Use of High-Flow Nasal Cannula Oxygen Therapy to Prevent Desaturation During Tracheal Intubation of Intensive Care Patients With Mild-to-Moderate Hypoxemia

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Objectives: Tracheal intubation of ICU patients is frequently associated with severe hypoxemia. Although noninvasive ventilation reduces desaturation during intubation of severely hypoxemic patients, it does not allow for per-procedure oxygenation and has not been evaluated in mild-to-moderate hypoxemic patients for whom high-flow nasal cannula oxygen may be an alternative. We sought to compare pre- and per-procedure oxygenation with either a nonrebreathing bag reservoir facemask or a high-flow nasal cannula oxygen during tracheal intubation of ICU patients.

Design: Prospective quasi-experimental before-after study (ClinicalTrials.gov: NCT01699880).

Setting: University hospital medico-surgical ICU.

Patients: All adult patients requiring tracheal intubation in the ICU were eligible.

Interventions: In the control (before) period, preoxygenation was performed with a nonrebreathing bag reservoir facemask and in the change of practice (after) period, with high-flow nasal cannula oxygen.

Measurements and Main Results: Primary outcome was median lowest Spo_2 during intubation, and secondary outcomes were Spo_2 after preoxygenation and number of patients with saturation less than 80%. One hundred one patients were included. Median lowest Spo_2 during intubation were 94% (83–98.5) with the nonrebreathing bag reservoir facemask versus 100% (95–100) with high-flow nasal cannula oxygen ($p < 0.0001$). Spo_2 values at the end of preoxygenation were higher with high-flow nasal cannula oxygen than with nonrebreathing bag reservoir facemask and were correlated with the lowest Spo_2 reached during the intubation procedure ($r = 0.38$, $p < 0.0001$). Patients in the nonrebreathing bag reservoir facemask group experienced more episodes of severe hypoxemia (2% vs 14%, $p = 0.03$). In the multivariate analysis, preoxygenation with high-flow nasal cannula oxygen was an independent protective factor of the occurrence of severe hypoxemia (odds ratio, 0.146; 95% CI, 0.01–0.90; $p = 0.037$).

Conclusions: High-flow nasal cannula oxygen significantly improved preoxygenation and reduced prevalence of severe hypoxemia compared with nonrebreathing bag reservoir facemask. Its use could improve patient safety during intubation. (*Crit Care Med* 2014; XX:00–00)

Key Words: hypoxemia; hypoxemic acute respiratory failure; oxygenation; patient safety; tracheal intubation

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Tracheal intubation is one of the most routinely performed invasive procedures in the ICU, but also one frequently associated with morbidity and, in some instances, mortality (1, 2). Almost one intubation out of three (28%) has been associated with at least one severe complication (3), and occurrence of severe hypoxemia was the complication the most often reported in this study (26%), which has been shown to increase mortality in specific populations (4, 5). Intubation is usually preceded by several minutes of preoxygenation through a nonrebreathing bag reservoir facemask (NRM) to delay desaturation. In healthy subjects such as in the anesthesia setting, preoxygenation allows for up to 9 minutes apnea without arterial desaturation below 90% (6). In the ICU however, preoxygenation is much less efficient, mainly due to patients' unstable cardiovascular or respiratory status (7). Alternative techniques have been proposed to reduce the prevalence of severe hypoxemia during intubation. A pivotal study by Baillard et al (8) convincingly showed that noninvasive ventilation (NIV) could reduce prevalence and magnitude of desaturation during intubation by enhancing preoxygenation. However, because this technique is interrupted during intubation (in order to allow laryngoscopy), there is no apneic oxygenation, and thus, serious desaturation may still occur, as evidenced by Baillard et al (8) in their study. In addition, patients with neurological impairment cannot benefit from this technique that requires patient's acceptance and cooperation. Finally, only a subset of ICU patients was evaluated in this study, those with profound hypoxemia. For all these reasons, an alternative technique that is more easily implemented and suitable for all patients including comatose ones merits investigation. High-flow nasal cannula oxygen (HFNC) is a device that allows the delivery of humidified and heated oxygen up to 60 L/min, with a modifiable inspired concentration of oxygen of up to 100%. It has become increasingly popular in the ICU to manage patients with acute hypoxemic respiratory failure (9–12) and may find other applications in ensuring oxygenation during invasive procedures (e.g., bronchoscopy [13, 14] or intubation). Indeed, HFNC has the advantage over the other techniques of preoxygenation (NIV and NRM) of being maintained during laryngoscopy and intubation allowing for apneic oxygenation. For these reasons, we believe that HFNC may improve the quality of pre- and per-intubation oxygenation. We thus conducted a prospective quasi-experimental before-after study to determine if HFNC is able to improve preoxygenation and reduce the prevalence of severe hypoxemia during intubation in comparison with NRM. We deemed that conducting a randomized trial would not be ethical due to obvious lack of equipoise between the two techniques.

