Non-invasive Ventilation (NIV) in the Micropremature Infant: Proceed With Caution

Rob Graham, R.R.T./N.R.C.P.

I dedicate this column to the late Dr. Andrew (Andy) Shennan, the founder of the perinatal program at Women's College Hospital (now at Sunnybrook Health Sciences Centre). To my teacher, my mentor and the man I owe my career as it is to, thank you. You have earned your place where there are no hospitals and no NICUs, where all the babies do is laugh and giggle and sleep.

"Although evidence incontrovertibly supports the use of NIV to decrease the incidence of chronic lung disease, evidence to support its use in the extremely premature population is lacking. In a previous column in NT, I have identified "practice creep" in this regard, with NIV being used with smaller and smaller babies utilising increasing pressures."

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"CPAP belly" is a ubiquitous phenomenon in the NICU and is typically viewed as CPAP's benign companion. Just how benign this condition has not been investigated sufficiently, in the writer's opinion, nor have other common occurrences that accompany NIV, namely bradycardic and apneic episodes.

A study of 343 infants published in 2009 did not find any correlation between the use of CPAP and necrotising enterocolitis (NEC) (1), although it must be noted that at that time, NIV was not commonly used in the micro-premature population. In addition, not so long ago, a CPAP level of 7 cmH_2O was considered high, and this must be contrasted against much higher levels, i.e., 12 cmH_2O or more, as well as newer modalities such as NIV using high-frequency oscillation.

Every body system is underdeveloped in the premature infant, especially with decreasing post-menstrual age (PMA). While the pulmonary system is most susceptible to damage from medical interventions, the gastrointestinal system is as well. We are obsessed (often rightfully so) with pulmonary over-distention, but distended bowel resulting from CPAP belly stretches the intestinal wall. While the aforementioned study found this to be of no consequence, is this true with much smaller infants of lower PMA? Since the use of NIV on extremely small babies is a recent (and largely unsupported) phenomenon, evidence of its safety is lacking. It also takes time to reveal associations with treatment, especially in the case of something as pervasive as NEC.

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There are several reasons apneas and bradycardias (A&Bs) are common occurrences in premature infants. The immature respiratory centre is the primary culprit, but they are also the hallmark of more serious factors such as infection. A common causation in a tiny infant on NIV is their tiring out and failing the modality. Because of the possibility of more serious etiology, clinicians often perform a full or partial septic workup to rule out sepsis. This is not benign; it represents an additional (and often unnecessary) procedure(s) and requires a significant volume of blood. The lab at my workplace requires 1.5 mL of blood for culture and CBC. This contributes to iatrogenic anemia, which may be more detrimental to the extremely premature than those of greater PMA.

The PINT study was conducted between 2001 and 2005 (2). 23-week PMA infants were not routinely offered resuscitation at that time. Thus, no conclusions regarding the safety of accepting low hemoglobin in these infants can be drawn. The PENUT study also did not include infants of less than 24 weeks PMA but did raise a flag regarding transfusions: each transfusion negatively affected cognitive and motor outcomes (3). Erythropoietin (EPO) was given in this study, and interestingly, those infants who received EPO did not suffer deficits in BDSI-III scores, but those who did not receive EPO did (3). The takeaway was to reduce the need for transfusion wherever possible. Unnecessary blood withdrawals do not fit that narrative. Since CPAP belly and associated abdominal distention may obfuscate more serious conditions like NEC (4), clinicians can hardly be faulted for being cautious.

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Another consequence of A&Bs is decreased perfusion and oxygen saturation. The premature gut is very susceptible to injury from under-perfusion and tissue hypoxia. One meta-analysis showed a significant increase in severe NEC in infants managed with lower SpO_2 targets (85-89%) c.f. those whose SpO_2 was targeted at 91-95% (5). More recently, transfusion re-perfusion injury to the gut has been suggested (6), leading to the withholding of feeds during transfusion in some units; the practice is the subject of an ongoing study (7) and debate. A patent ductus arteriosus, a risk factor for NEC (8), may amplify the effect of periodic A&B-related gut hypoperfusion.

