ADC-FNN Online First, published on June 28, 2017 as 10.1136/archdischild-2017-312640

Volume guaranteed? Accuracy of a volume-targeted ventilation mode in infants

Olivia Farrell,[1,2] Elizabeth J Perkins,[1] Don Black,[1] Martijn Miedema,[1,3] Joel Don Paul,[1,2] Prue M Pereira-Fantini,[1,2] David Gerald Tingay[1,2,4]

► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/archdischild-2017-312640).

[1]Neonatal Research, Murdoch Children's Research Institute, Melbourne, Australia
[2]Department of Paediatrics, University of Melbourne, Melbourne, Australia
[3]Neonatology, Academic Medical Centre, Amsterdam, The Netherlands
[4]Neonatology, Royal Children's Hospital, Melbourne, Australia

Correspondence to
Dr David Gerald Tingay, Neonatal Research, Murdoch Childrens Research Institute, Royal Children's Hospital Flemington Rd., Parkville 3052 Victoria, Australia.; david.tingay@rch.org.au

Received 5 January 2017
Revised 28 April 2017
Accepted 1 May 2017

ABSTRACT

Objectives Volume-targeted ventilation (VTV) is widely used and may reduce lung injury, but this assumes the clinically set tidal volume (V_{Tset}) is accurately delivered. This prospective observational study aimed to determine the relationship between V_{Tset}, expiratory V_T (V_{Te}) and endotracheal tube leak in a modern neonatal volume-targeted ventilator (VTV) and the resultant partial arterial pressure of carbon dioxide ($PaCO_2$) relationship with and without VTV.

Design Continuous inflations were recorded for 24 hours in 100 infants, mean (SD) 34 (4) weeks gestation and 2483 (985) g birth weight, receiving synchronised mechanical ventilation (SLE5000, SLE, UK) with or without VTV and either the manufacturer's V4 (n=50) or newer V5 (n=50) VTV algorithm. The V_{Tset}, V_{Te} and leak were determined for each inflation (maximum 90 000/infant). If $PaCO_2$ was sampled (maximum of 2 per infant), this was compared with the average V_{Te} data from the preceding 15 min.

Results A total of 7 497 137 inflations were analysed. With VTV enabled (77 infants), the V_{Tset}–V_{Te} bias (95% CI) was 0.03 (−0.12 to 0.19) mL/kg, with a median of 80% of V_{Te} being ±1.0 mL/kg of V_{Tset}. Endotracheal tube leak up to 30% influenced V_{Tset}–V_{Te} bias with the V4 (r^2=−0.64, p<0.0001; linear regression) but not V5 algorithm (r^2=0.04, p=0.21). There was an inverse linear relationship between V_{Te} and $PaCO_2$ without VTV (r^2=0.26, p=0.004), but not with VTV (r^2=0.04, p=0.10), and less $PaCO_2$ within 40–60 mm Hg, 53% versus 72%, relative risk (95% CI) 1.7 (1.0 to 2.9).

Conclusion VTV was accurate and reliable even with moderate leak and $PaCO_2$ more stable. VTV algorithm differences may exist in other devices.

What is already known on this topic?

- Volume-targeted ventilation (VTV) modes aim to stabilise tidal volume delivery and meta-analysis suggests improved outcomes when used.
- The benefits of VTV are reputed to be due to less atelectasis and volutrauma and more stable arterial carbon dioxide levels.
- The lung protective ability of VTV requires the ventilator's algorithm to reliably deliver the tidal volume set by the clinician.

What this study adds?

- In more than 7 million analysed inflations, the set tidal volume was delivered within a clinically acceptable range for most inflations using VTV.
- This is the first study to show that VTV targeting expiratory tidal volume, with good endotracheal tube leak compensation, stabilises arterial carbon dioxide.
- The first confirmatory evidence that a modern neonatal ventilator delivers the theoretical benefits of VTV.

