



Preoxygenation for tracheal intubation in critically ill patients: one technique does not fit all

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Introduction

Tracheal intubation is a common procedure in critically ill patients (1). Despite its frequent occurrence, tracheal intubation in this setting remains a risky procedure (2,3), mainly due to the combination of two synergistic and negative factors: the unique respiratory and hemodynamic instability of critically ill patients, and the high incidence of difficult airway in this population (4). Intubation-related life-threatening hypoxemia, hypotension, arrhythmia, cardiac arrest and death are frequently reported (2,3). Recently, a multicenter retrospective trial on tracheal intubation in Intensive Care Unit (ICU) observed a 2.7% rate of cardiac arrest (strongly predicted by hypoxemia prior to intubation and lack of preoxygenation), with a high 28-day mortality in patients who had experienced an intubation-related cardiac arrest (5).

Given this premise, it is not surprising that a strong effort to improve our daily practice is ongoing, including a growing number of randomized trials, the proposal of bundles, the publication of expert opinions, systematic review and guidelines (4,6-10). Unfortunately, findings from trials evaluating single interventions or bundles are often contradictory and overall insufficient to identify and recommend the best protocol (10): more research is urgently needed and every new trial on this topic is warmly welcome.

High-flow nasal oxygen for preoxygenation

Preoxygenation techniques aim to stock as much oxygen as possible in the patient's blood lungs in the few minutes (or seconds, in emergency scenarios) before attempting intubation, to increase the safety of the procedure by preventing or minimizing hypoxemia during the apneic phase. When time permits, preoxygenation is a key intervention and is considered mandatory by guidelines (4): however, the same guidelines warn that operating room standard techniques can be ineffective in critically ill ICU patients.

High-flow nasal oxygen (HFNO), consisting in the delivery of high flow rates (up to 60 L/min) of heated and humidified oxygen through the nostrils, has been proposed to treat hypoxemic acute respiratory failure (11). The potential preoxygenation benefits of HFNO, often including the application also during the apneic phase ("apneic oxygenation") was evaluated in several trials and meta-analysis (10): limited evidence based on five trials suggested that HFNO applied for apneic oxygenation does not reduce the rate of severe hypoxemic events, but might improve the peri-procedural lowest oxygen saturation without reducing the rate of severe hypoxemic events (10). Several reasons could explain the limited efficacy of HFNO, the most important being the low level—if any—of positive end-expiratory pressure (PEEP) generated by HFNO

particularly in patients breathing through the mouth. This prevents an improvement in lung volume and an increase in lung oxygen reserve (12).

Recently a multicenter, randomized trial focused on intubation of non-severely hypoxemic critically ill adult patients, excluding patients with a pO_2/FiO_2 ratio below 200 mmHg and comparing HFNO (pure oxygen, with flow set at 60 L/min) to standard bag-valve mask oxygenation (SMO, oxygen flow 15 L/min by a self-inflating resuscitator with reservoir, manually and firmly held in place) (13). The study took place in seven French ICUs; preoxygenation lasted 4 minutes in both groups, but HFNO was maintained also during intubation to offer an apneic oxygenation. The administered drugs were not standardized. The trial enrolled 184 patients, while 922 assessed for eligibility were excluded. Most patients were intubated for neurological reasons.

The primary outcome was the median lowest SpO_2 during the intubation (from laryngoscopy until connection to the ventilator): no significant difference was observed between groups.

Secondary outcomes included several minor and major endpoints, like predefined moderate or severe adverse events, time on ventilation, organ failure during the first 5 days, length of stay in ICU, incidence of ventilator associated pneumonia, and mortality rate at day 28. The average time to intubation was significantly longer in the HFNO group (1 *vs.* 0.8 min) and the incidence of difficult intubation was higher with HFNO (10% *vs.* 1%). Despite this, significantly more patients in the SMO group experienced drops in SpO_2 : 23% in SMO group *vs.* 12% in HFNO group experienced a drop of SpO_2 below 95%, 14% *vs.* 6% of patients experienced a drop below 90% ($P=0.1$) and 2% *vs.* 8% of patients showed values of SpO_2 below 80% ($P=0.06$). Overall, a significant higher incidence of severe adverse events was observed in the SMO group (16% *vs.* 6%); the same was true for moderate complications. The multivariate analysis confirmed the association of HFNO with less desaturation episodes below 90% (OR 0.21 *vs.* SMO) and with less intubation-related complications (OR 0.26). The Authors concluded that HFNO was associated with improved safety during intubation of non-severely hypoxemic critically ill patients, likely secondary to an apneic oxygenation effect.

