Volume-controlled ventilation in the newborn

Neonatal ventilation has traditionally been accomplished using time-cycled pressure limited ventilation. Volume-controlled ventilation has only recently been available for use in newborns. This article reviews volume-controlled ventilation and other volume-targeted modes.

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Key points

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- Evidence from animal and adult studies suggests that volutrauma may be the key determinant of ventilator inducedlung injury.
- Volume control and other methods of ventilation that target tidal volume delivery may therefore have advantages over traditional methods that target pressure.
- Early evidence from randomised trials in newborns is promising and has set the stage for a large trial looking at long term outcomes.

Mechanical ventilation remains the cornerstone in the management of respiratory failure in neonatal intensive care units. Although life saving, mechanical ventilation is associated with short and long term complications such as air leaks and chronic lung disease. The pathogenesis of chronic lung disease in preterm infants is multi-factorial but artificial mechanical ventilation plays a major part in its development and the term ventilator-induced lung injury (VILI) has been coined to describe the damage caused to lungs during mechanical ventilation^{1,2}.

Traditionally clinicians have believed that the amount of pressure delivered to the lungs was the primary cause of lung injury, described as barotrauma. New evidence from animal and adult studies however suggests that it may actually be the amount or volume of gas delivered to the lungs (the tidal volume) rather than the pressure it is delivered at, which is more likely to be the main cause of lung damage during mechanical ventilation. This has given rise to the concept of volutrauma caused by too much volume of gas leading to alveolar over distension and damage to the immature lungs³.

Volume-controlled versus pressure-limited ventilation

Since its introduction, neonatal ventilation has been accomplished using traditional time-cycled pressure-limited ventilation (TCPL). In this mode of ventilation, a peak inspiratory pressure is set by the operator, and during inspiration gas flow is delivered to achieve that set pressure, hence the term pressure-limited (PL) ventilation. The volume of gas delivered to the patient in this mode however varies depending on pulmonary mechanics such as compliance or stiffness of the lungs. At low compliance ('stiff lungs') such as occurs early in the course of respiratory distress syndrome (RDS), a given pressure generates lower tidal volume as compared to later in the course of the disease when the lungs are more compliant ('less stiff') when the same set pressure will lead to delivery of larger tidal volumes. This is illustrated in **FIGURE 1A**. This is important clinically as with improvement in compliance such as after exogenous surfactant therapy, the ventilator pressure has to be weaned by the operator to prevent alveolar over distension resulting from excessive tidal volume delivery.

The key differentiating feature of volume-controlled (VC) ventilation (Avea® and VIP Gold®, Viasys Health Care System) is that in this mode, the primary gas delivery target is tidal volume (not pressure) which is set by the operator, and the peak inspiratory pressure may vary from breath to breath to deliver this set tidal volume. Thus at lower compliance ('stiff lungs') such as in early stages of RDS, high peak pressures are generated to deliver the set tidal volume. As the compliance improves, the pressure needed to achieve the same tidal volume automatically reduces (also referred to as auto weaning of pressure). This is illustrated in FIGURE 1B.

If volutrauma is indeed important in the development of VILI then modalities of ventilation that target delivered tidal volume may have advantages over the PL modes of ventilation. Volume ventilation has been available for a long time in adult and paediatric intensive care units but it is only recently, since the introduction of microprocessor technology, that it became possible to ventilate preterm babies using VC ventilation as a primary mode of ventilation. Stability of tidal volume delivery may have advantages particularly in newborns with RDS in whom lung



Pressure

FIGURE 1A Schematic representation of pressure volume loops in pressure limited ventilation. In low compliance lung (broken line loop) the tidal volume delivered is lower than compliant lung (continuous line loop). Pressure delivered by the ventilator is same for the two breaths.



Pressure

FIGURE 1B Schematic representation of pressure volume loops in volume-controlled (VC) ventilation. Tidal volume delivered is same for the two breaths. In low compliance lung (broken line loop) the pressure needed to deliver the set tidal volume is higher than in compliant lung (continuous line loop).

compliance (and hence delivery of gas volume to the lungs) may rapidly change in response to the disease process or treatment such as surfactant therapy⁴.

Another important feature which differentiates VC from PL ventilation is the way that gas flows in during inspiration. This is illustrated in **FIGURE 2**. In VC ventilation a square flow waveform is generated and occurrence of peak volume delivery is at the end of inspiration⁴. In contrast, during PL ventilation the opening pressure is reached relatively quickly and after the target pressure is reached, flow decelerates in an exponential manner (ramp descending waveform) to maintain pressure at the target until inspiration is complete.

It is important to realise that there is a discrepancy between volume delivered by the ventilator and that reaching the patient. It is therefore important to measure volume delivery close to the patient. Most modern ventilators measure volume delivery at the proximal airway. This provides a better estimate of volume delivery to the patient as compared to ventilators which measure volume at the ventilator.

