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MINI-REVIEW

High flow nasal cannula for preoxygenation in rapid sequence intubation: a narrative review

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Abstract

Preoxygenation is a critical step in rapid sequence intubation (RSI) to reduce hypoxemia risk during airway management. High-flow nasal cannula (HFNC) delivers heated, humidified oxygen at high flow rates, enabling continuous delivery during both preoxygenation and apnea. This review summarizes evidence comparing HFNC with conventional methods, including face masks, bag-valve-mask (BVM) devices, and noninvasive ventilation (NIV) in critical care and emergency settings. Findings across randomized trials and observational studies are mixed: some report reduced desaturation and improved oxygenation with HFNC, while others show no significant benefit in lowest Peripheral oxygen saturation (SpO_2) or hypoxia rates. HFNC is well-tolerated and safe, but its superiority remains unproven. Current evidence supports selective use in high-risk patients, with further large-scale studies needed to clarify its optimal role in RSI.

Keywords

High-flow nasal cannula (HFNC); Preoxygenation; Rapid sequence intubation (RSI); Emergency airway management; Hypoxia

1. Background

Preoxygenation is a key step in emergency airway management and rapid sequence intubation (RSI), aiming to optimize oxygen reserves before laryngoscopy and intubation. The process increases oxygen concentration in the lungs, replacing nitrogen in the functional residual capacity, and provides a buffer that prolongs safe apnea time during intubation [1]. This is particularly crucial in critically ill patients, who often have reduced pulmonary reserves, increased shunt physiology, and diminished cardiac output, leading to shorter safe apnea durations [2].

There is significant clinical interest in extending safe apnea times and reducing the likelihood of hypoxic episodes. This goal is pursued while minimizing the use of high-pressure bag-mask ventilation (BMV) [3, 4] which has traditionally been thought to elevate aspiration risk in critically ill patients, though recent evidence has challenged this perspective [5]. Commonly employed preoxygenation strategies include standard nasal cannulas, non-rebreather masks, and oxygen-connected BVM masks without positive pressure breaths. More recently, the use of the humidified high-flow nasal oxygenation (HFNO) has emerged as a key preoxygenation strategy [6].

HFNO emerged as an alternative to continuous positive airway pressure therapy in the first decade of this century. This heated fresh gas mixture is delivered via purpose-designed nasal prongs at flow rates up to 70 liters per minute (L/min) and concentrations of up to 100% fraction of inspired oxygen (FiO_2) [7, 8].

Patel and Nouraei first described using HFNO for oxygenation until a definitive airway had been placed, coining the concept of peroxygenation, which included the pre-oxygenation and the subsequent period of apneic post-oxygenation, whether ventilation was provided or not [9].

The use of HFNC as a preoxygenation strategy prior to RSI offers both theoretical and practical advantages. It is increasingly employed in patients with hypoxemic respiratory failure who later require intubation, allowing for a seamless transition into RSI. HFNC may reduce the incidence of desaturation during the apneic phase, deliver continuous oxygenation without obstructing laryngoscopy, and is generally more comfortable and better tolerated than other noninvasive modalities [10–12]. However, these benefits must be weighed against certain limitations. HFNC setup may be relatively complex in time-sensitive situations, particularly during emergent airway interventions. Additionally, its use does not permit accurate measurement of end-tidal oxygen concentration, and its effectiveness may be compromised when patients breathe with an open mouth, potentially reducing the fraction of inspired oxygen delivered to the lungs [13].

2. Methodology

This narrative review synthesized literature on High-Flow Nasal Cannula (HFNC) for preoxygenation during Rapid Sequence Intubation (RSI) in critical care and emergency settings. A search was conducted in PubMed, Scopus, and Google Scholar using keywords like "HFNC", "Preoxygenation", and "RSI". Studies published in the English language from 2000 to 2024 were included.

