngoscopy,[13] and use of apnoeic oxygenation.[14] Flush rate denitrogenation alone is not adequate to provide a safe apnoea time in some patients. Instead, improving the ventilation/perfusion (V/Q) mismatch during preoxygenation enough to proceed safely with rapid sequence intubation becomes the priority, which can be accomplished with noninvasive positive pressure ventilation (NIPPV),[15] high-flow nasal oxygen (HFNO),[16–18] and upright positioning. However, the right hand tail of the curve is more complex, and represents the highest risk of desaturation because a safe apnoea time is not possible, even after optimal preoxygenation.

Optimal preoxygenation requires several components to provide a safe apnoeic interval: a sufficient volume of alveolar gas (the functional residual capacity [FRC]), oxygenation of that volume (denitrogenation), and availability of that volume of oxygen to resaturate haemoglobin.[19] Denitrogenation is best performed using a tight-fitting mask that eliminates entrainment of room air. If the mask loses its seal, the ability to denitrogenate is reduced, even if a nasal cannula is added.[19] Denitrogenation is even worse, as demonstrated by end-tidal O_2 (ETO_2) values in the 50% range, when reservoir-based non-rebreathing masks that are common in emergency departments and ICUs are used. Entrainment of room air can be reduced by applying flush rate oxygen when using such masks,[20] which improves denitrogenation by providing oxygen at flow rates that approach the inspiratory flow of a spontaneously breathing patient. This denitrogenated FRC creates a reservoir of oxygen to draw upon during apnoea that averages 30 ml kg^{-1} in healthy individuals, but decreases in proportion to the severity of airspace disease. In patients with severe acute respiratory distress syndrome (ARDS) and a Pao_2/Fio_2 ratio <100, the FRC is as few as 5–10 ml kg^{-1}.[21]

Tanoubi and colleagues[22] provided a useful method for estimating the safe apnoea time:

$$\text{Safe apnoea time} = \frac{\left(F_AO_{2_{\text{End preoxygenation}}} - F_AO_{2_{\text{O2 saturation of 90\%}}}\right) \times \text{FRC}}{V\dot{O}_2}$$

Holding VO_2 constant, this equation dictates that safe apnoea time is contingent upon the degree of denitrogenation and the size of the FRC. However, even in patients with severe ARDS, complete denitrogenation is easy to achieve and renders the EtO_2 value misleading. Knowing that the FRC in a 70 kg patient with severe ARDS can be as few as 5 ml kg^{-1}, we can estimate the safe apnoea time to be:

$$\frac{(0.95 - 0.10) \times 350}{250} = 72 \text{ s}$$

This equation also suggests that safe apnoea time should be essentially indefinite when using apnoeic oxygenation. Clinically, this explains the successes of THRIVE (transnasal humidified rapid insufflation ventilatory exchange) at maintaining oxygen saturation during surgery while clearing carbon dioxide through a combination of microturbulence in the large airways and cardiac oscillations.[23] However, clinically we see patients with ARDS desaturate much quicker than the predicted 72 s. There are several reasons for this. (1) If the source of oxygen is removed before the patient is fully apnoeic, renitrogenation can happen precipitously during the few breaths before apnoea. (2) This equation assumes normal V/Q mismatch, which results in a shunt fraction of 3–4%. The shunt fraction can be substantially higher—about 50% when the Pa_{O2}/Fi_{O2} ratio is <100.[24] The availability of the oxygen reservoir is the third requirement for preoxygenation. The greater the shunt, the less the FRC oxygen reservoir can resaturate haemoglobin, regardless of the size or adequacy of denitrogenation. Modifying the Tanoubi equation for shunt fraction in this hypothetical patient would decrease the safe apnoea time to 38 s:

$$\text{Safe apnoea time} = \frac{\left(\left[F_AO_{2_{\text{End preoxygenation}}} - F_AO_{2_{\text{O2 saturation of 90\%}}}\right] \times \text{FRC}\right) \times \%\,\text{shunt}}{V\dot{O}_2}$$