PATIENTS AND METHODS

Study Design

This prospective quasi-experimental before-after study took place in the 12-bed medico-surgical ICU of Louis Mourier University Hospital, Colombes, France. It was conducted from March 2011 to November 2012. During the control period (March to December 2011), all patients were intubated with our standard preoxygenation procedure that used a NRM. In the "change of practice" period (January to November 2012), use of HFNC as a preoxygenation device was applied to all our patients requiring tracheal intubation.

The Ethics Committee of the French Society of Intensive Care approved the study protocol and waived the need for written informed consent of the participants, according to French law. A specific information letter was given to the patient and/or to the family, describing the purpose of the study and the nature of the data collected. In addition, as part of our general policy on information provided to the patients and relatives, a leaflet is given at admission to the ICU, explaining that data gathered for usual care purposes may be used for medical research and publication.

Description of the Intubation Procedure

Rapid sequence induction with a hypnotic agent and a short-acting neuromuscular blocking agent was performed systematically before intubation. In the absence of contraindication, succinylcholine and etomidate are, respectively, the neuromuscular blocking and the hypnotic agents used in our unit for rapid sequence intubation. Two operators are present for each intubation. A first laryngoscopy is systematically attempted by a resident, as part of our training policy (15). The senior physician takes control if the attempt failed. The initial ventilator settings are determined by the senior clinician in charge according to needs of the patients, usually with a F_{IO_2} of 1.0. A blood sample for arterial blood gas analysis is systematically performed less than 1 hour after intubation. During the control phase, preoxygenation was performed with a NRM for at least 3 minutes before intubation with 15 L/min oxygen flow. The mask was removed during the intubation itself. As routinely done in our ICU, oxygen with a 6 L/min flow was administered to patients through a nasopharyngeal catheter during the apnea period. During the second phase, preoxygenation was performed with HFNC for 3 minutes before intubation. Oxygen flow was set at 60 L/min and the F_{IO_2} at 1.0. The device was maintained during the intubation itself. All other steps of the procedure were similar during the two phases of the study.

Patients

Adult patients admitted to our ICU and requiring endotracheal intubation were eligible. Noninclusion criteria were age under 18 years, intubation for cardiac arrest, severe hypoxemia (defined as Sp_{O_2} < 95% under a NRM with an oxygen flow of 15 L/min), patients already receiving HFNC, and patients under NIV. Although the final decision to intubate was left at the clinician's discretion, our ICU follows accepted indications for intubation, which include respiratory arrest, respiratory pauses with loss of consciousness, psychomotor agitation making nursing care impossible and requiring sedation, hemodynamic instability despite vasopressor administration and with systolic arterial pressure below 70 mm Hg, partial pressure of arterial oxygen below 45 mm Hg, loss of consciousness, or worsening encephalopathy (16).

