

## EDITORIAL VIEW

# Prevention of mechanical ventilation related iatrogenic injuries in neonates: Can we really succeed?

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**Citation:** Kojikj L. Prevention of mechanical ventilation related iatrogenic injuries in neonates: Can we really succeed? (Editorial). *Anaesth Pain & Intensive Care* 2012;16(1):1-3.

There has been an ongoing debate on the issue of how to prevent lung injury in neonates for almost half a century. The spectrum of topics is broad and involves many studies and many articles as well. But when it comes to practice, there have been two main concerns regarding prevention of lung injury. The first is endotracheal intubation itself as an aggressive procedure. The second and more complex one is the choice of ventilatory approach.

“When to start ventilating a neonate?” The only clear answer to this question is: “When he is apneic”. Or simply when the baby does not breathe, there is no way other than to intubate him. All the other scenarios, such as hypoxemia, hypercarbia, unstable cardiovascular function and increased work of breathing, deserve at least an attempt to be treated in a non-invasive way. Whenever possible, Continuous Positive Airway Pressure (CPAP) or some other mode of non-invasive ventilation should be attempted. Early CPAP is now used in many centers in preference to early intubation and IPPV. It's use has been associated with a reduction in the requirement for invasive mechanical ventilation.<sup>1</sup>

In premature babies of 25 to 28-weeks gestational age, introduction of early nasal CPAP, even though it did not significantly reduce the rate of death or bronchopulmonary dysplasia in comparison to intubation and even though it had a higher incidence of associated pneumothorax, resulted in fewer infants receiving oxygen at 28 days, and they had fewer days of ventilator support, if they had to be intubated.<sup>2</sup> If the patient does not respond to the non-invasive strategies, then conventional mechanical ventilation should be

initiated.

Intubation with an uncuffed tube in neonatology is consensus. The implications of inserting too large a diameter tube are clear. Inserting a tube larger than the appropriate, very likely will lead to severe injury to the trachea or the vocal cords.

But inserting smaller tube than the recommended size is also wrong, since if one places smaller tube, the air leak around the tube will be higher than 50%. Air leak greater than 50 percent is the problem that even most sophisticated microprocessor-based ventilators cannot compensate. The leak will lead to inefficient ventilation. This is mainly due to the insufficient tidal volume delivery that will result in inadequate minute ventilation. Hence you will have to increase the peak inspiratory pressure (PIP) in order to achieve acceptable blood gases. Higher PIP is associated with a risk of pneumothorax.

Not to mention the weaning process, in which if the tube is too small, you are increasing baby's work of breathing (WOB). Consecutively, the increased WOB is going to increase the oxygen consumption and fatigue, and is going to lead to a vicious circle that will result in ventilator dependency. Regarding the size of the tube, in almost every textbook or handbook for neonatal ventilation there is a chart with tube sizes that corresponds to the baby's size. It might be appropriate to follow that charts, but clinical judgment still reins supreme.<sup>3</sup>

The phase that comes after the intubation is the most tricky one: managing an already intubated baby

properly so as to prevent harm to the delicate lungs with the best possible strategies.

It was the mid-sixties of the past century when the first pressure controlled infant ventilators became available. Somehow, at the same time Northway has clearly stressed the bronchopulmonary dysplasia (BPD), or Chronic Lung Disease (CLD) as a consequence of inadequate ventilatory treatment of the premature lung. Even that many years ago it also became clear that high PIP did result in barotrauma (air-leak syndrome).<sup>4</sup>

Ever since, the traditional method of mechanical ventilation to treat neonatal respiratory failure has been time-cycled, pressure-limited ventilation (TCPL), which is actually pressure controlled (PCV) mode. Time-cycled, pressure-limited ventilation was easy to use and was considered to be protective against barotrauma, as the PIP could be limited and the ventilator would not exceed this pressure. This ventilator worked well along with the concept of 'barotrauma'. Pressure limited ventilation in newborn is reputable to be life-saving. But was it lung-saving?

The comprehension on the phenomenon of the so called 'post-surfactant era' CLD has somewhat changed over the past two decades as the knowledge of neonatal and premature neonate's lung mechanics was evolving.