Previously, the same research group had published a similar study but focusing on hypoxemic ICU patients, evaluating HFNO for preoxygenation versus high fraction-inspired oxygen facial mask in adult patients with a

pO_2/FiO_2 ratio <300 mmHg: no difference in any outcome was observed. Of note, at least one severe complication occurred in majority of patients (14).

New insights on HFNO and preoxygenation

Before the study by Guitton (13), according to guidelines and meta-analysis HFNO resulted to offer no relevant benefit but also no harm (4,10). In contrast, a very recent retrospective trial reported negative outcomes with HFNO (15). In a secondary analysis of the MACMAN trial on videolaryngoscope versus Macintosh laryngoscope, the Authors evaluated the efficacy of the four techniques applied for preoxygenation in adult ICU patients: bag-valve mask (BVM), non-rebreathing mask (NRM), HFNO and non-invasive ventilation (NIV). Two factors resulted associated with drops of SpO_2 below 90%: low baseline SpO_2 and preoxygenation device. Having BVM as reference, NIV significantly reduced the risk of hypoxemia (OR 0.1), NRM was not different from BVM, while HFNO significantly increased the risk (OR 5.75). It should be noted that the average pO_2/FiO_2 was well below 200 mmHg in all the four groups. The Authors concluded that the role of HFNO remained unclear and might be reserved in patients with mild hypoxemia, while NIV should be considered the first choice in severely-hypoxemic patients.

In a randomized controlled multicenter trial (the FLORALI-2 study) enrolling more than 300 patients, Frat *et al.* compared HFNO to NIV for preoxygenation (16). No difference in the rate of severe hypoxemic episodes or of other immediate or late severe complications; however, in the subgroup of patient with a pO_2/FiO_2 ratio below 200 mmHg at baseline, patients preoxygenated by NIV showed a significant lower incidence of severe hypoxemia (24% *vs.* 35%).

Finally, another multicenter randomized study recently published offers complementary data on preoxygenation in critically ill adults (6). Preoxygenation included bag-mask ventilation (BVM, different to bag-valve oxygenation, in which the device is simply maintained on the face of the patient, because ventilation is delivered) and a PEEP of 5–10 cmH₂O compared to no ventilation (in most cases in this group supplemental oxygen was delivered, by facemask or nasal cannula). In the BVM group the median lowest SpO_2 was significantly higher (a difference more marked in severely hypoxemic patients) and drops of SpO_2 below 80% significantly less numerous (11% *vs.* 23%). Moreover, the incidence of aspiration was not different. So, BVM appeared

Table 1 Preoxygenation and apneic oxygenation protocol based on the severity of acute respiratory failure

Severity of the acute respiratory failure	Suggested preoxygenation technique (3–4 minutes if time permits)
Mild (200 mmHg < pO ₂ /FiO ₂ <300 mmHg)	Face-mask or nasal cannula (standard or HFNO) or bag-mask oxygenation, at the highest possible FiO ₂ Maintain nasal cannula in place during laryngoscopy, if used for preoxygenation Bag-mask ventilation if SpO ₂ drops below 90%
Moderate (100 mmHg < pO ₂ /FiO ₂ <200 mmHg)	Non-invasive ventilation [also including continuous positive airway pressure (CPAP)] with PEEP 5–10 cmH ₂ O and FiO ₂ 100% Consider apneic oxygenation with nasal cannula oxygen (standard or HFNO) during intubation Bag-mask ventilation with PEEP 5–10 cmH ₂ O if SpO ₂ drops below 90%
Severe (100 mmHg < pO ₂ /FiO ₂)	Non-invasive ventilation (also including CPAP) with PEEP 5–10 cmH ₂ O and FiO ₂ 100% Consider awake fiberoptic intubation without interrupting non-invasive ventilation, through dedicated masks Otherwise, consider apneic oxygenation with nasal cannula oxygen (standard or HFNO) during intubation Bag-mask ventilation with PEEP 5–10 cmH ₂ O if SpO ₂ drops below 90%