INTRODUCTION

The optimal application of mechanical ventilation requires minimising the risks of ventilator-induced lung injury (VILI).[1 2] Both excessive and inadequate tidal volume (V_T) and applied pressure have been shown to increase VILI in neonates.[3 4] Volume-targeted ventilation (VTV) modes that adjust delivered pressure, aiming to maintain a constant V_T set by the clinician, have been shown to reduce the risk of death, chronic lung disease and short-term morbidity in preterm infants.[5] Despite this, VTV is not universally used in neonatal respiratory care.[6]

Critical to the lung protective potential of VTV is the accuracy and adaptiveness of the ventilators VTV algorithm and the ability of the clinicians to trust that the set V_T (V_{Tset}) is reliably delivered.[7 8] This is particularly important during spontaneous breathing and variable endotracheal tube (ETT) leak states.[8] To account for these factors, most modern ventilators target the measured expiratory V_T (V_{Te}). There are few reports addressing the reliability of specific VTV algorithms in neonates. The existing studies found a more stable V_T, with lower peak inflation pressures, when used in combination with patient-triggered ventilation than without.[5 9–11] However, on an inflation-to-inflation basis, inflating pressure fluctuations exceeded the manufacturer's guidelines in one of these studies.[11] Effective VTV should also result in more stable partial arterial pressure of carbon dioxide ($PaCO_2$), with less potentially injurious hypocarbia and hypercarbia episodes.[10 12 13] Despite the availability of VTV in neonatal ventilators for more than 15 years, the temporal relationship between $PaCO_2$ has not been reported.

The aim of this prospective observational study was to determine 1) the relationship between V_{Tset} and measured V_{Te} and 2) the relationship between V_{Te} and $PaCO_2$ with and without VTV.

To cite: Farrell O, Perkins EJ, Black D, *et al*. *Arch Dis Child Fetal Neonatal Ed* Published Online First: [*please include* Day Month Year]. doi:10.1136/archdischild-2017-312640

METHODS

The study was performed in the Neonatal Intensive Care Unit (NICU) at the Royal Children's Hospital, Melbourne, Australia, a referral tertiary unit, and approved by the Institutes Ethics in Human Research Committee. The study was performed in accordance with STROBE guidelines.[14]

The SLE5000 infant ventilator (SLE UK, South Croydon, UK), a neonatal ventilator (accelerating/decelerating flow waveform device) that measures pressure and flow (hot-wire anemometer) at the airway opening, was studied, being the only conventional ventilator used in our NICU. The study was performed in two epochs, as the manufacturer introduced a new VTV algorithm (with reported improved functionality, during the study) with a 2-year gap to allow for software updates and staff training of at least 1 year of clinical use with the new software: the first from April 2013 to March 2014 (V4 algorithm) and the second from March 2016 to August 2016 (V5 algorithm). Both algorithms target V_{Te} and offer leak compensation up to 20% (V4) and 50% (V5).

Intubated neonates less than 44 weeks corrected gestational age were studied if they were receiving mechanical ventilation in a patient-triggered modality with or without VTV enabled. Neonates were not studied if they were receiving high-frequency ventilation, muscle relaxants, had a major congenital abnormality or if extubation was anticipated within 24 hours.

At the commencement of the study, a custom-built data acquisition box (see online supplementary) was connected to the digital RS232 output port of the ventilator. From this port, the SLE5000 continuously outputs 40 parameters, including modality, VTV status, V_{Tset}, V_{Te} and measured ETT leak. These data were recorded for every inflation (text file onto an SD (Secure Digital) card) for up to 24 hours unless there was a clinical reason to remove it earlier. Clinicians could provide respiratory support at their discretion, including performing arterial blood gas analysis, changing modes and activating/deactivating VTV.

At the completion of each study period, the SD card was removed, data were extracted and the first 90 000 inflations per infant (or maximum within the 24 hours period if less) were exported into Prism V.7.02 for Windows (GraphPad Software, San Diego, California, USA) for analysis. For inflations with VTV enabled, matched V_{Tset}, V_{Te} and ETT leak data were extracted for each inflation and the $V_{Tset}-V_{Te}$ difference was calculated. $PaCO_2$ from any arterial blood gas analyses (maximum of 2 per infant) during the study period was manually recorded. The mean V_{Te} and minute ventilation for the 15 min prior to the $PaCO_2$ were calculated.

A convenience sample size of 100 (50 for each algorithm) was chosen to allow sufficient number of individual inflations within VTV permutations and a representative population of the broad spectrum of respiratory disease and ventilator settings. Descriptive statistics for the measured parameters were calculated. The Bland-Altman technique (using V_{Tset} as the comparator) and linear regression analysis were used to describe the inflation-to-inflation $V_{Tset}-V_{Te}$ differences and ETT leak relationships. Linear regression was also used to analyse the ETT leak$-V_{Te}$ and $V_{Te}-PaCO_2$ relationships. Fisher's exact test was used to determine whether VTV influenced the rates of hypocarbia or hypercarbia. All statistical analyses were performed using Prism, and $p<0.05$ was considered significant.

