Volume-targeted ventilation with a Fabian ventilator: maintenance of tidal volumes and blood CO_2

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ABSTRACT

Objective To analyse the performance of the Fabian +NCPAP evolution ventilator during volume guarantee (VG) ventilation in neonates at maintaining the target tidal volume and what tidal and minute volumes are required to maintain normocapnia.

Methods Clinical and ventilator data were collected and analysed from 83 infants receiving VG ventilation during interhospital transfer. Sedation was used in 26 cases. Ventilator data were downloaded with a sampling rate of 0.5 Hz. Data were analysed using the Python computer language and its data analysis packages.

Results ~107 hours of ventilator data were analysed, consisting of ~194 000 data points. The median absolute difference between the actual expiratory tidal volume (VTe) of the ventilator inflations and the target tidal volume (VTset) was 0.29 mL/kg (IQR: 0.11–0.79 mL/kg). Overall, VTe was within 1 mL/kg of VTset in 80% of inflations. VTe decreased progressively below the target when the endotracheal tube leak exceeded 50%. When leak was below 50%, VTe was below VTset by >1 mL/kg in less than 12% of inflations even in babies weighing less than 1000 g. Both VTe (r=–0.34, p=0.0022) and minute volume (r=–0.22, p=0.0567) showed a weak inverse correlation with capillary partial pressure of carbon dioxide (Pco_2) values. Only 50% of normocapnic blood gases were associated with tidal volumes between 4 and 6 mL/kg.

Conclusions The Fabian ventilator delivers volume-targeted ventilation with high accuracy if endotracheal tube leakage is not excessive and the maximum allowed inflating pressure does not limit inflations. There is only weak inverse correlation between tidal or minute volumes and Pco_2.

What is already known on this topic?

- Volume-targeted ventilation improves several long-term neonatal outcomes.
- Different ventilators use different algorithms for tidal volume targeting and leak compensation.

What this study adds?

- The Fabian +NCPAP evolution ventilator delivers tidal volumes during volume guarantee with accuracy comparable with other neonatal ventilators.
- When endotracheal tube leak exceeds 50%, tidal volume delivery is progressively impaired.
- Expiratory tidal volumes show weak but significant inverse correlation with partial pressure of carbon dioxide.

INTRODUCTION

Volume-targeted ventilation (VTV) is a ventilation mode where a clinician sets a target tidal volume (VTset) and the ventilator measures each expiratory tidal volume (VTe) and adjusts the next peak inflating pressure (PIP) to try to achieve an expiratory[1] or leak-compensated expiratory[2] tidal volume as close to the target as possible. In a Cochrane review, VTV compared with time-cycled, pressure-limited ventilation improved several short-term and long-term neonatal outcomes, including pneumothoraces, hypocapnia, days of ventilation, neonatal mortality, bronchopulmonary dysplasia and periventricular leucomalacia.[3]

VTV for neonates became available first on the Dräger Babylog 8000 ventilator as 'volume guarantee' (VG)[4] and is now available on many neonatal ventilators,[5] although different ventilator manufacturers probably use different algorithms to control the tidal volume. The question on how accurately the VTset is delivered has been extensively tested in bench models.[5–9] However, clinical data are only available for a few ventilators. Most clinical studies used the Dräger Babylog 8000 ventilator[10–13] and its successor the Babylog VN500.[2 14] Clinical data are also available for the SLE5000 ventilator.[15 16] Many studies have been difficult to interpret because they used low sampling rates, obtaining one data point per minute or less, and had only a few hundred or thousand data points.[10 13 15] More recently, clinical analyses based on millions of data points obtained with high sampling rate have been reported for the Dräger Babylog VN500[2 14] and SLE5000[16] ventilators.

The Fabian series of ventilators (Acutronic, Hirzel, Switzerland) have only been tested in a bench model.[5] In this study we collected >190 000 data points from infants ventilated using a 'Fabian +NCPAP evolution' neonatal ventilator during interhospital transfer and analysed how accurately the ventilator delivers the targeted tidal volume in VG ventilator modes and in babies of different weights and clinical characteristics.

