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EDITOR'S NOTES

Respiratory Support for Bronchiolitis Management in the PICU: What We Now Know and What We Want to Know

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In February 2023, *Pediatric Critical Care Medicine* (*PCCM*) published a systematic review and network meta-analysis of high-flow nasal cannula (HFNC) and other noninvasive ventilation (NIV) support therapies used in bronchiolitis (1). The focus was on studies carried out in the emergency department (ED) or hospital ward published up to 2022 that included patients younger than 2 years. At that time there were 14 randomized controlled trials (RCTs) with 3,367 patients and 14 non-RCT studies with 8,385 patients. Overall, as initial therapy, HFNC oxygen (O_2) therapy appeared no better than low-flow O_2-therapy; and, as a rescue intervention, support with HFNC O_2-therapy appeared no better than NIV.

Since 2023, there has been one additional RCT, which was published in the August 2024 issue of *PCCM* (2). This single center study–carried out in India (2019–2022)–aimed to compare HFNC versus nasal prong bubble continuous positive airway pressure (CPAP) in 118 children aged 1–23 months with moderate to severe bronchiolitis. The researchers concluded that using HFNC as opposed to bubble CPAP for early respiratory support was associated with lower failure rate within 24 hours of randomization, which in this case was taken as a composite outcome of deterioration in clinical asthma score, rise in respiratory rate, and escalation in respiratory support. The accompanying editorial was written by two accomplished trialists from the United Kingdom and it emphasized the need for pragmatic design in future RCTs in areas of clinical uncertainty, such as respiratory support for bronchiolitis (3).

There are two ongoing trials in bronchiolitis care that should be completed by 2026. There is the Respiratory Support and Treatment for Efficient and Cost-Effective Care (REST EEC, ClinicalTrials.gov NCT05909566) study in the United States (4). It is a single center, randomized, embedded, pragmatic, Bayesian clinical trial that focuses on clinical decision support for HFNC management in an expected population of 198 bronchiolitis patients. Then there is the Breathing Assistance in CHildren with bronchiolitis (BACHb; https://fundingawards.nihr.ac.uk/award/NIHR152262) trial in the United Kingdom. This group-sequential, two-stratum (moderate and severe) multicenter, RCT of respiratory support is seeking to recruit 1,508 infants with acute bronchiolitis managed in either the ED or hospital ward of 50 hospitals.

Given this background, the topic for *PCCM*'s third item in the 2025 series of Editor's Notes—the other two are in the February and April issues (5, 6)–is our

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field's progress in respiratory support for bronchiolitis management in the PICU. There is an opportunity here to reflect on recent *PCCM* reports that address four questions about bronchiolitis care: 1) What have we learned about clinical pathophysiology? 2) What clinical processes have others implemented? 3) What should we be thinking about for future clinical studies? and 4) What about patient outcomes?

UNDERSTANDING THE PATHOPHYSIOLOGY

Two studies–each with insightful editorials–have important bearing on how we quantify the underlying diaphragmatic physiology of breathing and respiratory support. First, a large population-based study of continuous monitoring of tonic diaphragmatic activity (Edi) proposed a definition of elevated tonic Edi episodes and diaphragmatic activity during expiration (7). In these researchers' experience, such monitoring can be used to identify patients who exert abnormal effort to defend end-expiratory lung volume, which may be evident during NIV failure in patients with bronchiolitis. The editorial provided a detailed discussion on this matter (8). Second–in a report that extended the first study (7)—the same group of researchers reviewed their center's experience (2016–2018) of using noninvasive neurally adjusted ventilatory assist (NIV-NAVA) in patients younger than 2 years with bronchiolitis (9). NIV-NAVA was used after first-tier noninvasive respiratory support (i.e., CPAP or HFNC) had failed, and this intervention was associated with a rapid decrease in respiratory effort, as determined by a decrease in Edi. The editorial recognized that "…use of NIV for management of work of breathing in bronchiolitis is here to stay…" but the writers' enthusiasm for a tiered approach to NIV-NAVA via facemask was tempered and their recommendation was for "…a future parallel design prospective study comparing conventional NIV protocolized escalation that includes transition to NIV-NAVA" (10).

Another two studies of bronchiolitis pathophysiology came from the 2019–2020 Bronchiolitis And COdetectioN (BACON) cohort, which was a multinational PICU study focused on children with bronchiolitis and lower respiratory tract infection aged younger than 2 years requiring intubation. The first BACON report found that bacterial codetection was present in almost one third of these children (11), but this finding was not associated with the need for prolonged invasive mechanical ventilation (IMV). Rather, a post hoc analysis of the BACON cohort showed that pediatric acute respiratory distress syndrome (i.e., PARDS, defined according to the 2023 second pediatric acute lung injury consensus conference criteria (12)) occurred in 42% of the 571 population on day 1 and was associated with longer duration of IMV (13). The editorial highlighted this PARDS pathophysiology in the context of 25 years of other observations about IMV for severe bronchiolitis and prolonged duration of IMV (14).