RESULTS

The demographic characteristics of the 100 infants studied (7 497 137 inflations) are summarised in table 1. There was no difference between the V4 and V5 groups, or the infants managed with and without VTV (data not shown). There was no difference in the use of synchronised intermittent mandatory ventilation and fully synchronised modes across all groups. Seventy-seven infants (5 477 530 inflations) had VTV enabled at some stage during the recording period with a median (range) 80 399 (352, 90 000) VTV inflations analysed per infant. The most common indication for respiratory support was primary parenchymal lung disease (n=55). At study commencement, five infants had either evolving or established chronic lung disease. Fifty-seven infants had at least one arterial blood gas analysis during the study period, with 42 infants contributing two sets of matched $PaCO_2$–V_{Te}/minute ventilation data (99 data triplicates). Forty of these infants were ventilated with VTV and 17 infants without VTV at the time of blood gas analysis. Infants receiving

Table 1 Subject characteristics at time of enrolment

Mean (SD), median (range) or n (%)	All infants (n=100)	V4 algorithm (n=50)	V5 algorithm (n=50)	Blood gas analysis cohort (n=57)
Gestational age (completed weeks)	34 (4)	35 (5)	34 (4)	35 (4)
Corrected gestational age (completed weeks)	36 (4)	36 (4)	36 (4)	36 (4)
Postnatal age (days)	4 (0, 84)	4 (1, 38)	4 (0, 84)	3 (0, 42)
Birth weight (g)	2483 (985)	2661 (1028)	2305 (915)	2728 (964)
Weight at study (g)	2630 (958)	2743 (1073)	2517 (823)	2830 (948)
Gender, female	44 (44%)	23 (46%)	21 (42%)	26 (46%)
Reason for mechanical ventilation (number) Primary respiratory disease: pneumonia (4), CLD (2), evolving CLD (3), MAS (4), RDS (22), prematurity (3), pneumothorax (1), RSV bronchiolitis (2), Pierre Robin syndrome (3), bilateral vocal cord palsy (1), TOF/OA (7), PDA (2), bilateral chylothoraces (1); shock/cardiac: sepsis (3), postoperative cardiac (2), metabolic acidosis (1); postoperative support of respiratory drive: laparotomy (15), choanal atresia repair (1), gastroschisis (8), NEC/peritonitis (3), myelomeningocele (1); other respiratory drive support: HIE (8), hypotonia (1), seizures (1) and renal failure (1).				
Relevant mediations at time of study (all infants) Opiate infusion (48), opiate+midazolam infusion (38), nidazolam infusion (2), one or more inotrope (31)				

Relevant medications prior to study (all infants).
Surfactant (30), antenatal corticosteroids (23), postnatal corticosteroids (12).
CLD, chronic lung disease; DORV, double outlet right ventricle; HIE, hypoxic ischaemic encephalopathy; MAS, meconium aspiration syndrome; NEC, necrotising enterocolitis; PDA, patent ductus arteriosus; RDS, respiratory distress syndrome; RSV, respiratory syncytial virus; TOF/OA, tracheo-oesophageal fistula/oesophageal atresia.

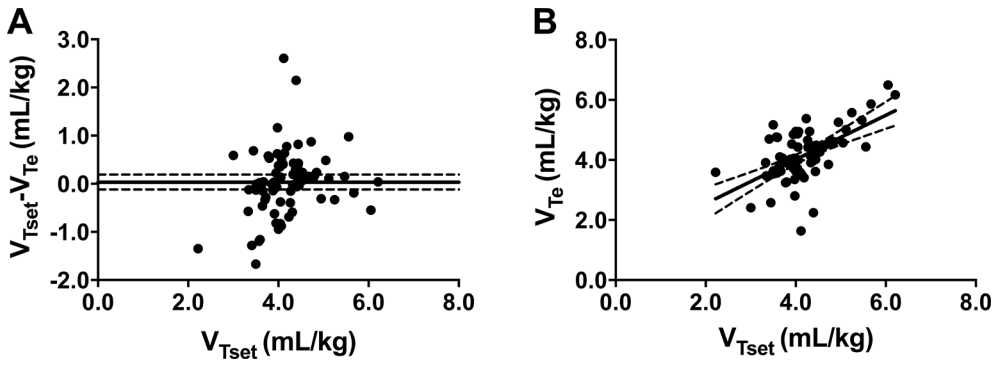

Figure 1 (A) Bland-Altman plot of V_{Tset} and expiratory tidal volume (V_{Te}) . Solid black line denotes the bias, dashed black lines denote the 95% CI of the limits of agreement. (**B**) Relationship between V_{Tset} and V_{Te}; y=0.736x+1.073 (r=0.34, p<0.0001; linear regression). Solid black line represents the line of best fit and dotted black lines represent 95% CI bands. To ease visual interpretation of figures, and after seeking statistical advice, symbols represent the average values for each infant rather than all values analysed (maximum 90 000/infant).

