Published in final edited form as:

Lancet Respir Med. 2019 April ; 7(4): 284–285. doi:10.1016/S2213-2600(19)30054-2.

“Ventilation before Intubation: Preventing Severe Hypoxemia during Tracheal Intubation in the ICU”

Jonathan D. Casey, MD¹ and Matthew W. Semler, MD, MSc¹

¹Division of Allergy, Pulmonary, and Critical Care Medicine, Vanderbilt University Medical Center, Nashville, TN

How can we prevent the millions of critically ill adults who undergo tracheal intubation each year from experiencing life-threatening hypoxemia? An answer to that question has recently begun to emerge from a series of critical care clinical trials comparing approaches to oxygenation and ventilation during different phases of the intubation procedure.

Rapid sequence induction and tracheal intubation occurs in three phases differentiated by the steps of the procedure, the respiratory effort of the patient, and the ability of the provider to administer supplemental oxygen and ventilation (Figure 1). The first phase (“preoxygenation”) occurs prior to induction of anesthesia. During this phase, patients are often spontaneously breathing, and supplemental oxygen may be provided through low-flow devices (e.g., nasal cannula, facemask, or bag-mask) or high-flow devices (e.g., high-flow nasal cannula [HFNC]). Alternatively, supplemental oxygen and ventilation may be provided together via non-invasive ventilation (NIV) or bag-mask ventilation. During the second phase of intubation, between induction and laryngoscopy, the same devices can apply supplemental oxygen or oxygen and ventilation, but medication-induced hypopnea or apnea may compromise the patient’s ability to assist in moving gas from the pharynx to the alveoli. During the third phase of intubation, between initiation of laryngoscopy and successful intubation of the trachea, the patient is usually apneic. The laryngoscope prevents provision of oxygen or ventilation by mask, but oxygen may be administered via nasal cannula (sometimes referred to as “apneic oxygenation”).

Because HFNC can deliver 100% oxygen at rates exceeding peak inspiratory flow, produce 2–3 cm H₂O of positive airway pressure,¹ and remain in place from preoxygenation through laryngoscopy, two recent trials hypothesized that providing supplemental oxygen with HFNC would be superior to a bag-mask or facemask. Disappointingly, however, neither trial observed a significant benefit to HFNC in preventing hypoxemia during intubation.^{2,3}

NIV and bag-mask ventilation deliver high flow-rates of 100% oxygen, elevate mean airway pressure, and facilitate movement of oxygen from the pharynx to the alveoli even when respiratory effort is impaired. Two randomized trials have compared preoxygenation with

Corresponding Author: Matthew W. Semler, MD, MSc, Assistant Professor, Division of Allergy, Pulmonary, and Critical Care Medicine, Vanderbilt University Medical Center, C-1216 Medical Center North, Nashville, TN 37232, Office Phone: (615) 322-3412; Fax: (615) 343-7448, matthew.w.semmler@vanderbilt.edu.

Conflicts of Interest: All authors completed and submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. The authors declared no potential conflicts of interest with the current work.

NIV vs facemask among adults with acute hypoxemic respiratory failure. The first trial found that NIV dramatically reduced the incidence of severe hypoxemia – from 46% in the facemask group to 7% in the NIV group.⁴ In the second trial, the incidence of severe hypoxemia was numerically (but not statistically significantly) lower with NIV (28%) compared to facemask (18%).⁵ Indirect inference from these trials has led some experts to recommend NIV as first line during intubation of adults with acute hypoxemic respiratory failure. However, the effects of NIV vs HFNC have never been directly compared.

In this issue of *Lancet Respiratory Medicine*, Frat and colleagues present the first randomized trial comparing NIV versus HFNC during intubation of critically ill adults (**LRM FLORALI-II citation). The trial enrolled 322 adults with a PaO₂/FiO₂ ratio 300 mm Hg undergoing intubation in 28 French ICUs. Patients randomized to NIV received 6–8 mL/kg breaths of 100% oxygen with 5 cm H₂O of positive end-expiratory pressure from the start of preoxygenation until laryngoscopy. Patients randomized to HFNC received 60 L/min of 100% oxygen via nasal prongs from the start of preoxygenation until intubation of the trachea. The primary outcome of severe hypoxemia (oxygen saturation less than 80%) was centrally adjudicated by blinded reviewers using pulse oximetry recordings – a strength of the study.