While relatively low CPAP pressure may not result in rising intragastric pressure (9), this cannot be assumed with higher pressure. Intra-thoracic pressure results in increased intra-abdominal pressure (4). This delays gastric emptying time, which is already increased in the premature infant, decreases intestinal blood flow and slows intestinal motility resulting in feeding intolerance (4). Furthermore, increased abdominal distention exerts upward pressure on the diaphragm, necessitating further increases in CPAP distending pressure to maintain adequate lung inflation (4). This is a perfect picture of a vicious circle.

The relationship between the pulmonary and gastrointestinal systems is complex. One affects the other; "how?" is a topic of an ongoing investigation. Remembering this when using ever-higher pressures on increasingly smaller babies behooves us. There are many factors in which one system affects the other and vice-versa. Intestinal inflammation contributes to pulmonary inflammation, and pulmonary inflammation contributes to intestinal inflammation (10). Indeed, pulmonary pathology increases the risk of NEC, and NEC increases the risk of pulmonary pathology (10).

Assessing tissue oxygenation via pulse oximetry does not necessarily reflect tissue (i.e., gut) oxygenation in and of itself, and intestinal hypoperfusion/hypoxia increases NEC risk (10). More accurate means of assessing oxygenation are needed, i.e., near-infrared spectroscopy (10).

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Other factors, including antibiotics, severe anemia, and hypotension, impact the bowel. Of interest, spontaneous breathing improves intestinal perfusion. This adds further weight to avoiding paralysis, and although many bedside caregivers conflate spontaneous breathing superimposed on high-frequency oscillation or jet ventilation as "fighting the ventilator." This is not the case; it is desirable (10).

Pulmonary/intestinal interactions are too numerous to expand here, but reference 10 is an excellent primer.

A&Bs may require vigorous stimulation to resolve. During the neurologically sensitive first 72 hours, is it prudent to regularly stimulate an infant to breathe when the goal is to minimise handling?

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The likelihood of failing NIV increases with decreasing birthweight and PMA, particularly below 25 weeks. Given the probability of failure and the lack of evidence supporting its safety (and other sequelae such as nasal damage from prolonged use of NIV interfaces), is it prudent to use this mode in the sub-25-week PMA population? It is not, particularly during the first 72 hours of life.

Finally, the fact that chronic lung disease can develop, despite using NIV is lost on many. This is particularly true if mode failure

is not recognised and the appropriate action is taken. Increasing FiO2 often reflects pulmonary derecruitment, which may lead to "atelectrauma." In the face of severe CPAP belly/abdominal distention, increasing pressure is likely, not helpful. It may make things worse. The increasing frequency and severity of A&Bs indicate that things are not going well.

As stated in a previous column, "With NIV, failure is not a four-letter word." Failing to recognise it should be.

References:

1. https://pubmed.ncbi.nlm.nih.gov/19564301/#:~:text=The%20impact%20of%20CPAP%20and%20oxygen%20on%20gut,necrotizing%20enterocolitis%20%28NEC%29%20has%20not%20been%20adequately%20addressed
2. https://clinicaltrials.gov/ct2/show/NCT00182390
3. https://www.nature.com/articles/s41390-020-01273-
4. https://www.scilit.net/article/a38b328b4b873992b7f9509d-8426b34e
5. https://www.sciencedirect.com/science/article/abs/pii/S0146000521000689?fr=RR-2&ref=pdf_download&rr=7b8aa11439f20fb5
6. https://www.liebertpub.com/doi/pdf/10.1089/bfm.2018.29082.efl#:~:text=gut%20injury%28TRAGI%29%20refersto%20the%20temporal%20association%20%28%3C48%20hours%29,opposed%20to%20the%20luminalside%2C%20of%20the%20mucosal%20barrier.
7. https://pubmed.ncbi.nlm.nih.gov/30890001/
8. https://link.springer.com/article/10.1007/s12098-014-1545-x
9. https://journals.lww.com/jpgn/Fulltext/2005/02000/Patent_Ductus_Arteriosus,_Indomethacin_and.19.aspx
10. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8440476/

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