VTV were a mean (95% CI) 2 (0 to 4) completed weeks gestation less mature in the cohort who had $PaCO_2$ samples (Welch's t-test). Demographic factors did not influence the VTV accuracy results (data not shown).

Volume-targeted ventilation accuracy

The mean (SD) V_{Tset} was 4.2 (0.7) mL/kg and V_{Te} was 4.2 (0.8) mL/kg, with a resultant V_{Tset}–V_{Te} bias (95% CI) of 0.03 (–0.12, 0.19) mL/kg (figure 1). There was a significant relationship between V_{Tset} and V_{Te} (r=0.34, p<0.0001; linear regression). There was no difference in the V4 (n=34; 2 305 076 inflations) and V5 (n=43; 3 172 454 inflations) algorithms, with the mean (95% CI) V_{Tset}–V_{Te} difference being 0.4 (0.2, 0.7) mL/kg and 0.3 (0.1, 0.4) mL/kg, respectively (paired t-tests; data not shown). VTV accuracy was not influenced by postnatal age (p=0.53, linear regression), birth weight (p=0.39) or dose of opiate infusion (p=0.96).

Figure 2 shows the percentage of V_{Te} that was equal to and within ±1.0, ±2.0 and ±3.0 mL/kg of the V_{Tset} for each infant. Overall V_{Te} equalled V_{Tset} in a median (range) of 4 (0, 28)% of inflations for each infant. Overall, 80 (15, 100)% of inflations were within ±1.0 mL/kg, and 73 (15, 100)% and 86 (30, 100)% of V4 and V5 inflations, respectively. Ninety-eight (30, 100)% and 99 (41, 100)% of inflations were within ±2.0 and ±3.0 mL/kg of V_{Tset}.

Overall, 93% of V_{Tset} were within 3.5–8.0 mL/kg and for these inflations, a median (range) of 12 (0, 99)% and 0 (0, 22)% of V_{Te} were less or greater than that range. V5 resulted in 92 (56, 100)% of V_{Te} being within the set 3.5–8.0 mL/kg, while this was 74 (1, 100)% with V4 and 26 (0, 99)% due to V_{Te} <3.5 mL/kg.

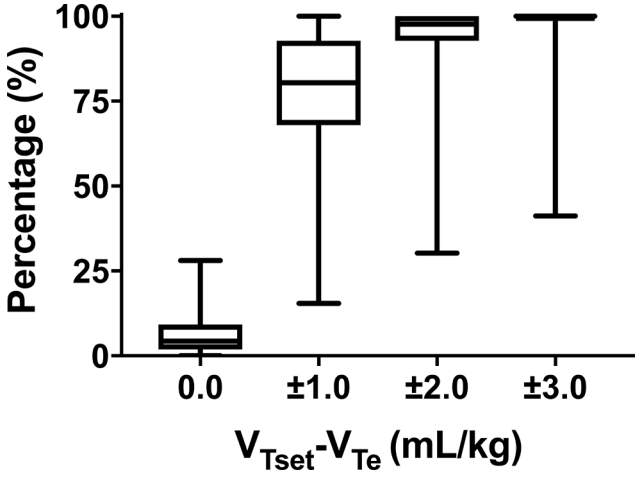

Figure 2 Percentage of inflations in each infant that expiratory tidal volume (V_{Te}) equalled to or was within ±1.0, ±2.0 and ±3.0 mL/kg of V_{Tset} using volume-targeted ventilation (n=77 infants). Box plots represent median and interquartile range with error bars showing minimum to maximum values.

Endotracheal tube leak compensation during volume-targeted ventilation

Figure 3 shows the relationship between measured ETT leak and V_{Tset}–V_{Te} difference for those infants receiving VTV with the V4 and V5 algorithms. Using the older V4 algorithm, there was a significant linear relationship (p<0.0001, linear regression). The relationship was non-significant for the V5 algorithm (p=0.2062) suggesting better ETT leak compensation within the range of ETT leaks measured.