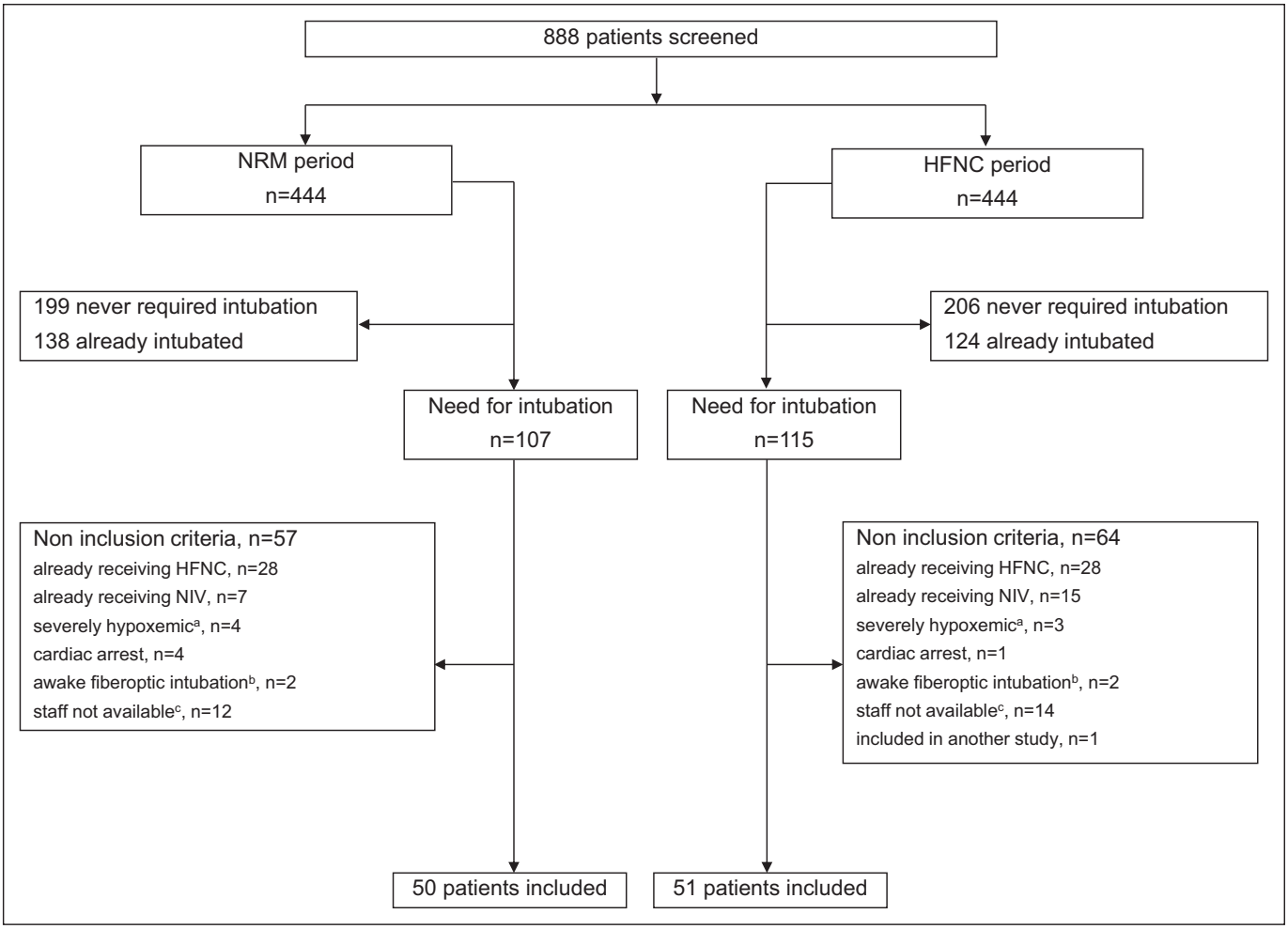

Figure 1. Patient flow chart indicating numbers of patients screened for eligibility, intubated in the ICU and finally analyzed in the study. HFNC = high-flow nasal cannula oxygen, NIV = noninvasive ventilation, NRM = nonrebreathing bag reservoir facemask. [a]Spo_2 below 95% while receiving 15 L/min oxygen through a NRM. [b]Awake fiberoptic intubation for planned difficult intubation. [c]Refers to a situation of intense activity in the ICU with work overload that precluded the physician from including the patient in the study.

Device Description

The HFNC device (Optiflow; Fisher & Paykel, Auckland, New Zealand) consists of an air-oxygen blender with adjustable Fio_2 (0.21–1.0) that delivers a modifiable gas flow (≤ 60 L/min) to a heated chamber (MR 850 passover humidifier; Fisher & Paykel) where the gas is heated and humidified. The gas mixture is then routed through a high-performance circuit (RT 310; Fisher & Paykel) to be delivered to the patient via short, wide bore nasal prongs at 37°C and containing 44 mg H_2O/L.

Conventional oxygen was given through a high Fio_2 NRM (Intersurgical, Wokingham, United Kingdom).