3. Mechanism of action and physiological benefits of HFNC oxygenation

The amount of oxygen delivered to the alveoli depends on the oxygen flow rate, its fraction of the total air delivered in the supplemental flow, how the applied device interfaces with the patient, and the patient's inspiratory demand [14, 15]. Traditional low-flow oxygen delivery systems, including nasal cannulas and simple face masks, are incapable of delivering a true FiO_2 of 100%, even at flow rates up to 15 L/min, due to the entrainment of ambient air during spontaneous inspiration. In healthy individuals, inspiratory flow rates typically approximate 30 L/min, exceeding the flow provided by these devices and resulting in dilution of the delivered oxygen with room air FiO_2 of 21%. This effect is significantly amplified in states of respiratory distress, where inspiratory flow rates may surpass 100 L/min, further reducing the effective FiO_2 and compromising alveolar oxygen delivery (Fig. 1) [16].

HFNC provides several theoretical advantages over conventional oxygen therapy. Standard oxygen therapy delivered through devices like nasal cannulas or non-rebreather masks often supplies cold and dry gas, which can lead to airway inflammation, increased airway resistance, reduced mucociliary function, and impaired secretion clearance [17]. Additionally, the body's effort to warm and humidify this gas consumes energy, which can further strain critically ill patients [18].

One of the primary advantages of HFNC is its ability to deliver continuous high-flow gas, effectively flushing the pharyngeal dead space that contains low oxygen and high carbon dioxide (CO_2) concentrations, and possibly providing positive airway pressure. With each subsequent breath, HFNC helps wash out CO_2 and replace it with oxygen-rich gas, thereby enhancing respiratory efficiency, improving patient comfort, and decreasing atelectasis (Fig. 2) [19, 20].

4. Current evidence comparing HFNC to other modalities for preoxygenation in acute care settings

Clinical evidence comparing HFNC and various oxygen delivery devices for preoxygenation before intubation is mixed. Although intubation-related mortality is rare, most comparative studies have focused on desaturation episodes as the primary outcome due to their direct link to cardiac arrest during intubation [21]. However, it is also essential to consider other potential complications.

With the increasing adoption of HFNC as a modality for treating hypoxemic respiratory failure, many patients who will ultimately require intubation and mechanical ventilation will already have the device to provide the preoxygenation needed [10].

In critical care settings, the effectiveness of HFNC for preoxygenation and apneic oxygenation during intubation has been evaluated in one before-after study and four randomized controlled trials (RCT) [22–26]. These studies shared similar outcome measures, such as lowest peripheral capillary oxygen saturation (SpO_2) levels and the number of episodes with SpO_2 below 80%, and used consistent HFNC settings (50–60 L/min and 100% FiO_2). In most studies, the comparator was a standard face mask with an O_2 reservoir, except in the study by Frat *et al.* [26], where noninvasive ventilation (NIV) was used as the comparator (Table 1, Ref. [6, 22–30]).

In patients with mild to moderate hypoxemia, the before-after study found that the use of HFNC improved preoxygenation and prevented the occurrence of profound desaturation compared to conventional preoxygenation [22]. In similarly sick patients, one multicenter RCT found a significant reduction in intubation-related severe adverse events with HFNC but no difference in the lowest SpO_2 value in comparison with conventional preoxygenation [25]. In another trial, a significant reduction in continuous SpO_2 levels during the apnea phase following preoxygenation with BMV was observed compared to those receiving HFNC [24]. In more severely hypoxemic patients, a multicenter RCT reported similar lower values of SpO_2 and several significant hypoxia episodes between conventional preoxygenation and HFNC [23]. In the Frat study, HFNC compared to NIV found no difference in the rates of serious adverse events between the two groups but notably found less severe hypoxic episodes in patients with baseline moderate to severe hypoxia [26].