METHODS

Patients and respiratory management

The Neonatal Emergency and Transport Services of the Peter Cerny Foundation (Budapest, Hungary)

Table 1 Summary of clinical details, ventilator settings and parameters

Number of cases	83	
	Median	**Range**
Recording duration (min)	74	20–237
Clinical details	**Median**	**Range**
Gestational age (weeks)	35	23–41
Postnatal age (hours)	5.22	1.32–3179
Corrected gestational age (weeks)	36	23–48.9
Birth weight (g)	2400	450–4650
Weight at transfer (g)	2400	560–4700
Primary reason for referral	**Cases (n)**	
Prematurity/respiratory distress syndrome	28	
Respiratory failure in term infants	11	
Patent ductus arteriosus	3	
Congenital heart disease	10	
Surgical	8	
Hypoxic-ischaemic encephalopathy	16	
Neurosurgical	6	
Retinopathy of prematurity	1	
Ventilator modes	**Recordings***	**Data points (n)**
SIMV-VG	56	121 566
SIMV-VG-PS	4	8193
SIPPV-VG	32	64 268
Ventilator settings†	**Median**	**IQR**
Fio_2 (%)	30	21–40
VTset (mL/kg)	4.8	4.3–5.4
PEEPset (cmH_2O)	6	5–6
Pmax (cmH_2O)	22	20–25
RRset (1/min)‡	38	30–43
Ti (s)	0.36	0.35–0.38
Te (s)	1.22	1.02–1.62
Circuit flow, inspiratory (L/s)	8	7.5–10
Circuit flow, expiratory (L/s)	4	4–4
Trigger sensitivity (1–10)§	1	1–1
Ventilator parameters†	**Median**	**IQR**
PIP (cmH_2O)	16.1	10.3–20.0
PEEP (cmH_2O)	5.9	5.0–6.1
MAP (cmH_2O)	7.9	6.3–9.4
VTi (mL/kg)¶	5.1	4.4–6.3
VTe (mL/kg)¶	4.5	3.8–5.6
Endotracheal tube leak (%)	0	0–0
MV (L/min/kg)**	0.27	0.22–0.33
VTdiff (mL/kg)	−0.06	−0.30 to 0.27
Absolute value of VTdiff (mL/kg)††	0.29	0.11–0.79
Pdiff (cmH_2O)	6.9	2.7–11.7

*Nine patients received more than one ventilation mode during the transport.
†Statistics were performed on all the ~194 000 data points combined. Statistics of the individual recordings are shown in the online supplementary tables.
‡The downloading software did not record the actual number of ventilator inflations only backup rates.
§Volume triggering was used in all cases. Trigger sensitivity is expressed in arbitrary units between 1 and 10, with 1 corresponding to 10% and 10 corresponding to 25% of the previous exhaled tidal volume, respectively.
¶VTi and VTe refer to the tidal volumes of ventilator inflations only, excluding spontaneous breaths.
**MV includes both ventilator inflations and spontaneous breaths.
††Absolute value of a number is its distance from zero, that is, its value without a sign.
Fio_2, fractional inspired oxygen; MAP, mean airway pressure; MV, minute volume; Pdiff, difference between the maximum allowed inflating pressure and actual peak inflating pressure of ventilator inflations (Pmax−PIP); PEEP, actual positive end-expiratory pressure; PEEPset, set positive end-expiratory pressure; PIP, actual peak inflating pressure; Pmax, the maximum allowed pressure during volume guarantee ventilation; RRset, set respiratory (backup) rate; SIMV-VG, synchronised intermittent mandatory ventilation with VG; SIMV-VG-PS, SIMV-VG with pressure support of spontaneous breaths; SIPPV-VG, synchronised intermittent positive pressure ventilation with VG; Te, set expiratory time; Ti, set inflation time; VG, volume guarantee; VTdiff, difference between the actual expiratory tidal volume and the target tidal volume of the ventilator inflations (VTe−VTset); VTe, expiratory tidal volume of ventilator inflations; VTi, inspiratory tidal volume of ventilator inflations; VTset, target expiratory tidal volume.

covers a geographical area in central Hungary with a population of ~5 million. The transport team comprises a fully trained neonatologist with experience in neonatal transport and an experienced neonatal transport nurse practitioner. Ventilator management, including the choice of ventilator mode and settings, is at the discretion of the transport team. The transport service started to use a Fabian +NCPAP evolution neonatal ventilator software (V.4.0.1) in 2015. VG ventilation was introduced in 2016 after formal staff training sessions but without an explicit guideline.

Clinical and ventilator data were collected from all 300 infants transferred over a 17-month period (between 20 March 2017 and 20 August 2018) who received invasive or non-invasive respiratory support during interhospital transport using a Fabian ventilator. This represented 29% of all transfers requiring any form of respiratory support in the period (n=1018). Of the 300 infants, 145 required mechanical ventilation via an endotracheal tube; of them 83 received VG ventilation for >15 min during transport and were included in this study and their data analysed.