Collected Data

We recorded baseline demographic and clinical data. Vital signs, with a particular attention to Spo_2, were monitored before and after preoxygenation, during the whole procedure, and until 30 minutes after intubation. Arterial blood gas analyses preceding and following intubation were collected when available. Difficulty of intubation was assessed with the following variables: Cormack score (17), duration of the procedure (from drug injection to connection to the respirator), number of attempts, use of specific devices for difficult airway management, and success or failure of intubation by the resident. The following adverse events were recorded: occurrence of arrhythmia, cardiac arrest, and death during or immediately following the procedure. A portable chest radiograph was systemically performed after intubation to confirm adequate position of the tube. Presence of gastric distension was also checked on the radiograph.

Endpoints and Statistical Analysis

The primary endpoint of the present study was the lowest Spo_2 value observed in each patient. Secondary endpoints were median Spo_2 obtained during intubation, after preoxygenation, and after intubation and prevalence of life-threatening hypoxemia (defined by a Spo_2 below 80%) during the procedure. Other prespecified outcome measures were the prevalence of serious adverse events (cardiac arrest, sustained arrhythmia, and hemodynamic instability).

For all the analyses, the main independent variable was the group membership (HFNC or NRM) and was included in all multivariate models.

TABLE 1. Baseline Characteristics, Intubation Conditions, and Reasons for Intubation of Study Patients

Variable	Nonrebreathing Bag Reservoir Facemask *n* = 50	High-Flow Nasal Cannula Oxygen *n* = 51	*p*
Age, yr, median (IQR)	61 (36–74)	59 (52–74)	0.90[a]
Gender, male/female, *n*	33/17	32/19	0.73[b]
Comorbidities, *n* (%)			
Chronic obstructive pulmonary disease	7 (14)	6 (12)	0.74[b]
Sleep apnea	2 (4)	0 (0)	0.24[c]
Chronic heart failure	5 (10)	3 (6)	0.70[b]
Coronary heart disease	6 (12)	4 (8)	0.71[b]
Hypertension	22 (44)	16 (31)	0.19[b]
Diabetes	4 (8)	10 (20)	0.09[b]
Atrial fibrillation	3 (6)	8 (16)	0.12[b]
Chronic renal failure	2 (4)	1 (2)	0.62[b]
Cancer	3 (6)	3 (6)	1.00[b]
Cirrhosis	10 (20)	11 (22)	0.85[b]
HIV	0 (0)	1 (2)	1.0[b]
Smoking	22 (44)	18 (35)	0.37[b]
Alcohol abuse	18 (36)	20 (39)	0.74[b]
Simplified Acute Physiology Score II, median (IQR)	44 (35–61.5)	47 (32–57)	0.77[a]
Difficulty of intubation			
Cormack 3–4, *n* (%)[d]	7 (14)	2 (4)	0.15[b]
Intubation duration, min, median (IQR)	2 (2–4)	2 (2–3)	0.21[a]
Use of Eschmann tracheal tube introducer, *n* (%)	11 (22)	6 (12)	0.17[b]
Success of intubation by a junior resident, *n* (%)	28 (56)	37 (72.5)	0.08[b]
Oxygenation variables (IQR)			
Spo_2, median	100 (98–100)	100 (100–100)	0.02[a]
O_2 nasal flow, median	3.5 (2–9)	5 (2–10)	0.58[a]
Reason for intubation, *n* (%)			
Shock	15 (30)	20 (39)	0.22[c]
Altered consciousness	12 (24)	19 (37)	
Acute respiratory failure	14 (28)	7 (14)	
Status epilepticus	6 (12)	3 (6)	
Acute-on-chronic respiratory failure	3 (6)	2 (4)	

IQR = interquartile range.
[a]Wilcoxon rank-sum test.
[b]Pearson chi-square test.
[c]Fisher exact test.
[d]Versus Cormack score 2–3.

TABLE 2. Oxygenation Variables, Adverse Events During and After Intubation, and ICU Mortality

