The Search for Accuracy in Neonatal Volume-Targeted Ventilation: For Whom, the Manufacturer, the Physician, or the Patient?

Since the development of volume-targeted ventilation, which has become the most recommended mode for lung-protective ventilation in neonates, many investigators (sometimes driven by corporate interests) have measured the accuracy of tidal volume (V_T) delivery for various ventilators primarily by using bench-testing while simulating various respiratory system conditions, including the introduction of an airway leak (ie, endotracheal tube [ETT] leakage). Such studies have repeatedly shown some discrepancies between various ventilators for desired and effectively measured V_T, observations that have often been used as an argument for some inconsistent outcomes of clinical studies that investigate the superiority of volume-targeted ventilation versus various modes of pressure-controlled ventilation.

What might be the real clinical advantage of volume-targeted ventilation? It is true that volume-targeted ventilation has shown some superiority over pressure-control modes in meta-analytic outcome analysis for death and/or chronic lung disease, although the quality of data varied from moderate to low and there were important heterogeneity among individual studies (of note, all of them were unblinded).[1] One more advantage of volume targeting would be to have stable minute ventilation and, therefore, stable P_{aCO_2} values, which allow for a better neurodevelopmental outcome. In fact, CO_2 stability and a lower incidence of hypocarbic events have been shown to be more achievable with volume-targeted ventilation than with synchronized intermittent pressure ventilation. However, this was only the case for infants at >25 weeks of gestation.[2]

Targeted V_T values are commonly in the range of 4 to 6 mL/kg, with the recommendation to use even larger V_T values in very small premature infants because of a proportionally larger instrumental dead space from the ETT and pneumotachograph inserted at the Y-piece.[3] However, there exists no single study that investigated in the best protective VT (in ml/kg bodyweight) range in neonates and/or infants who presented with respiratory distress. Therefore, and with the concept of a "safe" range of V_T, the question becomes, to what extent accuracy of V_T measures for volume-targeted ventilation as the primary control parameter, regulated either on the expired, the inspired, or a combination of both, is really of clinical relevance. Note that it has also been shown that the displayed, and for volume-targeted ventilation algorithms used, V_T from the ventilator may differ up to 10% from measures by a device independent pnumotachograph,[4] an observation that, in general, questions the accuracy of measures of very small V_T.

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The question to ask in the end, is not which ventilator is the best machine to regulate the V_T most precisely under any respiratory system condition, but what would be best in terms of respiratory support for the patient's clinical condition. In that, the study by DiBlasi et al[5] in this issue of RESPIRATORY CARE looked closer to the patient while investigating in an in vivo study (sedated but spontaneous breathing animals) the physiologic effects of different neonatal volume-targeted algorithms and V_T-measurement concepts of 3 neonatal ventilators. They addressed not only V_T measures and the accuracy of volume-regulation algorithms but also ventilation efficiency, as measured by gas exchange, trigger efficiency, and imposed work of breathing in the presence or absence of a graduated ETT leak.

One machine (Babylog VN500, Draeger, Lubeck, Germany) that offers adaptive leak compensation by using complex and proprietary algorithms that take into account the inspired and expired V_T, managed to keep the exhaled V_T value, as measured by an independent flow meter, within a 5% error of the preset value for both leak and no leak conditions. This resulted in stable P_{aCO_2} values, despite the observation that the spontaneous breathing rate decreased by 12%, which resulted in a reduction of calculated minute ventilation by 8%. This might suggest, as the authors hypothesized, that, in the presence of leak when the machine adds additional flow, CO_2 might be better washed out from the airways, similar to the concept of tracheal insufflation or high-flow nasal cannula therapy.

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DOI: 10.4187/respcare.06962

Whether this effect might increase the risk of hypocarbia in a subject without spontaneous breathing efforts remains unclear. With the second device (AVEA, CareFusion, Yorba Linda, CA), when regulating on the exhaled V_T only, the P_{aCO_2} values significantly decreased in the presence of an ETT leak, which suggests some leak overcompensation and the effect of CO_2 washout. Interestingly, with the third device (Servo-i, Maquet/Getinge, Solna, Sweden), which offers, in the model and version tested, no leak compensation and regulates on inspired V_T, which will lead in the presence of an ETT leak to a reduction of the Δ-pressure (ie, pressure above PEEP) to keep the inspired V_T constant. In this scenario, the measured exhaled V_T decreased below the target as would be expected, while spontaneous respiratory rates slightly increased, which resulted in unchanged P_{aCO_2} values.