$$\frac{[(0.95 - 0.10) \times 350] \times 0.5}{250} = 38 \text{ s}$$

This physiology suggests that flush flow oxygen, upright positioning, apnoeic oxygenation, and preoxygenation with NIPPV will provide an apnoea time conducive to placing a tracheal tube before critical desaturation in the absence of predicted anatomical difficulty and with a skilled operator. However, several clinical observations challenge these assumptions (represented by the far right of the bell curve in Fig. 1). (1) Patients can desaturate precipitously and immediately upon induction. (2) Patients oxygenating well on NIPPV with 5 cm H_2O of PEEP often require substantially higher PEEP after intubation. Higher PEEP requirements between preoxygenation on NIPPV and mechanical ventilation immediately after intubation would imply that the function of PEEP while on NIPPV is not entirely alveolar recruitment in this population. (3) Patients who are intubated awake and spontaneously breathing using supplemental HFNO at 40–60 L min^{-1} can often desaturate immediately upon administering the sedative after tube placement, despite no apnoea time for laryngoscopy. These observations are not explained mathematically by either the Tanoubi equation or after inclusion of the shunt fraction. There is no safe apnoea time for these patients. The Tanoubi equation, with the shunt modification, still predicts an acceptable apnoea time. Yet, these patients desaturate too quickly for this to be explained by rapid depletion of the FRC, with or without apnoeic oxygenation, and even despite a large shunt.

The explanations for these phenomena can be found in leading edge research into ARDS physiology. Although the FRC does indeed decrease in proportion to the severity of airspace disease, the space is dynamic rather than a fixed anatomical space.[25] Positron emission tomography scans show metabolic activity in the collapsed lung units,[26] and CT imaging before and after proning show that oedema migrates to remain in the lung's dependent portions.[25] Expressed another way, the 'baby lung' is more like a complicated 'moody teenager lung'. The lungs are inhomogeneous with at least four areas with varying gas/tissue ratios.[27] The elastic network between these areas function as stress multipliers. These stress multipliers are present in nearly half the lung in severe ARDS and regionally amplify the transpulmonary pressure.[27,28] Electrical impedance tomography data in patients breathing spontaneously on positive pressure show that this amplification of transpulmonary pressure leads to a regional redistribution of intrapulmonary gas before any increase in tidal volume occurs (the *pendelluft phenomenon*).[29,30] In normal cases, pendelluft flow is inconsequential as it is exhaled gas composition, moves from the dependent to non-dependent portions of the lung, and represents only 2% of the tidal volume.[31] However, pendelluft flow with severe ARDS is in the opposite direction and gas is pulled from the non-dependent to dependent portions of the lung. This pendelluft flow approaches 100% oxygen, can represent a 200% increase in regional tidal volume,[30] flows in a direction that reduces V/Q mismatch, and ceases immediately upon cessation of spontaneous respiration.[30] This likely causes a sudden severe worsening of the V/Q mismatch and immediate desaturation. In addition, right ventricular dysfunction is common with severe ARDS, and this immediate desaturation will be accompanied by a precipitous increase in pulmonary vascular resistance that is further increased with the subsequent aggressive mask ventilation to recover the oxygen saturation. The combination of these puts the patient at an extremely high risk of cardiac arrest.[24]

For these extremely critical patients, it is less important how you preoxygenate and more important that you preserve spontaneously breathing. If this physiologic rationale correctly explains the rapid desaturation seen in the patients on the right tail of the bell-shaped curve, then it is also possible that 100% oxygen may also precipitate consequential regional atelectasis and accelerate V/Q mismatch. Spontaneous breathing with high-flow oxygen, potentially pulmonary vasodilators (inhaled nitric oxide or epoprostenol) or hypoxic vasoconstrictors (almitrine), and a gentle transition from spontaneous breathing to mechanical ventilation should