Variable	Nonrebreathing Bag Reservoir Facemask *n* = 50	High-Flow Nasal Cannula Oxygen *n* = 51	*p*
Spo_2 after preoxygenation, %, median (IQR)	100 (98–100)	100 (100–100)	0.01[a]
Lowest Spo_2, median (IQR)	94 (83–98)	100 (95–100)	< 0.0001[b]
Adjusted lowest Spo_2, %, median[c]	94	99.2	0.007
Spo_2 upon respirator connection, %, median (IQR)	98 (92.5–100)	100 (99–100)	0.0004[b]
Spo_2 5 min after intubation, %, median (IQR)	100 (98.8–100)	100 (100–100)	0.002[b]
Spo_2 30 min after intubation, %, median (IQR)	100 (99–100)	100 (100–100)	0.024[b]
Spo_2 < 80%, *n* (%)	7 (14)	1 (2)	0.03[a]
Pao_2 after intubation, mm Hg, median (IQR)	280 (143–359)	239 (128–440)	0.59[b]
Sustained arrhythmia during intubation, *n* (%)	1 (2)	0 (0)	0.31[a]
Cardiac arrest during intubation, *n* (%)	1 (2)	0 (0)	0.31[a]
Death in ICU, *n* (%)	8 (16)	7 (14)	0.75[a]

IQR = interquartile range.

[a]Pearson chi-square test.

[b]Wilcoxon rank-sum test.

[c]Lowest Spo_2 was adjusted for the following variables (quantile regression of the median): study phase, baseline Spo_2, diabetes, difficulty of intubation (use of an Eschmann tube introducer, Cormack score 3 or 4, and success of intubation by a junior resident), and reason for intubation. See supplemental data (Supplemental Digital Content 1, http://links.lww.com/CCM/B139) for details.

Results are expressed as median (25–75%) or frequencies and percentages (%), as appropriate. Categorical variables were compared by chi-square or Fisher exact test, and continuous variables were compared by Student *t* test or Wilcoxon rank-sum test, as appropriate.

Between-groups difference in lowest Spo_2 was adjusted for baseline covariates significantly associated with lowest Spo_2 or with the group membership ($p < 0.2$). As lowest Spo_2 was not normally distributed, univariate analysis of lowest Spo_2 was performed using Wilcoxon rank-sum test (for median comparisons) or Kendall correlation coefficient, and multivariate analysis used quantile regression of the median (18). Quantile regression differs from standard linear regression: quantile regression models the relation between a set of explicative variables and specific percentiles (e.g., the 50th percentile, i.e., the median) of the response variable, whereas linear regression models the mean of the response variable. Unlike linear regression, quantile median regression does not assume a normal error distribution, but it has a similar interpretation: it quantifies change in a central measure (the median) of the response variable (lower Spo_2) as a function of other predicators.

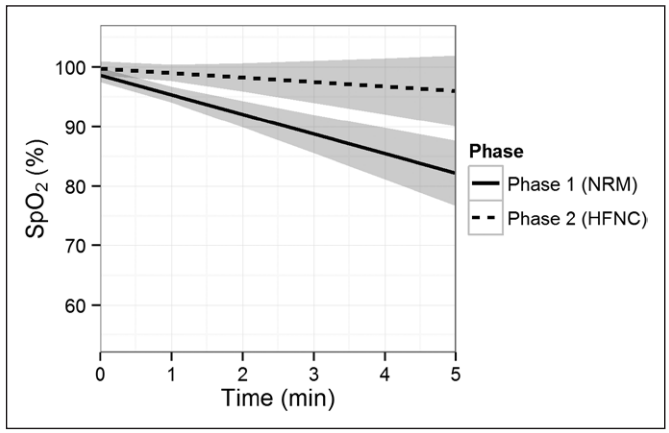

Figure 2. Predicted Spo_2 during the first 5 min of intubation. The two *black lines* represent the predicted Spo_2 during the first 5 min of intubation, using a linear mixed-effect model for each group (nonrebreathing bag reservoir facemask [NRM] and high-flow nasal cannula oxygen [HFNC]). For each prediction, the CI is figured by the gray region. There was a statistical difference for predicted Spo_2 drop between the two groups. Modeling took into account all the measures before the success of intubation (maximal duration of 10 min), but only the first 5 min of the predicted Spo_2 is represented (as the intubation procedure lasted < 5 min for 90% of patients). Variables of the mixed-effect model are presented in supplemental data (Supplemental Digital Content 1, http://links.lww.com/CCM/B139).