Volume Controlled Ventilation (VCV) and PCV, each have some characteristics that might be considered beneficial and other characteristics that might be considered limiting. Typical VCV in classic sense will deliver a preset tidal volume, regardless of the pressure, at fixed flow rate. Limitations of this mode in neonates are large tube leaks, the compressible volume loss and incompatibility with continuous flow. Therefore, it was not suitable for use in neonatology. During pressure control ventilation (PCV or TCPL), on the other hand, the delivered tidal volume will vary depending upon the specific characteristics of the lung (mainly compliance, and to a lesser extent the resistance). In other words, there is no consistency in tidal volume delivery. Today we know that lung mechanics, in particular, change rapidly after the administration of surfactant and if the peak inflating pressure is not altered, excessive tidal volume delivery can lead to overexpansion and volutrauma.<sup>5</sup>

In the late nineties, several studies on animal models introduced the concept of 'volutrauma' and lung damage due to over distension because of large tidal volume (VT) delivery. At the same time, the delivery of small VT has also been recognized and named as

'atelectotrauma'. 'Biotrauma' was the term coined for an inflammatory response of the immature lungs to mechanical ventilation on grounds of underlying infection.<sup>6-8</sup>

These concerns have lead to the development of alternative ventilator techniques. Since microprocessor was incorporated into ventilator design technology, there has been abundance of new ventilator techniques and strategies such as HFV (jet or oscillatory) and NO ventilation. And they all have proven to be useful, but not for extensive use or are just not available for use in each and every NICU.<sup>9</sup>

One may argue that the many new modes of mechanical support available to us are just "fashion trends" in mechanical ventilation, since long-term outcomes have not been clearly shown to be improved by their use. But today, we have the technology to detect patients respiratory effort, to monitor and adjust tidal volumes, to assess and augment minute ventilation, and the last but not the least to allow the recovering patient to interact with the mechanical ventilator with much greater degree of synchrony. Thus we may increase the odds that the delivered support will match the physiologic need. Neonatologists were mainly trained to adjust ventilator variables manually. We got used to working in the dark. As the possibilities to make more accurate measurements and to allow the babies to interact more with their mechanical support, we should make better judgments.

Decade ago first studies on Volume-targeted modes of ventilation (VTV) were published. VTV aims at minimizing variation in the volume delivered to the infant.

For the above mentioned reason of being in exaltation over a new ventilation strategy and/or technique, only to find it not widely applicable (or too expensive), the VTV modes were approached with great restraint and studied meticulously. It is actually nothing but pressure-limited mode with volume targeting. It is essentially pressure-limited form of ventilation that utilizes microprocessor servo-controlled ventilation with an algorithm that adjusts the rise and fall of pressure for VT delivery within a desired range. The clinicians is setting the pressure limit that will allow the pressure to vary, but within the safe range as the compliance changes. But it also has the benefits of volume targeting: Consistent tidal volume delivery and auto-weaning feature of the pressure, as the compliance improves. In simple words-it is actually SIPPV, SIMV or PSV with Volume Target. So the chances of volutrauma or atelectotrauma are

reduced.<sup>10</sup>

The most extensively evaluated ventilation strategies are volume guarantee (VG), pressure-regulated volume control (PRVC), and volume-assured pressure support (VAPS). VG and PRVC use the VT of previous breaths as a reference, with follow-up adjustments in PIP on averages of 6-8 breaths in order to deliver the preset VT. Volume-assured pressure support (VAPS) makes intra-breath adjustments of inspiratory time and/or pressure, until the desired volume has been delivered. They all aim to optimize VT delivery.

## Clinical evidence

The Cochrane Collaboration has recently published systematic review comparing volume-targeted (VTV) to pressure-limited ventilation (PLV). The investigators extensively evaluated the literature and ultimately found 12 trials that met criteria to include in their analysis.

While no differences in mortality were found, there was reduction in the risk of death or bronchopulmonary dysplasia with volume-targeted ventilation. Additionally, the review found that VTV was associated with a decreased incidence of pneumothorax, shorter duration of ventilation, a decreased incidence of hypocarbia and even lesser neurologic injury (severe intra-ventricular haemorrhage or periventricular leukomalacia). There were no differences apparently in long-term neurologic outcomes (although only two studies evaluated this).<sup>11,12</sup>

Bottom-line, VTV can be a powerful tool in preventing neonatal lung injury. VTV offers new choices to clinicians. It even appears preferable in certain clinical circumstances, especially those characterized by a changing lung compliance.

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