The incidence of severe hypoxemia during intubation was 23.2% in the NIV group and 27.5% in the HFNC (absolute difference –4.2%; 95% CI –13.7% to 5.5%; P=0.39). Secondary outcomes did not significantly differ between groups. Interestingly, the effect of study group on the primary outcome appeared to differ based on baseline PaO₂/FiO₂ ratio (the variable on which randomization was stratified). Among 71 patients with a PaO₂/FiO₂ ratio > 200 mm Hg, the incidence of severe hypoxemia was 20.0% with NIV and 6.5% with HFNC (absolute difference 13.4%; 95% CI –2.2% to 33.1%; P=0.12). In contrast, among the 242 patients with a PaO₂/FiO₂ ratio 200 mm Hg, the incidence of severe hypoxemia was 23.9% with NIV and 35.2% with HFNC (absolute difference –11.3%; 95% CI –22.3 to 0.3%; P=0.06).

Frat and colleagues should be commended for conducting a rigorous trial addressing an important question in the difficult-to-study field of ICU intubation. But how should clinicians interpret the results? The primary analysis showed no statistical difference between groups – but the point estimate favored NIV and the confidence intervals included a clinically meaningful benefit. We feel the best approach is to consider these new data in the context of the prior trials examining oxygenation and ventilation during intubation in the ICU. Three trials have now compared NIV to oxygen administration without ventilation during intubation of ICU patients. In each trial, the point estimate for severe hypoxemia favored NIV. In each trial, NIV appeared safe, with no increase in reported rates of gastric or oropharyngeal aspiration. Moreover, the potential benefit of providing both oxygen and ventilation during tracheal intubation of critically ill adults is further supported by results of a recent randomized trial in which bag-mask ventilation between induction and laryngoscopy appeared to significantly decrease the incidence of severe hypoxemia (**NEJM PreVENT citation).

In summary, while important questions remain, the new findings of Frat and colleagues, combined with those of prior trials, suggest that providing both supplemental oxygen and ventilation from the start of preoxygenation until laryngoscopy may be the most effective approach to preventing life-threatening hypoxemia for patients undergoing tracheal intubation in the ICU.

Sources of Funding:

J.D.C. was supported in part by the NIH (T32HL087738–12). M.W.S. was supported in part by the NHLBI (K23HL143053). The funding institutions had no role in (1) conception, design, or conduct of the study, (2) collection, management, analysis, interpretation, or presentation of the data, or (3) preparation, review, or approval of the manuscript.

REFERENCES

1. Parke RL, McGuinness SP. Pressures delivered by nasal high flow oxygen during all phases of the respiratory cycle. *Respir Care* 2013; 58: 1621–4. [PubMed: 23513246]
2. Simon M, Wachs C, Braune S, de Heer G, Frings D, Kluge S. High-Flow Nasal Cannula Versus Bag-Valve-Mask for Preoxygenation Before Intubation in Subjects With Hypoxemic Respiratory Failure. *Respir Care* 2016; 61: 1160–7. [PubMed: 27274092]
3. Vourc'h M, Asfar P, Volteau C, et al. High-flow nasal cannula oxygen during endotracheal intubation in hypoxemic patients: a randomized controlled clinical trial. *Intensive Care Med* 2015; 41: 1538–48. [PubMed: 25869405]
4. Baillard C, Fosse J-P, Sebbane M, et al. Noninvasive Ventilation Improves Preoxygenation before Intubation of Hypoxic Patients. *Am J Respir Crit Care Med* 2006; 174: 171–7. [PubMed: 16627862]
5. Baillard C, Prat G, Jung B, et al. Effect of preoxygenation using non-invasive ventilation before intubation on subsequent organ failures in hypoxaemic patients: a randomised clinical trial. *British Journal of Anaesthesia* 2018; 120: 361–7. [PubMed: 29406184]

Figure 1. Oxygenation and Ventilation during Rapid Sequence Induction and Intubation.
HFNC is high flow nasal cannula; NIV is non-invasive ventilation.