Is Delivery of Aerosolized Medication via HFNC for Critical Asthma Effective Concurrent Therapy?

Treatment of children with respiratory distress often consists of concomitant therapies. The most common of these therapies is aerosolized medication and respiratory support devices such as high-flow nasal cannula (HFNC) or noninvasive ventilation. Aerosolization of medications, and the changes in delivery in relation to air-flow dynamics, stability of particle size, deposition, and interaction with respiratory support devices, is a continuing validation process.[1] Patient-specific factors, particularly the ventilatory pattern and anatomic differences, affect aerosol deposition to the lungs.[2-4] High respiratory rates and small tidal volumes affect deposition because less of the medication is drawn into the lungs.[2-4] In addition to these factors, we often use medication off label by patient age, indication, or delivery method. Therefore, we must consider the characteristics for each therapy for limitations as well as optimizing efficacy for therapeutic benefit and when they are in divergence during concurrent delivery. The optimal flow range for HFNC in pediatrics should target 1.5-2 L/kg/min to meet or exceed inspiratory flow demands of the patients.[5,6] The most recent bench study by Li et al[7] that investigated the delivery of aerosolized medication via HFNC by exploring flows of 0.125, 0.25, 0.5, 1, and 2 L/kg/min showed percentage of aerosol delivery higher with lower flows with a distressed toddler model as 14% ± 1%, 13.6% ± 0.5%, 3.5% ± 0.3%, 1.0% ± 0.1%, 0.7% ± 0.2%, respectively.

In this edition of RESPIRATORY CARE, Gates et al[8] performed a retrospective analysis that compared delivery of aerosol therapy via an aerosol mask or HFNC of 171 children ages 2–17 years who, between June 2014 and March 2020, were admitted to the pediatric ICU with critical asthma. Placement into each therapy group was determined by the initiating device on admission to the ICU and was broadly chosen by the preference of the clinician.[8] The determination of bronchodilator dose was in accordance with an established respiratory therapist-driven protocol by using the modified pulmonary index score. A cutoff value of ≥8 indicated critical asthma. For those on HFNC, the initial flow for HFNC was chosen by respiratory therapist

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assessment based on the patient inspiratory flow demands in accordance with local protocol not described. Primary and secondary outcome metrics were pediatric ICU and hospital length of stay, time on continuous albuterol, and the modified pulmonary index score over time with the primary hypothesis as no change in hospital length of stay between the HFNC and aerosol mask groups.[8] Additional comparisons were made between ≥0.5 and <0.5 L/kg/min HFNC to determine any flow-related effects.[8]

The results did not show any difference in hospital or pediatric ICU length of stay ($P = .47$ and $P = .95$, respectively); however, there was a difference in the time on continuous albuterol, with the HFNC group having a shorter duration ($P = .048$).[8] There was also no difference in any outcome metric between the 2 flow-range groups. Additional analysis of the need for escalation to noninvasive ventilation or heliox was also reported, with no difference seen between the HFNC and aerosol mask groups ($P = .93$).[8]

The strengths of this study include the controlled nature of albuterol dosing and the setting of HFNC flows with respiratory therapist-driven protocols, often a limitation of retrospective analysis. Detailed statistical analysis was performed, including the treatment effect model with propensity matching. Determining the combined effect of concurrent therapy such as HFNC and aerosol therapy is a common question not easily answered. The authors attempted to determine this within real-life practice in this retrospective analysis; however, the limitation stated in the study, as well as additional perceived limitations, suggest to me that different outcome metrics would have better served this analysis.

First, the authors state that discharge from the pediatric ICU was determined by bed availability and not readiness for transfer. This is likely why the total hospital length of stay and not the pediatric ICU length of stay was used as a primary outcome. It is also reasonable to conclude that

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Correspondence: Natalie Napolitano MPH RRT RRT-NPS FAARC, Respiratory Care Department, Children's Hospital of Philadelphia, 3401 Civic Center Blvd, Suite 7NW148, Philadelphia, PA 19104. E-mail: napolitanon@chop.edu.

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hospital discharge could also have the same limitation because there could be a reason to remain in the hospital beyond resolution of the asthma symptoms. In a prospective study, this metric can be altered to readiness for discharge versus actual discharge to eliminate social and logistical barriers. The reported HFNC flows ranged from 0.3 to 0.9 L/kg/min, lower than the optimal recommended flow setting in previous studies. Also, by reviewing the deposition/flow setting from Li et al,[7] we can estimate deposition to be between 13.6% and 1.0% for lower to higher flow rates seen in this study. By using these results, which show a significant change in deposition at flows of 0.5 L/kg/min, it would have been best to have a subanalysis cohort by estimated deposition rates of $\leq$0.25 L/kg/min, with $\sim$14% deposition, and $>$ 0.25 L/kg/min, when deposition significantly reduces to $<$ 10%.

Third, it is my opinion that escalation of the support metric to be a more important measure of comparing 2 therapies than was given credit for by the authors. This may be due to the operational definition applied for it as a need for noninvasive ventilation or heliox versus escalation to the next level of support that is generally used. By using this definition of escalation, there was an escalation of support of 28% in the aerosol group versus 9% in the HFNC group, and this comparison may have a statistically significant difference that favors the HFNC group. Fourth, it is also worth a mention of no estimation of the needed sample size or treatment effect to determine statistical significance for any of the outcomes and thus cannot speak to limitations to the lack of power in the ability to make conclusions from this analysis. Although retrospective reviews generally use a set time frame over a sample size, we cannot overlook appropriate primary statistical methods of determining a effect size and projected sample size needed to make conclusions. Calculation of this factor in advance can assist in determining the look back timeframe for retrospective analysis or if multi-center data are needed.

This study shows that utilization of concurrent therapy of aerosolized bronchodilators and HFNC for asthma exacerbation is at least as an effective delivery of bronchodilators via aerosol mask and may reduce the time requiring continuous aerosol delivery. Unfortunately, questions persist as to the effective delivery of aerosolized medication via HFNC.

Natalie Napolitano
Respiratory Care Department
Children's Hospital of Philadelphia
Philadelphia, Pennsylvania

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