Infants were intubated with uncuffed, non-shouldered endotracheal tubes, which were shortened to reduce dead space. Out of the 83 infants, 26 received sedation (morphine, fentanyl or midazolam infusion) during transport; in addition, some of the other infants received sedative medication prior to transfer as premedication for intubation. Muscle relaxation was used only in two cases. Three VG ventilation modes were used: synchronised intermittent positive pressure ventilation with VG (SIPPV-VG), synchronised intermittent mandatory ventilation with VG (SIMV-VG) and SIMV-VG with pressure support of spontaneous breath (SIMV-VG-PS). Information about the algorithm of the VG mode was obtained from the ventilator manufacturer. During VG ventilation with the Fabian ventilator, the PIP is changed at each inflation according to the percentage the VTe deviates from the target. The maximum pressure increment limit per inflation is 3 cmH_2O in order to prevent overcorrection. The ventilator's computer uses a different algorithm to calculate the PIP of triggered inflations (lower PIP) and untriggered backup inflations (higher PIP).

Data retrieval and analysis

A data logger developed by Acutronic for research purposes was used to download ventilator data. The software downloads ventilator parameters, settings and alarms with a 0.5 Hz (1 data point every 2 s) sampling rate. Data were retrieved with milisecond time stamps and exported as text files. The ventilator parameters correspond to the last inflation that occurred before the time stamp. For each data point we calculated the difference between actual and targeted expiratory tidal volumes (VTdiff) and the absolute value of VTdiff, that is, its deviation from zero (its value without a sign). We also calculated the difference between the maximum allowed inflating pressure (Pmax) and the actual inflating pressure. Minute volume (MV) is reported by the ventilator as a rolling mean over 30 s, and it includes both ventilator inflations and spontaneous breaths if available. Clinical data were collected from electronic healthcare records. Blood gases were performed by capillary sampling using heel-pricks in all cases except one, as babies did not have arterial catheters.

Data were analysed using Python (V.3.7.1; https://www.python.org) and its add-on packages. Anaconda (Continuum Analytics; http://docs.continuum.io/anaconda/pkg-docs) was installed on a MacBook Pro V.2014, with 2.6 GHz i5 processor and 8 Gb RAM memory. Programming was done using Jupyter

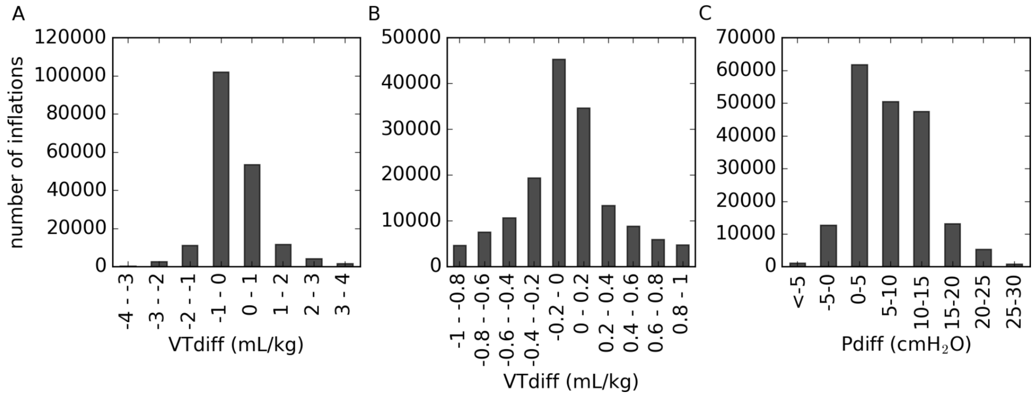

Figure 1 Histograms showing the distribution of the VTdiff and Pdiff in infants ventilated with volume guarantee ventilation. VTdiff is the difference between the target and actual expiratory tidal volume of ventilator inflations (VTe−VTset). Pdiff is the difference between the highest allowed inflating pressure and the actual inflating pressure (Pmax−PIP). (A–B) The actual tidal volume was within 1 mL/kg of the target in 80% of the inflations and very close to it (within 0.2 mL/kg) in 40% of them. (C) PIP was on average 7 cmH_2O below the Pmax but with significant variability.