TABLE 3. Risk Factors for Severe Hypoxemia (Spo_2 < 80%)

Variable	Spo_2 > 80% *n* = 93	Spo_2 < 80% *n* = 8
Age, yr, median (IQR)	60 (49–74)	47 (33.5–66)
Male sex, *n* (%)	60 (65)	5 (62)
Chronic obstructive pulmonary disease, *n* (%)	11 (12)	2 (25)
Chronic heart failure, *n* (%)	7 (8)	1 (12)
Coronary heart disease, *n* (%)	8 (9)	2 (25)
Hypertension, *n* (%)	34 (37)	4 (50)
Sleep apnea, *n* (%)	1 (1)	1 (12)
Diabetes, *n* (%)	13 (14)	1 (12)
Atrial fibrillation, *n* (%)	10 (11)	1 (12)
Chronic renal failure, *n* (%)	3 (3)	0 (0)
Cancer, *n* (%)	6 (6)	0 (0)
Cirrhosis, *n* (%)	21 (23)	0 (0)
HIV, *n* (%)	1 (1)	0 (0)
Smoking, *n* (%)	37 (40)	3 (38)
Alcohol abuse, *n* (%)	36 (39)	2 (25)
Eschmann tracheal tube introducer requirement, *n* (%)	15 (16)	2 (25)
Cormack 3–4, *n* (%)[e]	8 (9)	1 (12)
Success of intubation by a resident, *n* (%)	62 (67)	3 (38)
Duration of intubation, median (IQR)	2 (2–3)	3.5 (2.75–4.25)
Baseline O_2 nasal flow, median (IQR)	5 (2–12)	2.5 (2–3)
Baseline Pao_2, median (IQR)	102 (81–154)	88 (77–96)
Baseline Spo_2, median (IQR)	100 (99–100)	98.5 (97.5–100)
Preoxygenation with high-flow nasal cannula oxygen, *n* (%)	50 (54)	1 (12)

IQR = interquartile range, NA = not applicable.

[a]Wilcoxon rank-sum test.

[b]Fisher exact test.

[c]Adjustment on "sleep apnea" was not possible because there were only two patients with sleep apnea both belonging to the nonrebreathing bag reservoir facemask group. A multivariate model with the same variables excluding these two patients did not change the conclusion.

[d]Pearson chi-square test.

[e]Versus Cormack score 2–3.

Evolution of Spo_2 during the intubation procedure was analyzed through a linear mixed-effects model to take into account the existence of a correlation between repeated measurements (for a complete description of the model, see **supplemental data**, Supplemental Digital Content 1, http://links.lww.com/CCM/B139).

Multivariate analysis of the occurrence of a desaturation (< 80%) was performed using logistic regression. Variables associated ($p < 0.10$) with outcome or with the group membership were introduced into the multivariate model. Odds ratios (and their 95% CI) are provided. Significance was defined as p values of less than 0.05. Statistical analyses were performed using R 3.0.1 (http://www.R-project.org).

RESULTS

Patient flow chart is shown in **Figure 1**. Eight hundred and eighty-eight patients were admitted to our ICU during the two study periods. Two hundred and sixty-two were already intubated and 405 never required endotracheal intubation. Finally, 101 patients (50 during the first phase and 51 during the second phase) were included in the study and analyzed.

Baseline characteristics of the studied patients are reported in **Table 1**. The two study groups were similar in terms of age, sex, underlying comorbidities, and the Simplified Acute Physiology Score (19). Arterial blood gases were not systematically drawn prior intubation. When available, these samples were classified according to the time of

Univariate Analysis			Multivariate Analysis		
Odds Ratio	95% CI	*p*	Odd Ratio	95% CI	*p*
0.98	0.94–1.01	0.21[a]			
1.09	0.21–4.73	1.0[b]			
2.49	0.34–12.45	0.27[b]			
1.76	0.09–12.11	0.50[b]			
3.54	0.47–18.65	0.18[b]			
1.74	0.39–7.77	0.71[b]			
13.14	0.49–357.70	0.15[b,c]			
0.88	0.045–5.55	1.0[b]	2.74	0.12–30.26	0.46
1.19	0.06–7.71	1.0[b]			
NA	NA	1.0[b]			
NA	NA	1.0[b]			
NA	NA	0.20[b]			
NA	NA	1.0[b]			
0.91	0.18–3.93	1.0[d]			
0.53	0.08–2.44	0.70[d]			
1.73	0.24–8.40	0.62[b]			
1.52	0.08–10.22	0.54[b]			
0.3	0.06–1.30	0.13[b]	0.26	0.04–1.32	0.10
1.20	0.87–1.58	0.035[a]			
0.80	0.55–0.99	0.07[a]	0.77	0.50–0.98	0.026
0.99	0.96–1.00	0.17[a]			
0.83	0.64–1.13	0.06[a]			
0.12	0.006–0.73	0.06[d]	0.14	0.01–0.90	0.037

