Apneic Oxygenation for Intubation in the Critically Ill. Let's Not Give Up!

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In this issue of the *Journal*, Semler and colleagues (pp. 273–280) reported the effect of apneic oxygenation with 15 L/min nasal cannula oxygen on the lowest oxygen saturation during the intubation procedure (1).

The authors performed a randomized trial in a medical intensive care unit (ICU), enrolling 150 patients. In the usual care group and in the apneic oxygenation group, respectively, 73 and 77 patients were included. The administration of 15 L/min nasal cannula oxygen in the apneic oxygenation group was not associated with a significantly less drop in arterial oxygen saturation (from 92% in the apneic oxygenation group to 90% in the usual care group [$P = 0.16$]). The authors concluded that apneic oxygenation does not increase the lowest arterial oxygen saturation during intubation in critically ill patients compared with usual care.

In 1959, one study reported about eight patients scheduled for minor operations intubated and paralyzed to prevent breathing (2). Pure oxygen was administered in the endotracheal tube. The patients drastically increased their carbon dioxide tension (up to 250 mm Hg) and developed respiratory acidosis (up to a pH of 6.72) while maintaining 100% oxygen saturation. Indeed, whereas carbon dioxide tension depends on minute ventilation, oxygenation depends on positive end-expiratory pressure (PEEP) and $F_{I_{O_2}}$. The aim of using apneic oxygenation throughout the intubation procedure in ICUs would be to reduce the occurrence of severe hypoxemia and its associated complications (3), such as cardiac arrest (4). Indeed, if noninvasive ventilation can be used to enhance preoxygenation (5, 6), the mask has to be removed during the laryngoscopy, and the patient is deprived of oxygen during the procedure. Apneic oxygenation increased the time to severe desaturation during the intubation procedure in acute lung injury in an experimental study in piglets (7). Miguel-Montanes and colleagues (8) compared 3 minutes of preoxygenation using a nonrebreathing bag reservoir face mask with 60 L/min of high-flow nasal cannula oxygen in patients with mild to moderate hypoxemia. With the face mask, the median lowest oxygen saturation as measured by pulse oximetry during intubation was 94% versus 100% with high-flow oxygen.

Contrary to the positive effects of high-flow nasal cannula oxygen reported in the study by Miguel-Montanes and colleagues (8) on the prevention of oxygen desaturation during intubation, Vourc'h and colleagues (9) did not report similar results. They found no difference on lowest arterial oxygen during intubation in hypoxemic patients between 60 L/min of high-flow nasal cannula oxygen and 4 minutes of preoxygenation with a face mask (92% vs. 90%; $P = 0.44$). Finally, among these three randomized studies (1, 8, 9) that evaluated apneic oxygenation during tracheal intubation, only one study (8) reported superiority with high-flow nasal cannula oxygen, and two studies (1, 9) showed no significant difference between preoxygenation devices. The discrepancies between the results of these three studies (1, 8, 9) could mainly be explained by the oxygen flow used for the apneic oxygenation group (from 15 to 60 L/min) and the different studied populations in term of hypoxemia. Efficacy of apneic oxygenation mostly depends on delivered $F_{I_{O_2}}$, oxygen flow, position of the patient, and degree of hypoxemia. High-flow oxygen therapy generates a flow-dependent positive airway pressure that could prevent extubation failure compared with Venturi mask (10). However, in the current study, oxygen was administered by nasal cannula with a flow of 15 L/min, which does not allow a positive airway pressure (11). As suggested by Semler and colleagues (1) in their discussion, increasing the flow of oxygen from 15 to 60 L/min could improve apneic oxygenation. Moreover, the position of the mandible was not standardized, whereas subluxation of the temporomandibular joint during preoxygenation could improve oxygen diffusion by liberating the airway, displacing the tongue at a ventral position, and thus increasing the oropharyngeal space (12). Furthermore, mouth closing or opening during preoxygenation was not specified, whereas PEEP effect is only significant when the mouth is closed (11). Nor was the position of the patient during preoxygenation standardized, which influences the duration of nonhypoxic apnea after anesthetic induction. Similarly, the choice of preoxygenation devices as reported in Semler and colleagues' Table 1 (nonrebreather mask, bilevel positive airway pressure, bag–valve mask ventilation, standard nasal cannula) was left to the physicians' appreciation. This is also a confounding factor, given that noninvasive ventilation in hypoxemic patients has been shown to increase lowest oxygen saturation during intubation procedure (5).

In the study of Semler and colleagues (1), the lowest oxygen saturation was 91% in the usual care group versus 92% in the apneic oxygenation group. In the literature, reported lowest oxygen saturation during intubation procedure of hypoxemic patients is between 80 and 85% (5, 13). Apneic oxygenation could particularly benefit to this specific population of hypoxemic patients. Further, patients in whom a specific laryngoscopy device was required, such as a video laryngoscope (14, 15), were excluded. In this population at risk for difficult intubation, apneic oxygenation could also be very relevant, given the potentially increased length of intubation associated with an increased incidence of hypoxemia. It is worth noting that hypoxemia *per se* is a factor of difficult intubation (13) and associated complications.

It bears noting that an important limitation of the study is the absence of a blinded design. Assessors of oxygen saturation could have been influenced by their own opinion. Another limitation, also related to the design, is the number of subjects needed, based on an optimistic hypothesis of a 4.6% difference between groups. The saturation in usual care being 91%, the mean lowest oxygen saturation in the apneic oxygenation group should have been 96%, which is very high for an intubation performed in an ICU (13).

To conclude, the study of Semler and colleagues (1) is a randomized nonblinded study showing there is no difference between apneic oxygenation with a flow of 15 L/min nasal cannula oxygen and usual care in the lowest oxygen saturation experienced by nonselected critically ill adults undergoing endotracheal intubation. The effect of apneic oxygenation during intubation procedure in the ICU could interestingly be now assessed in a specific population of hypoxemic patients, particularly at risk for oxygen desaturation. At least 60 L/min of high-flow nasal cannula oxygen should be applied to allow higher $F_{I_{O_2}}$ with a moderate level of PEEP. ■

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