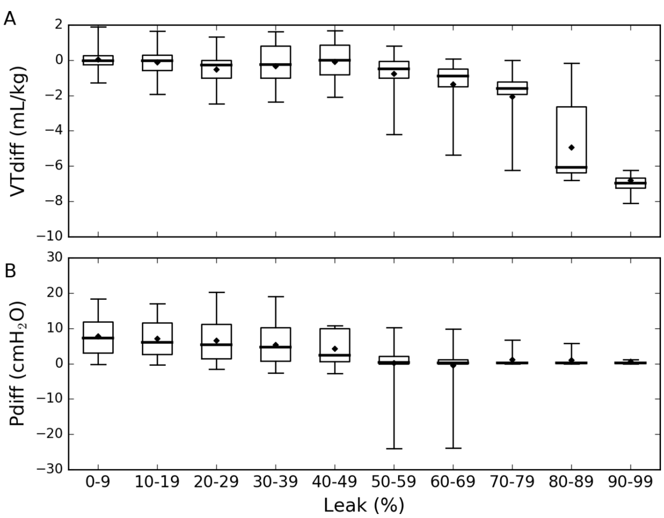

Figure 2 Boxplots showing the distributions of VTdiff (A) and Pdiff (B) for different levels of endotracheal tube leak. Medians (bold lines), means (diamonds), IQRs (boxes) and 5th–95th centiles (error bars) are shown. (A) The actual expiratory tidal volume shows significant variability at each level of leak, but on average it is maintained close to the target when leak is <50%. With >50% leak the expiratory tidal volume progressively falls below the target (VTdiff becomes negative). (B) With progressively increasing leak, the PIP gets closer to Pmax and reaches it more frequently (Pdiff becomes zero). Pdiff, difference between the highest allowed inflating pressure and the actual inflating pressure (Pmax−PIP); VTdiff, difference between the target and actual expiratory tidal volume of ventilator inflations (VTe−VTset).

Notebook (V.7.2.0; http://ipython.org/notebook.html). Data were represented, manipulated and analysed using NumPy (V.1.15.4; http://www.numpy.org) and pandas (V.0.23.4; http://pandas.pydata.org). Statistical analysis was performed using SciPy (V.1.1.0; www.scipy.org). We calculated and presented medians and interquartile ranges (IQRs) since ventilator parameters were not normally distributed due to outliers and, in case of some parameters, skewed distribution. $P<0.05$ was considered statistically significant. Visualisation was done using Matplotlib (V.3.0.2; http://matplotlib.org). All software are open-source and freely available. The Jupyter Notebook containing and explaining all steps of data processing and statistical analysis can be viewed on GitHub code repository at https://github.com/belteki/Fabian_VG.

RESULTS

We analysed ∼107 hours of ventilator data from 83 infants. As ventilator data were recorded once every 2 s, our analysis is based on ∼194 000 data points. Details on gestation, weight, duration of recordings and primary reason for transfer are shown in table 1. Cumulative statistics and distributions of ventilator settings and measurements are also shown in table 1 and in online supplementary figure 1, respectively. Statistics of ventilator settings and measurements in the individual recordings are shown in online supplementary tables 1–3.

Tidal volumes

Overall, VTdiff, the difference between the actual VTe of the ventilator inflations and the target value (VTset), was close to zero; its mean was −0.04 mL/kg (median: −0.06 mL/kg, IQR: −0.30 to 0.27 mL/kg). The absolute value of VTdiff (its deviation from zero to either direction) was also low; its mean was 0.72 mL/kg (median: 0.29 mL/kg, IQR: 0.11–0.79 mL/kg). Of the inflations 80% were within 1 mL/kg of the target and 40% were within 0.2 mL/kg (figure 1A,B).

Endotracheal tube leaks affected VTe delivery significantly; when the leak was ≥50%, the VTe decreased progressively below the target and PIP increased to the set maximum allowed inflation pressure (Pmax; figure 2).

In babies weighing <1000 g, the delivered VTe was well below the target in a considerable proportion of inflations due to endotracheal tube leak and/or PIP reaching Pmax (figure 3A,B). However, when inflations with ≥50% leak or when the Pmax was reached were excluded, VTe was below target by >1 mL/kg in less than 12% of inflations in each weight category (figure 3C,D). Importantly, VTe sometimes exceeded the target by more than 2 mL/kg due to the baby's large inspirations during ventilator inflations. There was no difference in VTdiff among the three modes used (SIPPV-VG, SIMV-VG and SIMV-VG-PS; online supplementary figure 2).