Like PL ventilation, VC ventilation can be provided in a variety of ways. These include intermittent mandatory ventilation (IMV), synchronised intermittent mandatory ventilation (SIMV), and assist control ventilation (A/C).

Hybrid modes of ventilation

Volume-controlled ventilation is different from volume guarantee (VG), pressureregulated volume control (PRVC) or volume assured pressure support ventilation (VAPS), which are hybrid modes of ventilation. These are essentially PL modes of ventilation that use dual loop control in an attempt to maintain tidal volume delivery in the target range (volume targeted). Loop control means that the tidal volume is monitored by the ventilator and if the tidal volume is not being achieved in the target range, the peak pressure setting is automatically adjusted by the ventilator.

Volume guarantee (VG) is available on the Draeger Babylog 8000 plus[®]. This mode uses time-cycled PL breath type ventilation but allows the pressure to be adjusted to guarantee tidal volume delivery in the target range. Potential advantages of VG include less risk of volutrauma, as clinician set tidal volume is not exceeded when lung compliance improves, and

automatic reduction in peak pressures when compliance improves i.e. reduced barotraumas. However, clinicians should be aware of certain limitations which may be associated with the feedback loop mechanism. For example, as adjustments to PIP are made in small increments to avoid overcompensation, the delivered tidal volume may not compensate for large breath to breath fluctuations. Thus although VG leads to more constant tidal volume delivery, this may not always be the actual set tidal volume. As the expired tidal volumes are used in the presence of large leaks, the ventilator may underestimate tidal volume delivery and overcompensate subsequent breaths. So far the published studies have not shown any potential harm in using VG5-9.

Volume assured pressure support (VAPS) is another hybrid mode that



FIGURE 2 Schematic representations of pressure and flow waveforms to illustrate the difference between volume-controlled (VC) and pressure-limited (PL) ventilation.

VENTILATION

combines VC ventilation and PL ventilation. A guaranteed tidal volume delivery is provided with each breath. Each breath starts as a pressure support (PS) breath. The ventilator will measure the delivered tidal volume when the inspiratory flow has decelerated to a minimum set level. If the delivered tidal volume equals or exceeds the set tidal volume, the PS breath is allowed to continue and is flow cycled. If the targeted tidal volume is not achieved the breath changes to a VC breath and inspiration is continued until the set tidal volume is delivered. Clinical experience with this mode is limited except for individual units.

Pressure-regulated volume control (PRVC) is another mode of ventilation which attempts to combine the benefits of pressure control (PC) and VC ventilation. This is available on the Servo 300A® and the Servo-i[®] ventilators (Maguet). It is a flow-cycled mode that offers the variable flow rate of PC ventilation with the advantage of setting a targeted tidal volume. Like VG, PRVC is also a form of closed loop ventilation in which pressure is adjusted according to tidal volume delivered. The new Servo-i ventilator features Y-sensor measurement ensuring better measurement and more accurate delivery of set tidal volume.

Clinical studies

As VC and volume-targeted hyrbrid modes of ventilation have only recently become available for use in the neonatal population, there are not many controlled studies describing their safety and efficacy.

The first reported randomised controlled trial of true VC ventilation, which controls the delivery of tidal volume as a primary variable against traditional TCPL ventilation, in preterm infants was conducted by Sinha et al10. Fifty preterm infants, weighing 1200g or more at birth, who developed RDS and required mechanical ventilation, were randomly allocated to receive either VC or TCPL mode of ventilation. The ventilator used in this trial was the VIP BIRD® (Bird products Corp, Palm Springs). Tidal volume delivery was kept deliberately at 5-8 mL/kg in both groups so that the only difference between the two groups was the ventilatory mode. The two modes of ventilation were compared by determining the time required to achieve a pre-set 'success criteria' using the alveolar-arterial oxygen gradient (AaDO₂) or the mean



airway pressure (Paw) as a standard, against which the speed of weaning could be objectively assessed. Infants randomised to VC ventilation met the success criteria faster (mean time 65 vs 125 hours, p < 0.001) and had a shorter total duration of ventilation (mean time 122 vs 161 hours, p<0.001). These babies also had a significantly lower incidence of large intraventricular haemorrhages and abnormal peri-ventricular echo-densities on ultrasound scans, although this finding should be interpreted with caution due to the small number of babies randomised. As tidal volumes were kept similar at 5-8 mL/kg in both groups, it appears that infants assigned to the VC mode could have benefited from better alveolar recruitment and ventilation perfusion matching.

