High-Flow Nasal Oxygen Therapy Outside the Intensive Care Setting: How Safe Is Safe Enough?

Oxygen interface choices have recently been broadened with the arrival of high-flow nasal canula (HFNC) oxygen therapy. HFNC avoids several drawbacks of low-flow interfaces:[1-3] the F_{IO_2} can be precisely adjusted, with a flow that better matches patient's inspiratory flow demand; the humidified and heated gas provides better comfort compared with other interfaces;[4,5] and the high flow induces a certain level of positive expiratory pressure,[6,7] which, therefore, contributes to lung aeration enhancement[8,9] and anatomic dead space clearance.[10]

Its use in the ICU comprises use for evaluations at ICU admission (or respiratory failure onset), during the preoxygentation period,[11-14] and after extubation.[15-17] HFNC for treatment of hypoxemic respiratory failure has been investigated in different populations. The FLORALI randomized controlled trial[18] became a landmark in HFNC evaluation. It provided evidence of a significant reduction in ICU and 90-d mortality in subjects treated with HFNC compared with subjects who received conventional oxygen therapy or a combination strategy of noninvasive ventilation and HFNC. Such enthusiastic results were not confirmed in patients who were immunocompromised.[19,20] A recent meta-analysis including subjects in the emergency department found no effect of HFNC over conventional oxygen therapy on mortality, but a significant reduction of the need for invasive mechanical ventilation or escalation of oxygen therapy.[21] In the ICU, a next step would be the investigation of hypercapnic respiratory failure.[22]

This promising technique has scarcely been investigated outside the ICU. Nevertheless, applying HFNC outside the ICU is an important challenge. The shortage of ICU beds and the high cost of ICU stays might contribute to the spread of this technique outside the ICU. The main challenge, therefore, would be the identification of patients who could benefit the most from HFNC, outside the ICU, with less risk of an unfavorable outcome.

Although some studies focused on its emergency department use,[23-28] which showed that HFNC is safe and effective in the emergency department compared with noninvasive ventilation and conventional oxygen therapy, a limited number of those studies reported HFNC use outside the ICU. Kang et al[29] focused on subjects for whom the therapy failed and who were eventually transferred to the ICU. In this study, a fourth of subjects for whom the therapy failed were intubated after 48 h of HFNC therapy, with a median HFNC duration of 126 h. This group had a significantly higher ICU mortality than subjects intubated in the first 48 h after HFNC therapy (39.2% vs 66.7%, $P = .001$). This study raised important concerns regarding the safety of HFNC outside the ICU, and its potential risks in delaying intubation when patients with severe conditions are hospitalized in a ward where monitoring is less frequent than in the ICU or the emergency department.[30] In the study by Pirret et al,[31] the 67 subjects who received HFNC in the wards significantly improved physiologic variables (ie, breathing frequency, S_{pO_2}, and heart rate) after the initiation of HFNC, and a very limited proportion of subjects suffered deterioration and were transferred to the ICU or a high-dependence unit (4.5% and 4.5%, respectively).

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Zemach et al[32] add very interesting data on HFNC use outside the ICU. In their real-life prospective observational study, they included consecutive adult subjects who required HFNC for respiratory failure in medical wards, the intermediate care unit, and the emergency department of their institution. In total, 111 subjects were included, and a composite outcome was defined as the absence of intubation, ICU admission, and death during a hospital stay.[32] The investigators report a significant alleviation of respiratory distress and dyspnea after HFNC in the wide majority of subjects (81%, 95% CI 72.5%–87.9%).[32] Interestingly, the alleviation of dyspnea was significantly lower in subjects who were unable to reach the composite outcome. Overall mortality reached 50%, but, when the investigators limited their analysis to subjects without do-not-escalate therapies orders, overall mortality was 26%.[32]

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Although limited, the mortality rate of this cohort[32] remains high. One might wonder if the high mortality is primarily the effect of applying HFNC in a setting of less frequent monitoring than in the ICU to subjects with acute respiratory failure and if a closer monitoring would have allowed a better prognosis. To date, physicians' tools to predict HFNC failure have only been assessed in the ICU.[33-36] The resolution of clinical respiratory failure features (breathing frequency, thoraco-abdominal asynchrony)[35] and the persistence of respiratory discomfort after the first hour[33] have been associated with a worst outcome. Roca et al described[34] and validated[36] the ROX index, a physiologic index defined as the ratio of oxygenation (assessed by S_{pO_2}/F_{IO_2}) to the breathing frequency. A ROX index that exceeds 4.88 at 12 h of HFNC less likely to fail than the noninvasive strategy.[34] In the present study by Zemach et al,[32] the ROX index was calculated much sooner (30 min after HFNC initiation) and was the only independent predictor of successful therapy in multivariate analysis, which indicates that the ROX index might be a valuable tool to predict HFNC failure in patients who are receiving HFNC, even outside the ICU.

An additional point is of paramount importance: the use of HFNC in patients with do-not-resuscitate orders. Obviously, these subjects would not have benefited from ICU admission in terms of escalation of life support. However, the alleviation of dyspnea, similar to patients without a do-not-resuscitate order as well as the decrease in breathing frequency are major reasons to provide HFNC treatment to patients who, in a vast majority (93% in this study), will finally die. Furthermore, it has previously been shown that HFNC could actually treat hypoxemic acute respiratory failure in patients with a do-not-resuscitate order[37] and allow a favorable outcome.

Although convincing, the data provided by Zemach et al[32] should be taken with caution. First, although the study was prospective, no predefined criteria for intensivist consultation or ICU admission were determined; and the high mortality rates in the subjects without a do-not-resuscitate order renders questionable their initial assessment. One can assume that some subjects' severity might have been underevaluated. Next, the flows applied were relatively low, with mean flows between 45 and 50 L/min, which is clearly underdosing the therapy.

HFNC is definitely a therapy that can be used outside the ICU. In their article, Zemach et al[32] provide data that support the diffusion of this technique into the wards. Nevertheless, caution should be the rule, and close monitoring, if not continuous, should be applied by skilled teams. Simple clinical parameters, or their combination using the the ROX index, ought to be scrutinized to avoid a delayed intubation. A misuse would result in jeopardizing this useful and effective technique.

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