Inflating pressures

The median difference between Pmax and the actual inflating pressure (PIP) was 7.1 cmH_2O (IQR: 2.7–11.7 cmH_2O; figure 1C). PIP reached Pmax in only 7.2% of inflations despite

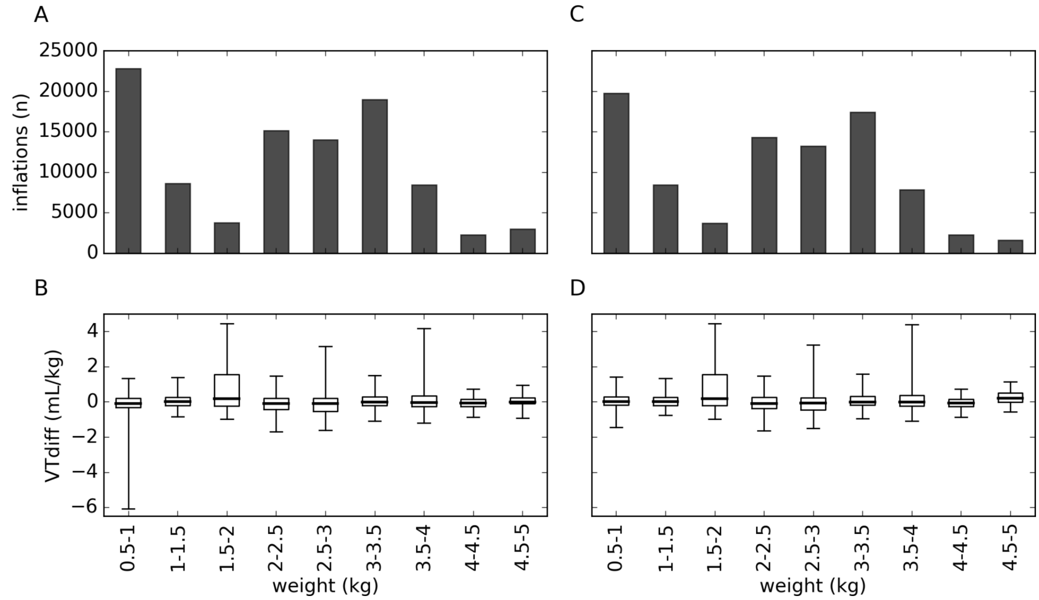

Figure 3 Tidal volume delivery in babies of different weights. (A–B) All ventilator inflations are included. (A) Bar plots showing the number of inflations analysed for the various weight categories. (B) In babies weighing less than 1000 g, the expiratory tidal volume frequently fell considerably below target. (C–D) Only ventilator inflations when leak was <50% and Pmax was not reached are included. (C) Bar plots showing the number of inflations analysed for the various weight categories. (D) The delivered tidal volume is close to the target in each weight category (VTdiff is close to 0). The boxplots show medians (bold lines), IQRs (boxes) and 5th–95th centiles (error bars). Pmax, maximum allowed inflating pressure; VTdiff, difference between the target and actual expiratory tidal volume of ventilator inflations (VTe–VTset).