McCallion et al in a recent Cochrane review identified eight randomised trials comparing the use of volume-targeted versus traditional PL ventilation in neonates, of which only four, including the trial by Sinha, met the eligibility criteria for inclusion in the meta-analysis11. These four trials recruited a total of 178 preterm infants. The trials used different ventilators and techniques (one trial used VC ventilation¹⁰, two used VG^{5,7} and one used PRVC¹²) to investigate the putative advantages of controlling tidal volume delivery in the 'optimal' range amongst babies who required mechanical ventilation. All trials recruited babies during the first 72 hours of life. Given the nature of neonatal ventilation, none of the trials were masked. No significant difference was found in the review for the primary outcome of death before discharge. Analysis of the trials however

showed that volume-targeted ventilation resulted in a significant reduction in the duration of ventilation [weighted mean difference -2.93 days (-4.28, -1.57)] as well as the rates of pneumothorax [typical relative risk (RR) 0.23 (0.07, 0.76), risk difference (RD) -0.11 (-0.20, -0.03), number to treat (NNT) 9]. There was also a significant difference in the rate of severe (Grade 3 or 4) intraventricular haemorrhage favouring the volumetargeted group [typical RR 0.32 (0.11, 0.90), RD -0.16 (-0.29, -0.03), NNT 6]. There was a reduction in the incidence of bronchopulmonary dysplasia (BPD) (supplemental oxygen at 36 weeks) amongst surviving infants, of borderline statistical significance [typical RR 0.34 (0.11, 1.05), RD -0.14 (-0.27, 0.00), NNT 7]. None of the trials looked at growth, death after discharge from hospital or neuro-developmental outcome.

The initial trial on VC ventilation carried out by the authors' group, by design only included babies more than 1250 grams in weight, because the ventilator available at the time could not deliver tidal volumes deemed suitable for smaller babies. However, these are precisely the type of babies who are more likely to sustain VILI and develop complications including death and BPD. This, along with improvements in ventilator technology enabling the delivery of smaller tidal volumes allowing the use of VC ventilation in smaller babies, prompted the same group of investigators to compare the safety and efficacy of VC ventilation in very low birthweight infants who had respiratory failure at birth and required mechanical ventilation. The results of this study, published this year, are the most recent on this subject and should

FIGURE 3 An infant receiving volumecycled ventilation.

only strengthen the findings of the metaanalysis in support of volume-targeted ventilation.

In this study by Singh et al, 109 newborns weighing between 600 to 1500 g and 24 to 31 weeks' gestation with RDS, were randomised to receive either VC or TCPL ventilation¹³. All infants in this study were treated with the VIP BIRD Gold ventilator (Viasys Healthcare Systems, Palm Springs, California) by using a standardised ventilatory management protocol designed for this study. In both groups, ventilator variables were set to target an exhaled tidal volume (V_{Te}) of 4 to 6 mL/kg. This was monitored and adjusted on an hourly basis. In the VC group, delivered tidal volume was adjusted, and in the TCPL group, the peak inspiratory pressure was adjusted. During the acute phase of illness, infants in both study groups were placed in the assist/control mode. Once the infants were recovering from their acute respiratory illness (peak inspiratory pressure <16 cm H₂O and FiO₂ <0.3), the ventilatory mode was changed from assist/control to synchronised intermittent mandatory ventilation with pressure support ventilation. The two modalities were compared by determining the time required to achieve a predetermined success criterion, on the basis of either the alveolar-arterial oxygen gradient <100 mm Hg or the mean airway pressure < 8 cm H₂O. Secondary outcomes included mortality, duration of mechanical ventilation and complications commonly associated with ventilation. The mean time to reach the success criterion was 23 hours in the VC group versus 33 hours in the TCPL group (P=0.15). This difference was more striking in babies weighing <1000g (21 vs 58 hours, P=0.03). Mean duration of ventilation with VC was 255 hours versus 327 hours with TCPL (P=0.60).

There was no significant difference in the incidence of complications in the two groups in this study. However, all deaths in the first week of life were related to respiratory disease and occurred exclusively in infants randomised to receive TCPL ventilation. This was unexpected, because the two study groups were closely matched for the factors affecting the severity of RDS. Although the modality of ventilation per se did not show an independent effect on survival on multivariate analysis, there was a trend towards better survival among babies treated with VC ventilation (odds ratio,

0.5; 95% CI, 0.2-1.2; P =0.010). These findings, however, should be interpreted with caution because of the small size of this study.

Future implications

Volume-controlled ventilation and other 'volume-targeted' modes of ventilation such as VG, PRVC and VAPS are new to neonatal intensive care units and represent a departure from the traditional TCPL modes. Not surprisingly, there are only a few published randomised controlled clinical trials using these modes in the newborn population. Nonetheless, the evidence so far is encouraging. It would appear that the consistency of tidal volume delivery during VC ventilation, in the face of varying lung compliance and the auto weaning of airway pressure, may be clinically advantageous. Although the benefits of volume-targeted modes in the published studies have been restricted to only short-term outcomes such as duration of ventilation, pneumothorax and intraventricular haemorrhage, they are still important findings and should not be ignored. They also have laid the groundwork for a large multi-centre trial of a sufficient size to be able to address the question - "Does volume-targeted ventilation improve the long term respiratory and neuro-developmental outcome"14. Such a trial would also establish whether the results can be replicated in units where staff have not as yet developed expertise in these modalities.

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