Relationship between volume-targeted ventilation and partial arterial pressure of carbon dioxide

There was no significant correlation between V_{Te} or minute ventilation and $PaCO_2$ in the 40 infants managed with VTV at the time of an arterial blood gas (figure 4). In contrast, there was a significant inverse relationship between V_{Te} and $PaCO_2$ (but not minute ventilation) in the 17 infants ventilated without VTV. The use of VTV was also more likely to be associated with a $PaCO_2$ between 40 and 60 mm Hg, although this did not reach significance; 72% versus 53%, relative risk 1.7 (1.0, 2.9); p=0.1 (Fisher's exact test).

DISCUSSION

Within the era of antenatal corticosteroids and exogenous surfactant therapy, VTV is one of the few neonatal ventilator modes that has been shown to reduce lung injury in preterm infants.[5] However, achieving tight V_T control during the dynamic conditions of neonatal lung disease is complex and little has been reported regarding the accuracy of the different VTV options. In our pragmatic prospective observational study of >7 million inflations in a diverse population of 100 infants, we found that the VTV algorithms of a modern neonatal ventilator (SLE5000) were able to accurately and reliably deliver V_T and adapt to ETT leak and were associated with more stable $PaCO_2$ than without VTV.

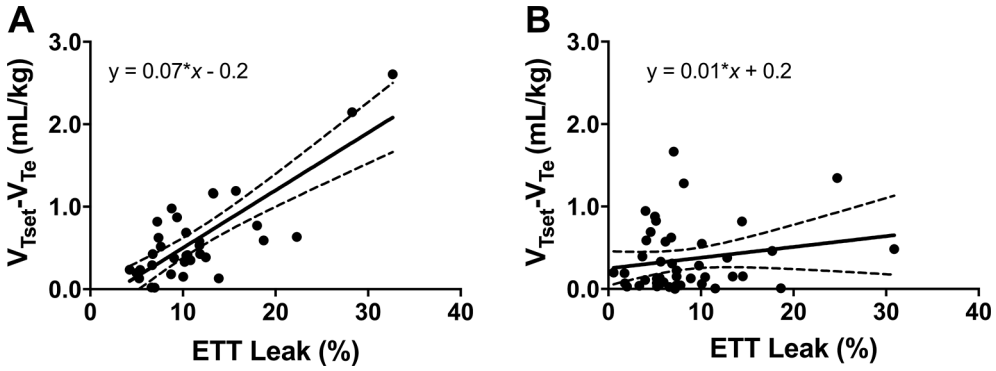

Figure 3 Relationship between endotracheal tube (ETT) leak and the V_{Tset}–V_{Te} difference for infants receiving VTV using the V4 (n=34; **A**) and V5 (n=43; **B**) algorithms. There was a significant relationship between ETT leak and V_{Tset}–V_{Te} difference using the V4 (p<0.0001, r=0.64; linear regression) but not the V5 (p=0.2062, r=0.04) algorithms. Solid black line represents the line of best fit and the dotted black lines 95% CI. Linear regression equation shown in figure panel. As per the rationale detailed in figure 1, symbols represent the average values for each infant rather than all values analysed. V_{Te}, expiratory tidal volume.

For the ventilator used in our study, overall V_{Te} was delivered within ±1.0 mL/kg of the V_T the clinician intended (V_{Tset}) in 80% of inflations with VTV enabled, although the intersubject and intrasubject variability suggests a clinically acceptable degree of reliability. The accuracy of VTV has been reported before in a benchtop study[7] and in small sample size neonatal studies limited to a relatively small number of inflations or reporting of averaged V_T over time.[8–11 15] In contrast, by accessing the large amount of data generated by modern ventilators, we were able to extract inflation-to-inflation data for >7 million inflations from 100 infants, the largest to date. Understanding the inflation-to-inflation variability is important when considering VTV accuracy, providing insight as to why V_{Tset}–V_{Te} discrepancies might occur, as even short periods of inappropriately delivered ventilation may cause VILI.[16 17]

Discrepancy between V_{Tset} and V_{Te} may have occurred due to factors beyond control of the ventilator algorithm, such as highly variable patient respiratory effort or the contribution of