IMPLEMENTATION AND QUALITY IMPROVEMENT STUDIES IN BRONCHIOLITIS

Next, despite what we know from RCTs (1, 2), there have been two key studies about practice improvement or implementation. The first study was a single center 2018–2020 quality improvement (QI) project–using 2017–2018 historical controls and published in 2023 (15)—which aimed to reduce hospital and PICU length of stay (LOS) by 10% between two bronchiolitis seasons. The main part of the intervention was a HFNC protocol with guidance on initiation and weaning; the strategy was associated with decreased LOS in the PICU and hospital and less time on HFNC, while also avoiding any increase in readmission or adverse event rates. The editorial brought an added dimension and referred to other QI and "process improvement" studies published in *PCCM* (16). The second study implemented a respiratory therapist-driven HFNC protocol in a single center (17). The work started in 2017 with subsequent iterative cycles through 2021 (and published in 2023) and found that protocol changes with standardized discharge criteria led to clinical improvements (i.e., less use of NIV and lower readmission rate) without any increase in adverse events.

Taken together these implementation/improvement studies must be considered as viable alternatives to RCTs: we can learn from others' experiences and the cycles of improvement with planning, testing, observing, and acting on what has been learned may be faster in producing changes in clinical care than any result from a RCT (18).

HYPOTHESIS-GENERATING FOR FUTURE BRONCHIOLITIS RESEARCH

A data review of therapies used in 350 infants with bronchiolitis managed in 13 U.K. PICUs

(November–December 2019) was published in 2023 (19). The report identified early management choices associated with the duration of IMV. For example, after adjustment for confounders, fluid restriction, route of endotracheal intubation, and using alpha-2 agonist were each associated with duration of IMV. The editorial highlighted the variation in practice across the 13 centers and the potential for Bayesian approaches to future study (20) (see also the Introduction and references [3] and [4]).

More recent work by the U.K. group included a post hoc subgroup analysis of 784 bronchiolitis patients in the Sedation AND Weaning In CHildren (SANDWICH) cluster-RCT carried out 2018–2019 (21). The report published in the April 2025 issue of *PCCM* showed that exposure to the sedation/weaning protocol, rather than not, was associated with clinically significant reduction in time to successful extubation. The editorial discusses this endpoint used in the SANDWICH trial—extubation failure and time to successful extubation—and wondered whether time to liberation from any respiratory support was now the more relevant outcome (22). Interestingly, the ongoing U.K. BACHb trial uses the endpoint of time to liberation from any respiratory support.

OUTCOMES OF RESPIRATORY SUPPORT FOR BRONCHIOLITIS

The endpoints outlined in the above respiratory support studies for bronchiolitis and their associated editorials have included outcomes such as changes in composite severity scores, need for escalation in support or duration of IMV, rate of adverse events and readmission, and total time to liberation from any respiratory support.

In contrast to these PICU-focused outcomes, there is one new study that has focused on a different outcome: that is, the long-term cognitive, functional, and quality of life outcomes after IMV for bronchiolitis (23). The investigators used a non-prespecified secondary analysis of 6-month follow-up data of patients in the 2009–2013 Randomized Evaluation of Sedation Titration for Respiratory Failure trial (RESTORE; ClinicalTrials.gov NCT00814099) to support their argument. Out of 232 randomly sampled patients aged under 2 years receiving IMV as support for bronchiolitis, 12% (95% CI, 8%–17%) had new functional and/or cognitive morbidity by 6-month follow-up. At one level, we could ignore these data because they are 12 to 16 years old, and we may wonder whether practices have improved over the years. However, regarding patients undergoing IMV for bronchiolitis support, as the authors acknowledged "…prospective evaluation of critical bronchiolitis is urgently needed…" and "…such children warrant targeted study in order to better understand the mechanisms (of significant morbidity)…" (23).

Therefore, given the other studies of IMV support for bronchiolitis reviewed in these Editor's Notes and the potential impact on how we should best design future studies, we must inquire about the mechanism underlying these new morbidities. Are the morbidities a function of PARDS-related complications, as described in the 2023 second pediatric acute lung injury consensus conference supplement (24)? Or are they a reflection of cumulative exposure to analgesic and sedative agents (19, 21)? Alternatively, is excessive supplemental-O_2 exposure the issue? For example, the 2020–2022 conservative versus liberal oxygenation targets in critically ill children (Oxy-PICU) multicenter RCT found that among children undergoing IMV with supplemental-O_2 as an emergency, a conservative rather than liberal oxygenation target (pulse oximetry saturations 88%–92% versus > 94%) resulted in greater probability of better outcome (25). Of note, out of the 1,872 pediatric patients recruited to the Oxy-PICU trial, 37% had bronchiolitis; although these data have been debated in *PCCM* (26, 27), as yet there is no post hoc bronchiolitis subgroup analysis. However, *PCCM* did publish a single-center retrospective study (2008–2020) of 176 PICU patients aged younger than 2 years who required IMV for severe bronchiolitis (28). The investigators found that even though moderate to high-dose pulmonary supplemental-O_2 exposure and potential overuse of O_2 were common, such practice was not accompanied by high systemic O_2 burden. Thus, the researchers' conclusion: "…further studies are needed to determine optimal oxygenation targets to prevent overzealous use of oxygen in this vulnerable population…" (28).

Hence, in answer to the question "what do we now know about respiratory support for bronchiolitis management in the PICU?," we know a great deal. Our *PCCM* authors have provided us with details about

contemporary pathophysiology and implementation of clinical reforms. In answer to the harder question, "What do we want to know about respiratory support for bronchiolitis management in the PICU?," we want to know a great deal more and expect our *PCCM* authors to focus on these aspects of clinical research: what are the mechanisms underlying new morbidities; and what are the appropriate endpoints for clinical trials? At *PCCM* we look forward to advancements in the field and welcome post-2023 multicenter studies.

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