Guitton and colleagues compared HFNC to standard BMV to preoxygenate patients with mild to moderate hypoxemia requiring tracheal intubation [25]. The study was a multicenter, open-label RCT, HFNC was set at 60 L/min and preoxygenation oxygen flow was 15 L/min in the standard group, and 184 patients were analyzed. The median lowest SpO_2 during intubation was not significantly different between the two groups, despite a greater incidence of reported difficult intubations in the HFNC group. Similarly, fewer patients in the HFNC group experienced mild drops in SpO_2: 12% *vs.* 23% in the standard oxygen group. Overall, the standard oxygen group had a significantly higher incidence of moderate and severe adverse events than the HFNC group.

Rodriguez *et al.* [27] analyzed a subgroup of obese patients in the previously mentioned Frat trial comparing NIV *vs.* HFNC for preoxygenation. They observed that patients with obesity and acute hypoxemic respiratory failure had a higher risk of severe hypoxemia during the intubation procedure than patients without obesity, but preoxygenation with noninvasive ventilation did not reduce this risk when compared with HFNC oxygen therapy [27].

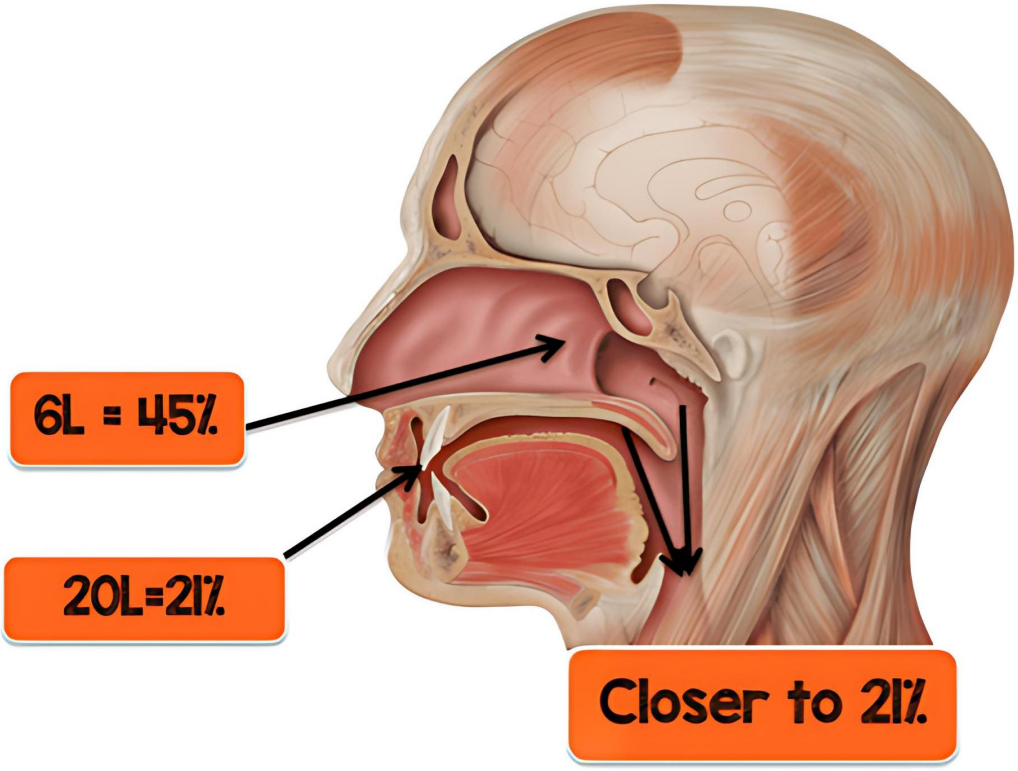

FIGURE 1. Oxygen dilution with standard oxygen therapy. FiO_2 (%): Fraction of inspired oxygen; L: Liter. Reprinted from "High-flow Nasal Cannula: Mechanisms of Action and Adult and Pediatric Indications" by FJ Lodeserto, 2018, Cureus, Adapted with permission.