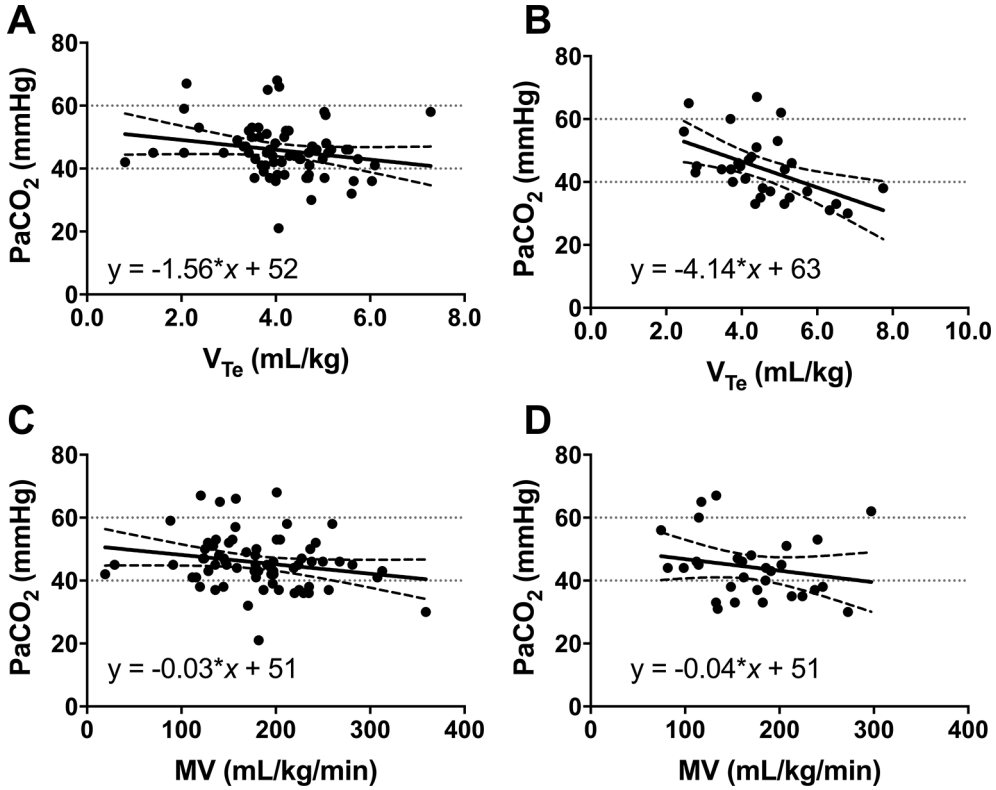

Figure 4 Relationship between expiratory tidal volume (V_{Te}) and partial arterial pressure of carbon dioxide ($PaCO_2$) (**A and B**) and minute ventilation (MV) and $PaCO_2$ (**C and D**) for infants managed with volume-targeted ventilation (VTV) (69 arterial gases, n=40 infants; **A and C**) and without VTV (30 arterial gases, n=17 infants; **B and D**). There was no relationship between $PaCO_2$ and V_{Te} (p=0.10, r=0.04; linear regression) and MV (p=0.08, r=0.05) with VTV. Without VTV, there was a significant relationship between $PaCO_2$ and V_{Te} (p=0.004, r=0.26) but not MV (p=0.281, r=0.04). Linear regression equations are shown in each panel. Solid black line represents the line of best fit and dashed lines 95% CI. Dotted black lines represent the normocapnia (40–60 mm Hg) range.

unsupported and therefore unregulated patient breaths.[11] No VTV mode can be 100% accurate due to inherent errors in the flow sensors[18] and the fact that the ventilator cannot prevent an infant from generating volumes higher than V_{Tset} or anticipate a lower respiratory effort. In such situations, the algorithm will need a few inflations to readjust the delivered pressure and may overshoot and undershoot while doing so. We could not address these concerns in the current study, due to the high level of computer processing needed for the large number of inflations. This limited the ability to individually assess patient effort and algorithm reaction.

To our knowledge, this is only the second report of inflation-to-inflation accuracy during VTV in vivo. McCallion and coworkers reported the accuracy of the Dräger BabyLog 8000+ to deliver VTV using a V_{Te}-based algorithm over 10 min of patient-triggered ventilation in 10 preterm infants (6540 inflations).[11] Although unable to determine long-term patterns, the authors found that, overall, VTV was accurate but they observed that there were large variations in V_T between adjacent inflations by up to 2.2 mL/kg. Our results confirm the observation that inflation-to-inflation V_T delivery can be highly variable in an infant. Notwithstanding the different ventilator and study design, together, the similar results are reassuring and indicate that the lung protective features of VTV identified in randomised controlled trials appear being delivered.