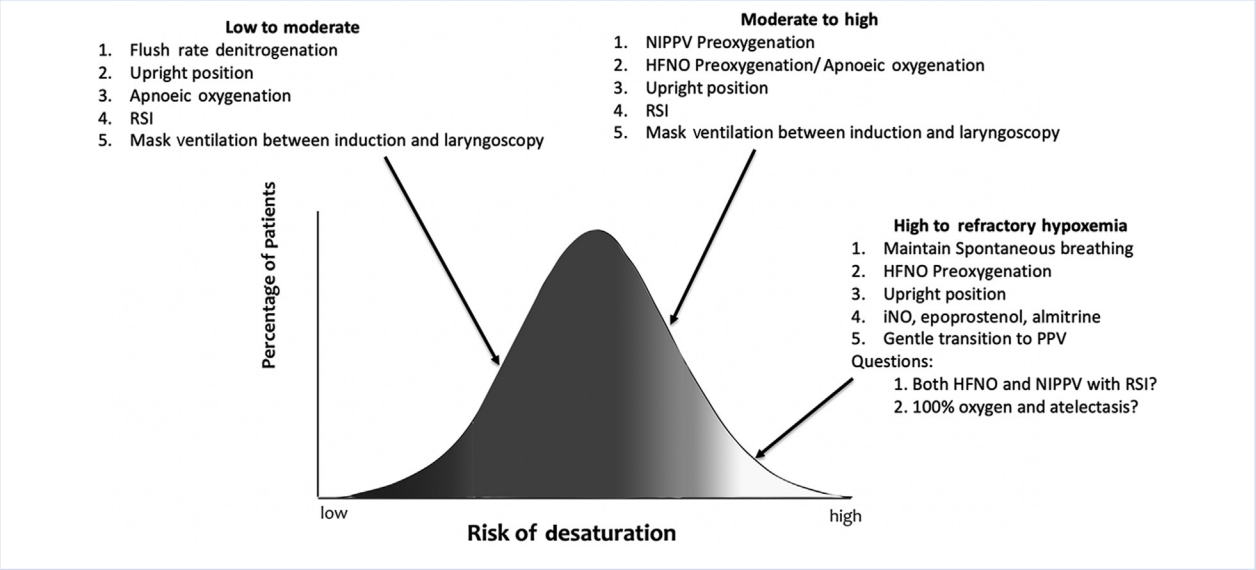

Fig 1. Interventions based on the risk of haemoglobin oxygen desaturation. Interventions aimed at preventing haemoglobin desaturation have varying efficacy based on the pre-intubation risk of desaturation. In patients at low to moderate risk of desaturation, usually those with a large functional residual capacity and low shunt fraction, optimal denitrogenation is the critical step. Thus, flush flow oxygen in the upright position with mask ventilation between injection of induction anaesthetics and laryngoscopy and use of apnoeic oxygenation should allow for a prolonged safe apnoea time amenable to proceeding with rapid sequence induction. In patients at moderate to high risk of desaturation, those with reduced functional residual capacity and increasing shunt fraction, functional residual capacity and ventilation-perfusion mismatch are the limiting factors. As such, more aggressive measures are required such as preoxygenation with positive pressure ventilation, high flow nasal oxygen, and ramped positioning to safely proceed with rapid sequence intubation, although with a reduced safe apnoea time. In those at highest risk of desaturation, usually those with refractory hypoxaemia because of high shunt fractions and airspace disease, safe apnoea may not be possible and an awake, spontaneous breathing approach is the safest approach as any hypoventilation leads to a rapid increase in V/Q mismatch and immediate desaturation. HFNO, high-flow nasal oxygen; iNO, inhaled nitric oxide; NIPPV, noninvasive positive pressure ventilation; RSI, rapid sequence intubation; V/Q, ventilation/perfusion.

reduce the risk of peri-intubation cardiac arrest until focused research in this population can guide us further.

Declaration of interests

The author declares no conflicts of interest.

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