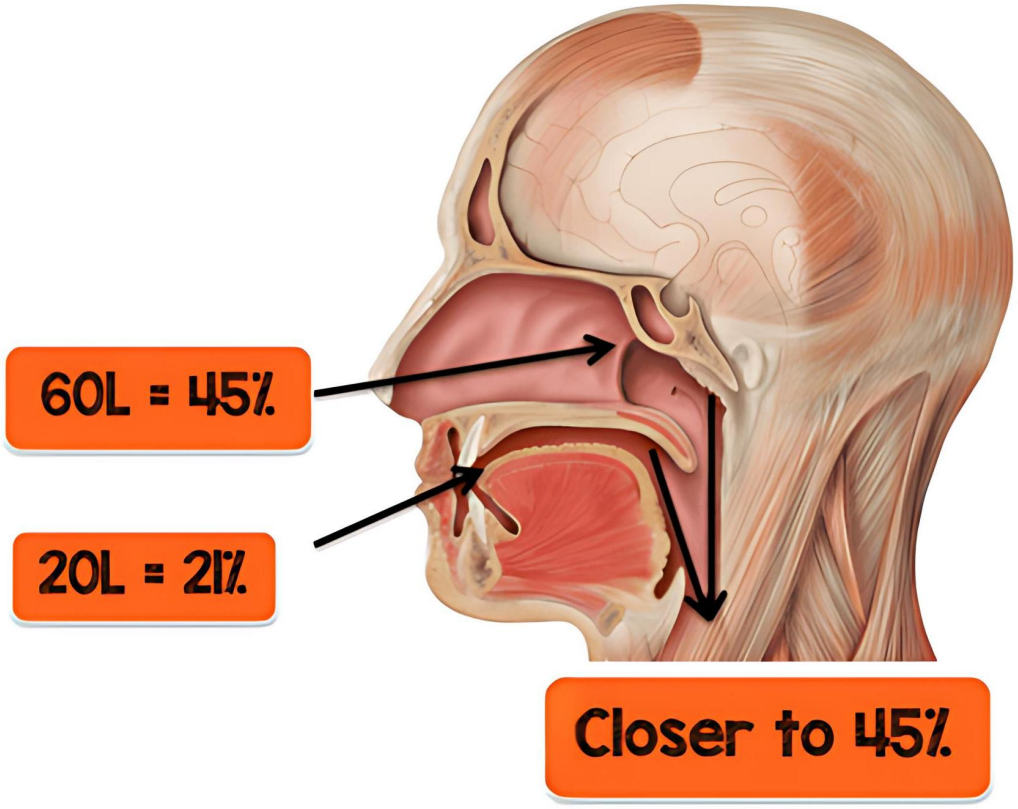

FIGURE 2. Oxygen dilution with HFNC. FiO_2 (%): Fraction of inspired oxygen; L: Liter. Reprinted from "High-flow Nasal Cannula: Mechanisms of Action and Adult and Pediatric Indications" by FJ Lodeserto, 2018, Cureus, adapted with permission.

TABLE 1. Synopsis of the available evidence comparing HFNC and other modalities for preoxygenation in different settings.

