VIEWPOINT

High-Flow Nasal Cannula Therapy for Pediatric Patients With Bronchiolitis

Time to Put the Horse Back in the Barn

Shawn L. Ralston, MD, MS
Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Maryland.

The proliferation of observational literature on the topic of high-flow nasal cannula (HFNC) as a therapy for acute viral bronchiolitis is nothing short of remarkable. A brief PubMed search reveals a ratio of observational studies to randomized trials of at least 10 to 1 in the past 3 years alone. This proliferation suggests that, right or wrong, we have embraced the widespread use of HFNC clinically. This ratio also hints at a bigger problem, which is that we have moved on to answering somewhat peripheral questions about the therapy prior to answering the most important questions about clinical utility.

A recent meta-analysis concluded that HFNC, when compared with standard nasal cannula, reduced the incidence of treatment failure in bronchiolitis.[1] However, treatment failure in the standard cannula group universally led to crossover to HFNC in the 2 relevant trials[2,3]; thus, a potentially more accurate representation of the trials to date would be that they compare early vs rescue use of HFNC. Furthermore, key findings in both trials were that there were no differences in overall duration of oxygen use, transfer to the intensive care unit (ICU), hospital length of stay, or adverse events between groups. A layman's summary of the current literature would be this: if you start HFNC early in bronchiolitis, you can avoid needing to start it later, although it will not really alter the overall hospital course either way. If you find this situation a little confusing, you are likely not alone.

A closer look at the details of the 2 trials comparing standard cannula therapy with HFNC for patients with moderate bronchiolitis may provide clarity. Kepreotes et al[2] studied 201 children younger than 24 months with moderate bronchiolitis in a single Australian hospital. The primary outcome of the trial was time receiving oxygen therapy, for which there was no difference (20 hours in the HFNC group vs 24 hours in the standard cannula group; hazard ratio, 0.9; 95% CI, 0.7-1.2). There were differences in initial treatment failure rates between the 2 groups (14 patients [14%] receiving HFNC vs 33 patients [33%] receiving standard cannula therapy); however, all 32 children in the standard cannula group were deemed to have treatment failures and were switched to receive HFNC. Of those, 20 were successfully rescued and 12 transferred to the ICU. In the HFNC group, the same proportion (14 patients) were deemed to have treatment failures and transferred to an ICU; thus, the final outcome was equivalent for both groups.

Franklin et al[3] studied 1472 infants younger than 12 months in 17 hospitals in Australia and New Zealand and used a flow rate of 2 L/kg, thus, younger infants and higher flow rates than the study by Kepreotes et al.[2] Treatment failure was chosen as the primary outcome, with higher failure rates in the standard therapy group (23% [167 of 733]) compared with the HFNC group (12% [87 of 739]); however, the same pattern of events occurred after treatment failure as in the trial by Kepreotes et al. Of the 162 patients in the standard cannula arm who experienced treatment failure, 102 (61%) were considered rescued by HFNC, almost exactly the same percentage considered to have been rescued in the study by Kepreotes et al (62.5%). Ultimately, only 9% of children receiving standard therapy went on to have failed rescue HFNC and experience admission to an ICU, which is equivalent to the 12% transfer rate in the early HFNC group. Furthermore, there were no differences in overall duration of hospital stay or duration of oxygen therapy between groups.

While both trials had the stated purpose of comparing low-flow with high-flow oxygen, owing to therapeutic crossover both trials really evaluated early vs rescue use of high flow. It is worth noting that the original title of the study by Franklin et al, as evidenced by the published protocol, was "Early High Flow Nasal Cannula Therapy in Bronchiolitis: A Prospective Randomized Control Trial (protocol)."[4] Thus, an accurate interpretation of this evidence is that the 2 strategies (early vs rescue) appear equivalent in terms of outcomes. Furthermore, it has also been pointed out that a large proportion of patients in the standard care arms (77% in Franklin et al and 68% in Kepreotes et al) were successfully treated without escalation of care.[5] Finally, the available economic analysis suggests HFNC costs 16 times as much as standard care.[2] Thus, another reasonable conclusion from these data might be that early initiation of HFNC is the inferior choice since it involves providing a costly therapy to a large number of children who will not benefit from it.

Given the reality of the situation represented by the observational literature, what can we do with the pressing clinical question about how to more appropriately use this ubiquitous therapy? An Australian pediatric emergency medicine research collaborative recently proposed that HFNC in patients with bronchiolitis should be limited to use as rescue therapy for infants with hypoxemia in whom standard cannula therapy has failed.[6] This suggestion seems appropriate since there is no evidence that a patient would have any different outcome or be placed at increased risk by delaying the use of HFNC. The suggestion also highlights a large gap in the existing literature: there are no clear initiation criteria for when to start HFNC for patients with bronchiolitis.

One possible strategy would be to use the treatment failure criteria in the existing randomized trials as initiation criteria for HFNC. The definition of treatment

Corresponding Author: Shawn L. Ralston, MD, MS, Division of Quality and Safety, Department of Pediatrics, Johns Hopkins Children's Center, 1800 N Orleans St, Baltimore, MD 21287 (sralsto3@jhmi.edu).

failure in the Kepreotes et al trial included a heart rate or respiratory rate in the "red zone" for age-based norms or an oxygen saturation below 90% (while receiving a maximum flow rate of 2 L/min with a standard nasal cannula), or a respiratory distress score in the severe range as well as a concurrent assessment by the treating clinician. Treatment failure in the trial by Franklin et al required 2 of the following 4 criteria: (1) heart rate or respiratory rate remaining unchanged or increased from admission, (2) failure to maintain oxygen saturations above 92% (or 94% at some sites) despite maximal therapy, (3) triggering of the hospital early warning tool, as well as (4) physician determination or confirmation of treatment failure. While these are notably distinct sets of criteria, the fact that treatment failure rates were so similar in each trial would suggest that either set of criteria would be reasonable.

Finally, it is important to remember the potential for a downside to HFNC other than the significantly increased cost. Infants often experience gastric distention and poor feeding while receiving HFNC, whereas some hospitals do not allow feeding while HFNC is in use. Other adverse effects include a risk of pneumothorax, particularly at higher flow rates.[7] Taken together, the 2 randomized trials suggest that, if we apply HFNC early in the course of bronchiolitis, we can expect approximately 70% of that use will be unnecessary. It is sometimes exceptionally difficult for us to understand small harms applied to large populations as a meaningful concern when we are hoping to help a single patient in the moment. However, it is highly likely that the liberal application of HFNC oxygen in bronchiolitis is doing more harm than good at the population level.

Given the risk of harm and the strong suggestion that we are wasting resources with our current use of HFNC, we urgently need prospective research to define the appropriate population in whom to use this therapy. Until then, limiting the use of HFNC to rescue therapy by protocolizing treatment failure criteria for standard, low-flow nasal cannula in the treatment of bronchiolitis is likely to do the most good with the least harm.

ARTICLE INFORMATION

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