Fundamental to ensuring the V_T the lung receives is consistent with the V_{Tset} during VTV is the ability to compensate for ETT leak. Most neonatal ventilators now offer leak compensation during VTV,[7] and the manufacturers of the SLE5000 report that the older V4 and newer V5 algorithms can adapt V_T delivery to ETT leaks up to 20% and 50%, respectively. We found that V_{Tset}–V_{Te} discrepancy increased linearly with increasing leak using the V4 algorithm, but not the V5. This suggests that the V5 algorithm was more effectively adapting to ETT leak. To our knowledge, this is the first time ETT leak compensation has been reported using VTV and suggests that other ventilators warrant investigation. Such investigation should consider differences in ventilator flow characteristics as this will influence the impact of leak on V_T generation.

More stable $PaCO_2$ has been proposed as one of the beneficial effects of VTV.[5] We observed that $PaCO_2$ was more stable in infants ventilated with VTV compared with infants ventilated without, with $PaCO_2$ 20% more likely to be within 40–60 mm Hg (the commonly targeted range on our NICU). These findings are similar to reductions in hypocarbia reported in an earlier small randomised cross-over studies using the BabyLog 8000+.[10 12] We did not record the clinician's intended target $PaCO_2$, which may have differed from 40 to 60 mm Hg, especially in infants with chronic lung disease, who also have different VTV needs due to higher respiratory dead-space volumes. Thus, conclusions regarding the physiological outcomes of the arterial blood gases, including whether the use of VTV altered the prevalence of normocarbia and the suitability of V_T choice, cannot be made.

CO_2 clearance is determined by minute ventilation (product of rate and V_T), so the negative direct relationship between $PaCO_2$ and V_{Te} when VTV was not enabled was expected. The lack of this relationship using VTV suggests that the mode was operating appropriately as the clinician determines the V_T based on a desired $PaCO_2$. Dawson and Davies also observed a lack of correlation between $PaCO_2$ and V_T using VTV (BabyLog 8000+), although V_{Tset} was reported, and there was little variability in the V_T values reported.[13] There was no definitive relationship between $PaCO_2$ and minute ventilation with and without VTV, suggesting that infants may have been contributing to CO_2 clearance independent of delivered rate and measured V_T.

This study has some limitations not previously mentioned. Our study was observational, resulting in unbalanced subgroups, and clinical care and ventilator settings were not a priori dictated. Conclusions regarding whether VTV was achieving lung protection cannot be assumed, especially as we did not standardise the mode of triggering. Only one ventilator was studied, the SLE5000, and we relied solely on the ventilators measured data, therefore caution is required regarding the generalisation of our findings to other ventilators.[7] Our choice of the SLE5000 was pragmatic and practical as it was the only ventilator in use on our NICU and the introduction of alternative ventilators would have required additional staff training to ensure accurate clinical use and avoid bias. In addition, the SLE5000 has an open source data output, allowing our unique data collection system to be used. We would encourage all neonatal ventilator manufacturers to allow open access to ventilator data. Our study was not limited to preterm infants with acute disease but rather a diverse range of neonatal conditions, including term infants and some without primary respiratory failure. Furthermore, our study population had a high rate of analgesia use, potentially decreasing patient effort. This may increase algorithm accuracy. Modern neonatal respiratory practices are changing, with non-invasive support predominating in early preterm care.[2] We contend that our intentionally large convenience sample size was robust enough to allow meaningful clinical conclusions.

Conclusions

A representative modern neonatal VTV algorithm, with good ETT leak compensation, was accurate, reliable and effective, delivering the V_{Tset} within a clinically acceptable range. Reassuringly, the use of VTV resulted in more stable $PaCO_2$ than without VTV. This study provides the first confirmation that modern neonatal ventilators are able to deliver the theoretical lung protective benefits of V_T targeting.

Acknowledgements The authors wish to thank Associate Professor Susan Donath of the Centre of Epidemiology and Biostatistics Unit (Murdoch Childrens Research Institute) for statistical advice and Professor Peter Davis (Royal Women's Hospital, Melbourne, Australia) for clinical interpretation of the data.

Contributors DGT developed the concept and designed the experiment. OF, EJP, DB and JDP enrolled and studied all infants. DB designed and built the data collection system used in the study. OF, DB, MM and EJP were involved in data analysis. OF, PP-F, DB, MM and DGT interpreted the data. OF and DGT wrote the first draft of the manuscript and all authors contributed to redrafting the manuscript.

Funding This study is supported by the Victorian Government Operational Infrastructure Support Program (Melbourne, Australia). DGT is supported by a National Health and Medical Research Council Clinical Career Development Fellowship (grant ID 1053889).