Authors, Year	Study Design	Sample Size	Primary Median Lowest SpO_2 between groups (IQR)	Outcomes Number and proportion of patients with severe hypoxic episodes[1]	Conclusion
Miguel-Montanes *et al.* [22] 2015	Quasi-experimental, non-severely hypoxemic ICU patients	HFNC (51), Facemask (50)	HFNC: 100% (95–100%), Facemask: 94% (83–98.5%) ($p < 0.0001$)	HFNC: 1 (2%), Facemask: 7 (14%) ($p = 0.03$)	HFNC was identified as a protective factor against severe hypoxic episodes.
Vourc'h *et al.* [23] 2015	Prospective multicenter RCT, hypoxemic ICU acute respiratory failure patients	HFNC (62), Facemask (57)	HFNC: 91.5% (80–96%), Facemask: 89.5% (81–95%) ($p = 0.44$)	HFNC: 16 (25.8%), Facemask: 13 (22.3%) ($p = 0.70$)	There is no difference between groups regarding adverse events.
Simon *et al.* [24] 2016	Open label RCT, respiratory failure ICU patients ($PaO_2/FiO_2 \leq 300$)	HFNC (20), BMV (20)	HFNC: 89 ± 18%, BMV: 86 ± 11% ($p = 0.56$)*	HFNC: 5 (25%), BMV: 5 (25%) ($p = 1.00$)	HFNC for preoxygenation is feasible and safe compared to BMV in mild-to-moderate hypoxemia.
Guitton *et al.* [25] 2019	Open-label multicenter RCT, non-severely hypoxemic ICU patients	HFNC (95), BVM (89)	HFNC: 100% (97–100%), BVM: 99% (95–100%) ($p = 0.30$)	HFNC: 2 (2%), BVM: 7 (8%) ($p = 0.06$)	HFNC did not improve the lowest SpO_2 but reduced intubation-related adverse events.
Frat *et al.* [26] 2019	Open-label multicenter RCT, acute hypoxemic ICU respiratory failure with two studied groups mild and moderate to severe hypoxia using P/F ratios	NIV (142), HFNC (171)	• P/F ≤200 NIV: 86% (12%), HFNC: 81% (17%) 5.0 (1.2–8.7) ($p = 0.02$)* • P/F >200 NIV: 90% (15%), HFNC: 93% (8%) −3.0 (−8.4–2.4) ($p = 0.31$)*	• P/F ≤200 NIV: 28 (24%), HFNC: 44 (35%) −11.3 (−22.3–0.3) ($p = 0.0553$) • P/F >200 NIV: 5 (20%), HFNC: 3 (7%) 13.4 (−2.2–33.1) ($p = 0.1197$)*	Preoxygenation with NIV or HFNC did not change severe hypoxemia risk in acute respiratory failure patients, with NIV possibly better at preventing severe hypoxia in patients with worse P/F ratios.
Rodriguez *et al.* [27] 2021	Post hoc analysis of RCT, obese ICU patients with acute hypoxemia	NIV (40), HFNC (51)	NIV: 87% (77–93%), HFNC: 86% (78–92%) ($p = 0.98$)	NIV: 15 (37%), HFNC: 16 (31%) ($p = 0.54$)	Preoxygenation with NIV did not reduce hypoxemia risk compared to HFNC in obese patients.

TABLE 1. Continued.

Authors, Year	Study Design	Sample Size	Primary Median Lowest SpO_2 between groups (IQR)	Outcomes Number and proportion of patients with severe hypoxic episodes[1]	Conclusion
Chua *et al.* [6] 2022	Open label multicenter RCT, ED patients requiring RSI	HFNC (97), Facemask (93)	HFNC: 100% (96.0–100%), Facemask: 100% (91.0–100%) 0 (0–4.0) ($p = 0.138$)	HFNC: 15 (15.5%), Facemask: 21 (22.6%) 0.68 (0.37–1.25) ($p = 0.213$)*	HFNC did not improve SpO_2 but may prolong safe apnea time.
Merry *et al.* [28] 2022	Prospective multicenter Randomized, no control group, elective surgery patients	HFNC (75), Facemask (74)	Assessing ease by operator and patient comfort[2]. HFNC: 0.89% (1.48%) Facemask: 1.62% (2.2%) −0.76 (−1.25–−0.27) ($p = 0.003$)*	HFNC: 3 (3.2%), Facemask: 4 (4.3%) 0.72 (0.14–3.43) ($p = 0.679$)*	HFNC is easier and more comfortable than facemask without significant clinical differences.
Mitsuyama *et al.* [29] 2022	Observational study with before-after comparison, ED patients requiring RSI	HFNC (20), Conventional (67)	HFNC: 94% (84–99%), Conventional: 85% (76–91%) ($p = 0.006$)	HFNC: 8 (40%), Conventional: 44 (63.9%) ($p = 0.037$) Using SpO_2 <90%	HFNC associated with higher lowest SpO_2 compared to conventional therapy in non-trauma ED patients.
Cırıl *et al.* [30] 2024	Open-label non-inferiority RCT, single-center, ED patients requiring RSI	HFNC (68), BVM (67)	HFNC: 96% (88.8–99.0%), BVM: 92% (86.0–97.5%) ($p = 0.161$)	HFNC: 9 (13.2%), BVM: 6 (8.9%) ($p = 0.429$)	HFNC did not improve lowest SpO_2 or reduce severe hypoxemia incidence compared to BMV; slight survival benefit at 30 days observed in HFNC.