Yet, it seems that two of the tested devices, despite complete opposite regulation algorithms, allowed the spontaneous breathing animals to maintain P_{aCO_2} stability in the presence or absence of an ETT leak. But what is the price that the subjects had to pay for this consistency? Whereas work of breathing as measured by the pressure-rate product calculated from esophageal pressure measures was equal for all 3 devices for the no-leak condition, it decreased with the Babylog VN500 and the AVEA when a leak was introduced. This would suggest that, in patients in whom spontaneous breathing efforts are supported, it would be best to search for an important ETT leak when using a device that regulates V_T leak compensated on the exhaled or on both inspired and exhaled V_T. Whereas, with a device that regulates the inspired V_T without leak compensation, the leak condition would not matter.

However, such interpretation of these findings might be flawed because, besides the various concepts and algorithms used for targeting a V_T for these 2 devices, asynchrony events (ie, inspiratory trigger failure), as observed with and without a leak condition with the Servo-i, might have had a major effect on imposed work of breathing. This observed important patient-ventilator asynchrony might be attributed to the fact that the flow sensor used for regulating V_T adjustments in this device is positioned within the device. Note, the manufacturer of the Servo-i, which does not have a leak compensation algorithm, does explicitly recommend not to use the volume-target mode in the presence of a major leak (ie, ≥50%). Therefore, it would have been desirable to compare ventilators of the same generation, where, at least in areas that accept CE-market (European Union approval), technology has for some years already been available with the Servo-u or Servo-n (Maquet/Getinge), which both offer leak compensation and regulate V_T on measures from a pneumotachograph at the Y-piece. Also, the latter may probably allow a reduction in asynchrony events. But this needs to be investigated.

All these observations and thoughts illustrate not only the complexity of comparative measures among devices but also that the individual's physiologic response to positive-pressure ventilation is more complex than we tend to think when testing devices on the bench. However, in the end, the essential questions that the clinician has to ask are the following:

1. What type and amount of support might be the best for my patient's actual disease condition?
2. How can my patient adapt to and interact optimally with the ventilator?
3. To what extent does the accuracy of numbers and measures matter for the patient?

In trying to partially respond to these questions, we need to better define what the ultimate outcome goals will be and what price to pay will be acceptable for a patient. In this search, the first maxim should be to cause no further harm, the second to improve short- and long-term outcomes, and the third to ensure patient comfort. This no harm and improve outcome concept that focused for many years on airway pressure limitation to protect the lung moved toward targeting V_T to protect the lung and ensure better P_{aCO_2} stability while trying to minimize alterations in cerebral perfusion. Targeting a specific V_T calls for high accuracy in V_T measures and assumes not only that V_T variability would be bad but that it also assumes that we know the specific best V_T for the patient's actual respiratory system conditions. However, for the latter, we do not have any data that would guide us when ventilating and/or assisting breathing in a neonate. Furthermore, irregular breathing with variable spontaneous V_T and variation of breathing frequency is highly physiologic in the preterm infant. Therefore, one might raise a further question, namely, whether some variability in V_T during ventilatory support would be desirable or beneficial for the patient.[6,7]

Patient-ventilator asynchrony is a second topic that has become a modern topic for device testing and altered since the appearance of neural adjust ventilatory assist. Although trigger and cycling asynchronies might increase the work of breathing of the patient and, in some conditions, call for more sedation, it has not conclusively been shown yet that minimizing asynchrony events would lead to better patient outcomes. However, better synchrony seems to be associated with better patient comfort.

Increased work of breathing and poor gas exchange are certainly 2 factors that might contribute to the severity of respiratory failure and an ongoing need for mechanical ventilation in premature infants. It would be highly desirable that ventilators are capable of delivering appropriate V_T and that they allow for effective triggering and cycling. However, this study by DiBlasi et al[5] did not help to confirm that the call for high accuracy and precision of V_T targeting, with almost a zero error allowance in measures and delivery of V_T, would be so essential for the patient and his or her outcome. It could be argued for this study

that the essential parameter that could explain the observed differences among ventilators would only be the observed patient-ventilator asynchrony. Therefore, we do not know yet whether it really matters for the patient if inspiratory, expiratory, or adaptive V_T targeting algorithms are used. Also we do not know yet how much precision in V_T measures and V_T regulation algorithms will finally be required to have an impact on patient outcome.

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