Competing interests DGT has presented at conferences and workshops in which SLE, UK, has paid unrestricted travel costs or sponsorship for the meeting. DGT has also presented at conferences and workshops supported (including speaker travel costs) by other ventilator manufacturers, including Carefusion, Dräger, Fisher Paykel and Acutronic. No author received an honorarium, grant or other forms of payment to produce the manuscript. The study was not commissioned and no commercial agencies were involved in any aspect of this study. The authors have no other competing interests to declare.

Ethics approval The Royal Children's Hospital Human Research and Ethics Committee. The study was approved as a low or negligible risk study meeting audit criteria and prospective parental consent was not deemed necessary.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement De-identified raw complete data (7 million inflations) for all 100 study subjects are available upon request from the corresponding author.

REFERENCES

1 Dreyfuss D, Saumon G. Ventilator-induced lung injury: lessons from experimental studies. *Am J Respir Crit Care Med* 1998;157:294–323.
2 Dargaville PA, Tingay DG. Lung protective ventilation in extremely preterm infants. *J Paediatr Child Health* 2012;48:740–6.
3 Dreyfuss D, Soler P, Basset G, *et al*. High inflation pressure pulmonary edema. respective effects of high airway pressure, high tidal volume, and positive end-expiratory pressure. *Am Rev Respir Dis* 1988;137:1159–64.
4 Muscedere JG, Mullen JB, Gan K, *et al*. Tidal ventilation at low airway pressures can augment lung injury. *Am J Respir Crit Care Med* 1994;149:1327–34.
5 Wheeler K, Klingenberg C, McCallion N, *et al*. Volume-targeted versus pressure-limited ventilation in the neonate. *Cochrane Database Syst Rev* 2010:CD003666.
6 van Kaam AH, Rimensberger PC, Borensztajn D, *et al*. Ventilation practices in the neonatal intensive care unit: a cross-sectional study. *J Pediatr* 2010;157:767–71.
7 Jaecklin T, Morel DR, Rimensberger PC. Volume-targeted modes of modern neonatal ventilators: how stable is the delivered tidal volume? *Intensive Care Med* 2007;33:326–35.
8 Abubakar KM, Keszler M. Patient-ventilator interactions in new modes of patient-triggered ventilation. *Pediatr Pulmonol* 2001;32:71–5.
9 Cheema IU, Ahluwalia JS. Feasibility of tidal volume-guided ventilation in newborn infants: a randomized, crossover trial using the volume guarantee modality. *Pediatrics* 2001;107:1323–8.
10 Keszler M, Abubakar K. Volume guarantee: stability of tidal volume and incidence of hypocarbia. *Pediatr Pulmonol* 2004;38:240–5.
11 McCallion N, Lau R, Morley CJ, *et al*. Neonatal volume guarantee ventilation: effects of spontaneous breathing, triggered and untriggered inflations. *Arch Dis Child Fetal Neonatal Ed* 2008;93:F36–F39.
12 Cheema IU, Sinha AK, Kempley ST, *et al*. Impact of volume guarantee ventilation on arterial carbon dioxide tension in newborn infants: a randomised controlled trial. *Early Hum Dev* 2007;83:183–9.
13 Dawson C, Davies MW. Volume-targeted ventilation and arterial carbon dioxide in neonates. *J Paediatr Child Health* 2005;41:518–21.
14 von Elm E, Altman DG, Egger M, *et al*. The strengthening the Reporting of Observational studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* 2007;370:1453–7.
15 Armstrong RK, Carlisle HR, Davis PG, *et al*. Distribution of tidal ventilation during volume-targeted ventilation is variable and influenced by age in the preterm lung. *Intensive Care Med* 2011;37:839–46.
16 Björklund LJ, Ingimarsson J, Curstedt T, *et al*. Manual ventilation with a few large breaths at birth compromises the therapeutic effect of subsequent surfactant replacement in immature lambs. *Pediatr Res* 1997;42:348–55.
17 Tingay DG, Rajapaksa A, Zonneveld CE, *et al*. Spatiotemporal aeration and lung Injury patterns are Influenced by the First inflation strategy at Birth. *Am J Respir Cell Mol Biol* 2016;54:263–72.
18 Mendiondo Luedloff AC, Thurman TL, Holt SJ, *et al*. Reliability of displayed tidal volume in healthy and Surfactant-Depleted piglets. *Respir Care* 2016;61:1605–12.

Volume guaranteed? Accuracy of a volume-targeted ventilation mode in infants

Olivia Farrell, Elizabeth J Perkins, Don Black, Martijn Miedema, Joel Don Paul, Prue M Pereira-Fantini and David Gerald Tingay

Arch Dis Child Fetal Neonatal Ed published online June 28, 2017