High-Flow Nasal Cannula Use in the Management of Acute Hypercapnic Respiratory Failure Due to Cardiogenic Pulmonary Edema: Heavyweight or Light Heavyweight?

Patients presenting to the emergency department with respiratory failure require rapid assessment and diagnosis, based on history and physical exam, so that early appropriate treatment can be initiated. Imaging, such as chest radiography and bedside ultrasound, can aid in tailoring treatment. Acute cardiogenic pulmonary edema (CPE) is a common cause of respiratory distress and failure.[1] Current standard treatment for respiratory failure from acute CPE includes diuretics, nitrates, antihypertensives, and noninvasive ventilation (NIV).[2] NIV has been demonstrated in randomized controlled trials to improve mortality and reduce the need for endotracheal intubation in patients with cardiogenic pulmonary edema.[3] High-flow nasal cannula (HFNC) use in the emergency department has increased in recent years because it is easy to apply, is well-tolerated, and offers some appealing physiologic benefits.[4] The benefits of HFNC include improved humidity, precise delivery of F_{IO_2}, meeting of inspiratory flow demand, reduced work of breathing (WOB), and decreased breathing frequency related to washout of anatomic dead space and small, variable amounts of PEEP.[5,6]

HFNC has been studied extensively in hypoxemic respiratory failure, and current evidence indicates that HFNC is superior to standard oxygen therapy for undifferentiated respiratory failure; however, when compared to NIV, low-quality evidence suggests similar outcomes.[7] For hypercapnic respiratory failure, there have been few randomized controlled trials to investigate HFNC. In a retrospective analysis of 200 subjects receiving HFNC and 378 subjects receiving NIV, Koga et al[8] reported that HFNC was associated with increased risk of treatment failure in subjects with CPE. Nearly half of subjects with CPE had treatment failure compared to 12% who received NIV.[8] In hypercapnic subjects, treatment failure was nearly double in the HFNC group.[8] In a randomized trial of HFNC in the emergency department, Doshi et al[9] reported that HFNC was noninferior to NIV; however, a number of subjects in the HFNC group were rescued with NIV. In a predefined subgroup analysis of hypercapnic subjects, there was no difference in treatment failure between the 2 groups.[10] Importantly, in this trial, 6 of 8 subjects who failed HFNC were successfully treated with NIV. In this subgroup analysis, HFNC reduced frequency by 4 breaths/min after 1 h, while NIV resulted in a reduction of 8 breaths/min, although there was no change P_{aCO_2} after 1 h in this study.[10] Thus, the role of HFNC in patients with hypercapnia in general is unclear.

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In this issue of RESPIRATORY CARE, Marjanovic et al[11] report the results of a prospective, observational, nonrandomized study of subjects with acute CPE and hypercapnia. They compared change in P_{aCO_2} between subjects receiving HFNC or NIV for 1 h at the discretion of the treating physician. There were no statistically significant differences between the 2 groups at baseline; however, the low sample size makes the study underpowered to detect any differences. The HFNC group had lower P_{aCO_2} at baseline (50 mm Hg vs 60 mm Hg) but similar pH (7.30 vs 7.29), indicating that the NIV group may have had undiagnosed chronic lung disease or may have been sicker upon presentation to the emergency department. The NIV group also had higher N-terminal prohormone of brain natriuretic peptide, creatinine, and baseline oxygen requirements, although these did not reach statistical significance. Interestingly, while the NIV group had a lower baseline frequency (29 vs 34 breaths/min, $P = .34$), there were similar decreases in breathing frequency in both groups, although there were no differences in WOB or WOB score after treatment. Subjects who received NIV had a lower frequency (median 26 vs 21 breaths/min, $P = .03$) at 1 h after treatment, and 75% of subjects in the HFNC group had a breathing frequency $\geq$ 25 breaths/min. After treatment, 75% of subjects in the NIV group had a breathing frequency $\leq$ 26 breaths/min. The primary outcome was achieved in both groups, although the NIV group had a greater change in P_{aCO_2} (8 vs 5 mm Hg), but this may be related to the lower baseline P_{aCO_2} in the HFNC group.

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In the emergency department, most patients present with undifferentiated respiratory failure, and hypercapnia is often determined after NIV or HFNC has been initiated. Indeed, in this study, approximately 1 in 5 subjects were excluded from analysis after discovering they had COPD exacerbations, sepsis, or other reasons.[11] Although the primary outcome was reasonable, it is unclear whether short-term changes in P_{aCO_2} and breathing frequency will translate into improved patient outcomes in larger studies. Importantly, for patients with severe heart failure and pulmonary edema, NIV likely offers several physiologic advantages over HFNC. First, positive pressure is maintained throughout the respiratory cycle, unlike HFNC, in which positive pressure is affected by flow, mouth opening, and cannula size. Positive pressure decreases preload to the right side of the heart, which will reduce the overall cardiac output and allow more efficient pumping by a failing left ventricle. In addition, the restoration of functional residual capacity reduces WOB and F_{IO_2} requirement. Lastly, positive-pressure ventilation results in a decrease in afterload for the left ventricle, which may help the patient recover until diuretics and antihypertensives have an effect.[12]

Given the physiology of CPE and the documented success of NIV in treatment of the pathophysiology and a high rate of HFNC failure documented by Koga et al[8] and Doshi et al,[9] we must have a high standard for alternative treatments. HFNC may yet emerge as a promising therapy in hypercapnic patients; however, we need to be cognizant that NIV in acute pulmonary edema has not only been shown to reduce intubation but also to improve mortality.[3] Further studies, with larger sample sizes and randomization, are needed to ascertain the clinical benefits of HFNC in patients with hypercapnic respiratory failure due to acute CPE. Thus, it seems that HFNC may be considered for patients with acute CPE with mild hypercapnia, but more severe cases should be treated with NIV. HFNC may also be considered for patients who are do not tolerate NIV, but with close monitoring in the event that clinical deterioration warrants intubation.

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