HFNO, high-flow nasal oxygen.

safer than no ventilation in terms of hypoxemic adverse events, without an increased risk of aspiration.

A work-in-progress, operative protocol

The study by Guitton and co-workers (13) showed that even the intubation of non-severely hypoxemic ICU patients presents a high incidence of adverse events; on the other hand, the enrolled patients were only a minority of the screened ones, with more patients excluded as they were severely hypoxemic. Hence, a standardized, well-constructed protocol for tracheal intubation (including the occurrence of difficult airway) should be in place in every ICU and all members of the team should be trained on it (7,9). While awaiting the results of future trials, we would offer a tentative summary relative to preoxygenation and apneic oxygenation for everyday practice based on best available evidence, published guidelines and personal experience, also following the ARDS Berlin definition as a pragmatic reference (*Table 1*) (4,6,10,15,17-20). The assumption is that there is no best technique to be adopted with every ICU patient; on the contrary, a progressive approach based on the severity of the acute respiratory failure (ARF, considered as the main non-modifiable risk factor for severe adverse event) should be adopted. Of course, safety is never too much and when in doubt one should choose the more prudent technique.

Three elements of the proposed protocol deserve further

comments. First, NIV should be considered the gold standard in the worst cases (4,10,15,21); at a minimum, it should never be interrupted before intubation if the patient is already on NIV, on the contrary NIV should be optimized for intubation setting FiO₂ at 100%. Second, a single trial suggested that the adjunct of HFNO for apneic oxygenation to NIV may be more beneficial than NIV alone in patients with pO₂/FiO₂ <300 mmHg (22). Finally, in extreme cases with pO₂/FiO₂ <100 mmHg we warmly suggest considering awake fiberoptic intubation *without* interrupting non-invasive ventilation, through dedicated masks: this technique allows to avoid major sedation and apneic periods, so avoiding or strongly minimizing the synergistic negative effects on hemodynamic and blood oxygenation of sedative agents and apnea. This technique has never been evaluated, but it appears logical and, in our experience, safe even in patients to be intubated for NIV failure (19).

Conclusions

The study by Guitton and co-workers (13) adds relevant data on the risky issue of intubation of critically ill patients. Even if the last words on HFNO is still to be said and contradictory findings have been reported, Guitton suggests that non-severely hypoxemic ICU patients are at risk for adverse events during intubation and might benefit from HFNO. While awaiting for conclusive results from future

trials, a stepwise protocol based on ARF severity could help make the procedure safer.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