RCT: randomized controlled trial; NIV: noninvasive ventilation; HFNC: high flow nasal cannula; BMV: bag mask valve; PaO_2: partial pressure of oxygen in the arterial blood; SpO_2: peripheral capillary oxygen saturation; FiO_2: fraction of inspired oxygen; P/F: ratio PaO_2 in mmHg to FiO_2; ICU: intensive care unit; ED: emergency department; RSI: rapid sequence intubation; IQR: interquartile range.

[1] *SpO_2 <80% events.*

[2] *Ease by anesthesiologists using visual analogue scale and comfort of patient using smiley face scale.*

**Using mean standard deviation (SD).*

An elective intubation anesthesia RCT study aimed to assess the ease and comfort of pre-oxygenation with HFNC *vs*. a face mask concluded that pre-oxygenation with HFNC was easier for anesthetists and more comfortable for patients than with a facemask, with no clinically relevant differences in end-tidal oxygen fraction after securing a definitive airway or time to secure the airway [28].

HFNC for preoxygenation prior to intubation has also been studied in the Emergency department (ED) settings, with overall findings similar as reported in critical care settings. Chua and colleagues in an RCT compared HFNC to standard care for preoxygenation and apneic oxygenation in ED patients. They observed that HFNC did not improve lowest SpO_2 during the first intubation attempt but potentially prolonged the safe apnea time [6]. Mitsuyama *et al*. [29] studied the effectiveness of HFNC for tracheal intubation in the ED, concluding that the use of HFNC during intubation had a higher lowest SpO_2 reading during the procedure in comparison to conventional oxygen administration in non-trauma patients in the ED. A more recent RCT compared HFNC versus BVM for preoxygenation during rapid sequence intubation in the ED. It found that the use of HFNC for preoxygenation, when compared to BVM, did not improve the lowest SpO_2 levels during intubation—also finding that the use of HFNC during intubation did not provide benefits in reducing the incidence of severe hypoxia. However, it was observed that 30-day survival rates were slightly better in the HFNC group on secondary analysis (Table 1) [30].

The current literature includes both small observational studies and larger randomized controlled trials, with mixed results. As such, strong conclusions regarding the superiority of HFNC remain premature. While several studies suggest that HFNC improves oxygenation without increasing adverse outcomes, its routine use as a preoxygenation strategy during RSI remains controversial. Some experts advocate for the expanded use of NIV with positive end-expiratory pressure (PEEP), citing a more robust evidence base supporting its efficacy [5, 31].

This narrative review is subject to several limitations. It does not use a systematic search strategy, which may introduce selection bias. Relevant studies published in languages other than English or outside the searched databases may have been missed. Additionally, heterogeneity across the included studies limits direct comparison, and many trials had small sample sizes or methodological limitations.

5. Conclusions

Although HFNC offers theoretical and practical advantages and has shown non-inferiority performance to standard approaches in several trials, current evidence does not support its superiority across all patient populations. Further comparative trials are needed to define its optimal role.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

AUTHOR CONTRIBUTIONS

MKA—conceptualized and designed the study, conducted the literature review, and drafted the manuscript. AA—contributed to the literature synthesis, data interpretation, and critical revision of the manuscript. RA, NA, OA, GA—assisted in literature review, manuscript preparation, and editing. ZAA—supervised the study, provided critical revisions, and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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