sampling (within 2 hr of intubation, between 2 and 4 hr, and > 4 hr). There was no significant difference in Pao_2 at any of the different time points between the two groups (**eTable 1**, Supplemental Digital Content 1, http://links.lww.com/CCM/B139). Oxygen flow delivered before inclusion was not different between the two groups. Initial Spo_2 was 100% (100–100) in the NRM versus 100% (98–100) in the HFNC ($p = 0.01$). Both groups were similar in term of indication for intubation, duration and difficulty of intubation, and organ failure at baseline (**eTable 2**, Supplemental Digital Content 1, http://links.lww.com/CCM/B139).

Changes in Spo_2 during intubation are shown in **Table 2** and **Figure 2**. The decrease in Spo_2 during intubation was greater in the NRM group as evidenced by the lowest values of Spo_2 reached in each group (NRM, 94% [83–98.5] vs HFNC, 100% [95–100]; $p < 0.0001$). After adjustment for significant ($p < 0.2$ with outcome and/or group status) baseline covariates (baseline Spo_2, diabetes, difficulty of intubation [use of an Eschmann tube introducer, Cormack score 3 or 4, and success of intubation by a junior resident], reason for intubation, atrial fibrillation, sex, chronic pulmonary failure, and coronary heart disease), the difference remained significant (94 vs 99; difference 5% [1–9], $p = 0.007$). The decrease in the Spo_2 during the intubation procedure was analyzed with a linear mixed-effects model to adjust for the effect of time. The difference was statistically significant (Fig. 2), although

this analysis should be interpreted with caution because of the heterogeneity of individual Spo_2 profiles. The prevalence of severe hypoxemia, defined by a Spo_2 less than 80% during the procedure, was significantly lower in the HFNC group (2% vs 14%, $p = 0.03$). One cardiac arrest was recorded in the NRM group, and it was due to severe hypoxemia. Postintubation chest radiograph revealed no episode of gastric distension during the study period.

The variables associated with the occurrence of severe hypoxemia in univariate and multivariate analysis are shown in **Table 3**. In the multivariate analysis, preoxygenation with HFNC was an independent protective factor of the occurrence of severe hypoxemia (odds ratio, 0.14; 95% CI, 0.01–0.90; $p = 0.037$). Spo_2 values at the end of preoxygenation were correlated with the lowest Spo_2 reached during the intubation procedure ($r = 0.38$; $p < 0.0001$).

DISCUSSION

The results of this study strongly suggest that HFNC significantly improved oxygenation during intubation in our patients and prevented life-threatening hypoxemia compared with NRM. Given the high rate of severe hypoxemia during intubation in the ICU, our results have major clinical consequences, directly applicable in the ICU worldwide.

Life-threatening hypoxemia is the most frequently reported complication of intubation in the ICU (3). These desaturations occur despite preoxygenation. Numerous reasons concur to limit efficiency of preoxygenation in ICU patients: cardiopulmonary underlying disease, anemia, low cardiac output, hypermetabolic states, ventilation/perfusion mismatch, obesity, pain, etc (6, 7, 20). Finally, the rate of difficult intubation is greater in the ICU, and a subset of patients require more than two attempts, prolonging duration of apnea and obviously risk of desaturation. Improving preoxygenation is a crucial issue to reduce morbidity of urgent tracheal intubation in the ICU. Efforts to improve preoxygenation through optimized conventional facemask oxygenation and ventilation were found to be only marginally effective to prevent desaturation (7). Thus, other oxygenation administration techniques are required. NIV has proven to be among the most successful, as clearly shown by Baillard et al (8) in their compelling study comparing conventional facemask preoxygenation and NIV. They showed that NIV reduced profound desaturation (< 80%) from 46% to 7%. Despite these impressive results, it seems that NIV has not been widely adopted as a preoxygenation device. To the best of our knowledge, these results were not confirmed by another team apart from the particular case of obese patients' intubation in the operating room (21, 22). In the authors' own ICUs, a subsequent study indicated that NIV was "spontaneously" used in only 42% of the patients requiring urgent intubation (23). NIV has inherent limitations; the main one is the necessary acceptance and cooperation of the patient, excluding all the patients with neurological impairment; and the removal of the positive pressure to allow for laryngoscopy, thus preventing any oxygen delivery during attempts.