- Jaber S, Amraoui J, Lefrant JY, et al. Clinical practice and risk factors for immediate complications of endotracheal intubation in the intensive care unit: A prospective, multiple-center study. *Crit Care Med* 2006;34:2355-61.
- Simpson GD, Ross MJ, McKeown DW, et al. Tracheal intubation in the critically ill: a multi-centre national study of practice and complications. *Br J Anaesth* 2012;108:792-9.
- Cook TM, Woodall N, Harper J, et al. Major complications of airway management in the UK: Results of the Fourth National Audit Project of the Royal College of Anaesthetists and the Difficult Airway Society. Part 2: Intensive care and emergency departments. *Br J Anaesth* 2011;106:632-42.
- Higgs A, McGrath BA, Goddard C, et al. Guidelines for the management of tracheal intubation in critically ill adults. *Br J Anaesth* 2018;120:323-52.
- De Jong A, Rolle A, Molinari N, et al. Cardiac arrest and mortality related to intubation procedure in critically ill adult patients: a multicentre cohort study. *Crit Care Med* 2018;46:532-9.
- Casey JD, Janz DR, Russel DW, et al. Bag-mask ventilation during tracheal intubation of critically ill adults. *NEJM* 2019;380:811-21.
- Jaber S, Jung B, Corne P, et al. An intervention to decrease complications related to endotracheal intubation in the intensive care unit: A prospective, multiple-center study. *Intensive Care Med* 2010;36:248-55.
- Janz DR, Semler MW, Joffe AM, et al; Check-UP Investigators; Pragmatic Critical Care Research Group. A Multicenter Randomized Trial of a Checklist for Endotracheal Intubation of Critically Ill Adults. *Chest* 2018;153:816-24.
- De Jong A, Jung B, Jaber S. Intubation in the ICU: we could improve our practice. *Crit Care* 2014;18:209.
- Cabrini L, Landoni G, Baiardo Radaelli M, et al. Tracheal intubation in critically ill patients: a comprehensive systematic review of randomized trials. *Crit Care* 2018;22:6.
- Ricard JD. High flow nasal oxygen in acute respiratory failure. *Minerva Anestesiol* 2012;78:836-41.
- Hanouz JL, Gérard JL, Fischer MO. Nasal high-flow preoxygenation for endotracheal intubation in the critically ill patient? *Con. Intensive Care Med* 2019;45:526-8.
- Guitton C, Ehrmann S, Volteau C, et al. Nasal high-flow preoxygenation for endotracheal intubation in the critically ill patient: a randomized clinical trial. *Intensive Care Med* 2019;45:447-58.
- Vourc'h M, Asfar P, Volteau C, et al. High-flow nasal cannula oxygen during endotracheal intubation in hypoxic patients: a randomized controlled clinical trial. *Intensive Care Med* 2015;41:1538-48.
- Bailly A, Ricard JD, Le Thuaut A, et al; Clinical Research in Intensive Care and Sepsis Group (CRICS-TRIGGERSEP). Compared Efficacy of Four Preoxygenation Methods for Intubation in the ICU: Retrospective Analysis of McGrath Mac Videolaryngoscope Versus Macintosh Laryngoscope (MACMAN) Trial Data. *Crit Care Med* 2019;47:e340-8.
- Frat JP, Ricard JD, Quenot JP, et al; FLORALI-2 study group; REVA network. Non-invasive ventilation versus high-flow nasal cannula oxygen therapy with apnoeic oxygenation for preoxygenation before intubation of patients with acute hypoxaemic respiratory failure: a randomised, multicentre, open-label trial. *Lancet Respir Med* 2019;7:303-12.
- Cabrini L, Nobile L, Cama E, et al. Non-invasive ventilation during upper endoscopies in adult patients. A systematic review. *Minerva Anestesiol* 2013;79:683-94.
- Pieri M, Landoni G, Cabrini L. Noninvasive Ventilation During Endoscopic Procedures: Rationale, Clinical Use, and Devices. *J Cardiothorac Vasc Anesth* 2018;32:928-34.
- Pieri M, Cabrini L, Landoni G. Preventing Intubation-Related Cardiac Arrest in ICU: A Promising New Ventilation Mask. *Crit Care Med* 2018;46:e715.
- ARDS Definition Task Force, Ranieri VM, Rubenfeld GD, et al. Acute respiratory distress syndrome: the Berlin Definition. *JAMA* 2012;307:2526-33.
- Baillard C, Fosse JP, Sebbane M, et al. Noninvasive

- ventilation improves preoxygenation before intubation of hypoxic patients. *Am J Respir Crit Care Med* 2006;174:171-7.
22. Jaber S, Monnin M, Girard M, et al. Apnoeic oxygenation via high-flow nasal cannula oxygen combined with non-

invasive ventilation preoxygenation for intubation in hypoxaemic patients in the intensive care unit: the single-centre, blinded, randomised controlled OPTINIV trial. *Intensive Care Med* 2016;42:1877-87.

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