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Non-Invasive Ventilation: Who, How and For How Long?

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.

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Non-invasive respiratory support in the NICU pre-dates invasive mechanical ventilation (IMV). Initially, bubble CPAP was the only adjunct available to clinicians. It is still widely used in units worldwide; its simplicity and low cost make it particularly attractive where available healthcare resources are limited. Today, there are more options for providing NIV. There are also several different modes as well.

With the introduction of mechanical ventilators, IMV became the standard of care for most premature infants. That IMV was not a panacea was almost immediately apparent: bronchopulmonary dysplasia (BPD), now referred to as chronic lung disease (CLD), became the hallmark of prematurity. Before the availability of surfactant supplementation, it was a necessary and undeniably life-saving therapy, CLD notwithstanding. As my late mentor, Dr. Andrew Shennan, would say, "you have to survive to have complications."

Surfactant therapy did not eliminate CLD as much as was hoped, and post-natal steroid use became commonplace as a treatment for CLD and to facilitate extubation to NIV. Concerns about brain development and neurodevelopmental outcomes led to steroid use falling out of favour in the late 1990s until demonstrably safer regimens such as the "DART" protocol were introduced.

The undeniable link between IMV and CLD begged the question of whether the duration of IMV could be decreased or avoided altogether. While gestational age alone was once the sole determinant of the need for intubation and IMV, it was also a common determinant for the transition from IMV to NIV. Intubating all infants of less than 30 weeks post-conceptual age (PCA) and/or continuing IMV until 30 or more weeks PCA may seem absurd today, but it was standard a generation ago.

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Earlier extubation was followed by selective intubation and increased use of NIV as first-line therapy, and later research supported its use at lower PCA. Intubation for surfactant administration followed by extubation to NIV (INSURE) is now common practice, and alternative "less invasive" methods of surfactant administration "LISA, MIST" are gaining acceptance. There is evidence to support both approaches. I suspect variations in how surfactant is delivered after intubation have implications for potential lung damage, i.e., hand-bagged in or delivered while on the ventilator, and may favour less invasive methods. The benefit may be secondary to not handbagging the baby, c.f., not intubating. To the best of my knowledge, no comparison study has examined whether handbagging surfactant contributes to poorer outcomes. (I suspect it does).

Although CLD, among other morbidities, has not declined, NIV is now routinely chosen as the first-line modality for respiratory support in ever younger and smaller infants (1). As PCA at birth decreases, the risk of lung damage increases. It has also been shown that extubation failure bodes poorly for outcomes, including CLD (2). The lungs are most susceptible to damage during

the recruitment phase, whether during initial resuscitation or de-recruitment. Oxidative stress is most deleterious in premature infants at birth, especially as PCA decreases. Stubbornly refusing to change course as a baby's FiO_2 increases will likely exacerbate the problem through progressive atelectasis, prolonged oxidative stress, and delaying surfactant administration (however given) should it be needed. Providing NIV should be weighed against the increasing likelihood of treatment failure as PCA falls.

"Radiologically diagnosed severe RDS increases the odds of failure but not uniformly; 50-80% will fail NIV but fewer than a third of infants failing NIV have radiological evidence of severe RDS. Not all babies with severe RDS will fail CPAP, and not all failing NIV have severe RDS (1)."

Other than PCA, other indicators are pointing to NIV failure. Surfactant deficiency (SD) is one. Historically chest films and FiO_2 have been used to determine SD, but their sensitivity is lacking; high FiO_2 correlates well with SD but may result from under-recruitment. Radiologically diagnosed severe RDS increases the odds of failure but not uniformly; 50-80% will fail NIV but fewer than a third of infants failing NIV have radiological evidence of severe RDS. Not all babies with severe RDS will fail CPAP, and not all failing NIV have severe RDS (1). Observationally it is not uncommon in units that do not administer surfactant prophylactically to see very premature infants who have not received surfactant in a FiO_2 of 0.21. It stands to reason that these infants are not SD but respond to adequate recruitment.

Another problem with incorporating FiO_2 into failure criteria is the lack of consensus on what level represents failure; some define failure at 0.6, some at 0.4, and some at 0.3. Decreasing failure criteria from 0.6 to 0.35 increases the failure rate by 16% and results in surfactant being given 2.5 hours earlier, ostensibly a good thing, especially at lower PCA. Interestingly, an FiO_2 of 0.3 on NICU admission has a 60% sensitivity in predicting NIV failure (1). This supports the European recommendation of FiO_2>0.3 as a failure criterion. Higher FiO_2 criteria decrease failure rates and result in truly SD infants not receiving surfactant (1). This management may be one reason pulmonary function in babies "successfully" managed on NIV is decreased later in life.

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Several modes of NIV are available today that were not available to our colleagues of yesteryear. In addition to CPAP, non-invasive positive pressure ventilation with or without synchronisation (Si) NIPPV, non-invasive HFO (NI-HFO), and non-invasive neurally assisted ventilation (NIV-NAVA) are available. Evidence favouring one mode over the other has been historically inconsistent or lacking, but more recent studies show decreased NIV failure with NIPPV (particularly if synchronised) and possibly NI-HFO. NIV-NAVA is the newest kid on the block and shows great promise, and those using the mode report great success, but further studies are needed (3). NIPPV should be initially considered as the first mode for those most at risk of failing NIV. NI-HFO is frequently used to good effect in my practice. Babies should be transitioned to CPAP as soon as possible.

How long babies should remain on NIV is a topic of great debate. Antenatal steroids (ACS) have increased dramatically since early NIV trials and have changed our patient population even as their PCA has become much lower. Trials involving non-ACS exposed infants and higher PCA are not applicable today, nor is it reasonable to expect the course of the extremely premature to mirror that of more mature infants. Before resuscitation of the sub-25-week PCA became routine, it was relatively uncommon (at least in the unit where I practice) for NIV to be required beyond 30 weeks PCA, give or take. An infant born at 23 weeks PCA cannot generally be expected to be free of NIV until much before 32 weeks PCA, perhaps much longer (4).

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Some propose leaving all infants on NIV until at least 32 weeks. I believe this blanket approach may not be in our patient's best interest as it will indubitably result in many infants being maintained on NIV longer than necessary. The proven benefits of NIV have blinded many to the fact that the modality is not benign and the duration of therapy increases the risk of adverse effects. Air leak, distal airway over-extension, reflux (itself, contributory to lung damage), and nasal injury are not beneficial. In addition, NIV can delay oral feeding and interfere with Kangaroo care, and may increase the length of stay if used unnecessarily. NIV can also result in many of the same problems as invasive ventilation, including cardiopulmonary compromise (4). I do not think it is a stretch to

say any medical intervention should not be continued beyond its utility.

"Treatment creep," the use of a proven therapy on patients for whom its beneficence has not been established, may not be appropriate in the case of NIV and may lead to unintentional harm. More research reflecting today's NICU patient population is needed before the indiscriminate application of NIV. That research should establish consistent failure criteria and involve long-term follow-up before the safety and efficacy of NIV in the highly premature can be established.

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