Our positive results with HFNC over conventional oxygen are consistent with the data reported in patients with acute hypoxemic respiratory failure and are related to the high Fio_2 delivered with the device (due to the absence of oxygen dilution), the pharyngeal dead-space washout, the optimal conditioning of inspired gases, and a certain amount of positive pressure (10, 11, 24–27). The extent to which the moderate positive pressure generated with HFNC (28) contributed significantly to the improved preoxygenation cannot be assessed, but these moderate levels of pressure have been shown to result in alveolar recruitment (29). Obviously, these levels are much smaller than those delivered during NIV (around 12 cm H_2O in the study by Baillard et al [8]) but may be sufficient in less hypoxemic patients. An important feature of HFNC and potential advantage over NIV is the possibility to pursue oxygenation during laryngoscopy, a technique known as "apneic oxygenation." Oxygen diffusion from the alveoli to the capillaries decreases alveolar pressure, generating a flow of air from the pharynx to the distal airway. Increasing pharyngeal oxygen content thus enhances apneic oxygenation, which has been shown to further delay desaturation (30–32). It is clear that features of HFNC make it ideal for apneic oxygenation. The respective contribution of each of them to the beneficial effect observed in the present study is difficult to establish.

A high Fio_2 NRM was used during the control period because it is the device used in our ICU for several years to provide preoxygenation. A recent study (33) compared bagvalve masks and NRM for preoxygenation and found that use of a NRM resulted in the same level of denitrogenation than the bagvalve mask. In addition, a greater difficulty to breathe through the bagvalve mask than through the NRM was reported in this study, and $Etco_2$ at the end of preoxygenation was higher with the bagvalve consistent with a certain level of rebreathing.

Limits and Strength of the Study

Our study has several limitations. First, it was not a randomized controlled trial (RCT). We believe that the choice of such a design would have been questionable for ethical reasons. Indeed, the prerequisite for performing an RCT is the high probability of clinical equipoise (which is supposed to be reached if most physicians agree they cannot decide a priori on the superiority of one arm over the other). In the present case, it is difficult to consider that equipoise exists for several reasons: by essence, HFNC was designed to deliver greater Fio_2 than NRM, and bench test evaluation provides clear evidence of this superiority (34), confirmed in several clinical studies unequivocally and systematically showing greater improvement in oxygenation with HFNC than with NRM in ICU patients (11, 24, 25, 29, 35). Our study was made ethically acceptable by the fact that we compared a period when limited availability of HFNC restricted its use to the sickest patients (which were not included in

this study) with another period when availability enabled to expand its use in all patients. In addition, as advocated by Concato et al (36), observational studies may provide valid results similar to RCT. We therefore believe that our results provide evidence supporting the use of HFNC for preoxygenation before intubation in the ICU. Second, inspired and end-tidal oxygen concentrations that may help determine optimal preoxygenation were not monitored in our study. Contrary to the operating room, they are seldom used in the ICU, and we failed to find a device that could adapt satisfactorily to the high-flow cannulas. Third, one may question the clinical significance of the difference in Spo_2 found in our study given that the SD of the pulse oximeter reading as a predictor of Hbo_2% is ± 2%. Figure 2 illustrates the prediction of Spo_2 evolution over time in the two groups. Although modest differences in Spo_2 exist initially, these become considerable over time and greater than the imprecision of Spo_2 reading with regard to Hbo_2. In addition, we deliberately chose other, more relevant outcome measures such as Spo_2 less than 80%. As such, and because we restricted inclusions to mild to moderately hypoxemic patients, desaturation less than 80% happened in only eight patients. Strengths of our study lie in the number of patients included (twice as many as in the study by Baillard et al [8]); the capture of real-life setting (all kinds of patients were studied, including patients with neurological impairment); and most importantly, the fact that we were able to show a significant decrease in prevalence of severe hypoxemia in a study patient population where the sickest patients were not included. Intuitively, one could infer that those patients would benefit even more from this technique.

CONCLUSION

In conclusion, use of HFNC for preoxygenation significantly reduced the prevalence of severe hypoxemia during intubation compared with NRM. We believe that the use of HFNC during intubations in the ICU represents a major advance in patient safety during these potentially high-risk procedures.

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