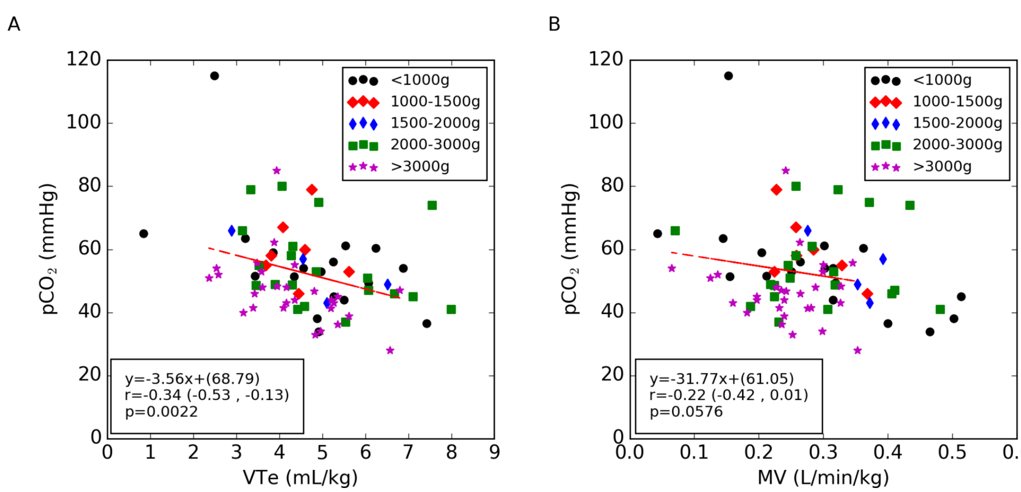

Figure 4 Correlation between expiratory tidal volume (A) or minute volume (B) before blood gases and Pco_2. The inverse correlation is poor in both cases although statistically significant in case of VTe. Weight-corrected tidal and minute volumes fall in the same range for all weight categories. MV, minute volume; Pco_2, partial pressure of carbon dioxide; VTe, expiratory tidal volume.

Pmax being set relatively low in most cases (the mean Pmax of the cases ranged between 14.5 and 46 cmH_2O, group median: 22 cmH_2O; online supplementary table 1).

Ventilation volumes and capillary CO_2

We analysed the relationship between capillary partial pressure of carbon dioxide (Pco_2) levels and the tidal and minute volumes averaged over a 10 min period before the blood gas as previously described.[17] VTe showed a weak inverse correlation with Pco_2 levels ($r=-0.34$, $p=0.0022$; figure 4A, online supplementary figure 3A). The correlation between MV and Pco_2 was also weak ($r=-0.22$, $p=0.0567$; figure 4B, online supplementary figure 3B). Interestingly, only 52% (28/54) of the normocapnic blood gases with Pco_2 between 5 and 8 kPa (37.5–60 mm Hg) were associated with VTe in the range of 4–6 mL/kg; 31% (17/54) had a VTe <4 mL/kg and 17% (9/54) >6 mL/kg. The VTset did not correlate with Pco_2 (online supplementary figure 4).

DISCUSSION

This is the first study analysing the performance of Fabian ventilators in infants. We found that overall the VTe was very close to the VTset during VG ventilation, irrespective of the weight of the infant or whether the ventilator mode was SIPPV or SIMV. However, VTe showed considerable short-term variability, and in some cases even the average value was well below or above the targeted volume.

The failure of VTe to reach the VTset may have been due to inappropriate ventilator settings or excessive leak around the endotracheal tube. If Pmax is set too low, the PIP cannot increase enough to deliver the VTset. This can occur even when the average Pmax is above the required 'working PIP', due to the short-term variability of PIP during VG ventilation.[14] The VTe will also be below the target if there is an excessive leak around the tube or there is a change in the clinical condition of the infant, such as splinting against the ventilator inflations. In this case the VG algorithm will increase the PIP to try and deliver the target VTe and so the PIP will quickly reach Pmax; if this is not able to compensate for the large leak, a low tidal volume alarm will be triggered. We found that in the case of the Fabian ventilator, this happened progressively above 50% leak (figure 2). Of note, with excessive leak, the actual VTe is somewhat larger than the VTe reported by the ventilator due tothe expiratory component of the leak.[2] Finally, the target VT may not be delivered if the inflation time is too short for the required PIP to build up in the lungs. This was unlikely in this study as the pressure rise time was significantly shorter than the set inflation time (Ti). When PIP is reached in the ventilator circuit, the inspiratory flow drops to zero quickly unless there is very high airway resistance. In any case, if the tidal volume was not delivered due to a short Ti, the VG algorithm would increase PIP to Pmax level within a couple of inflations. Therefore, excluding inflations with >50% leak or when PIP reached Pmax provides a more unbiased view about how closely the ventilator can maintain the VTe to its target.

Irrespective of the set parameters, the VTe can exceed the target value significantly if the baby takes large breaths from the ventilator circuit during synchronised inflations. During VG, the PIP is frequently low in these babies, sometimes close to the positive end-expiratory pressure level[10 14] because the VG algorithm determines that very little PIP is required to deliver the set VTe. The clinical significance of the large tidal volumes seen in actively breathing ventilated babies is uncertain.

Different ventilators use different algorithms for VG and leak compensation; therefore, how well they maintain the tidal volume may be different. In a study using SLE5000 ventilators with two different algorithms and combining SIMV and SIPPV inflations, the mean absolute value of VTdiff for the V4 algorithm was 0.4 mL/kg and for the V5 algorithm was 0.3 mL/kg, somewhat lower than in our study (0.72 mL/kg).[16] They did not report their Pmax settings or the effect of endotracheal tube leak. In a study with the Dräger VN500 ventilator, we found the mean VTdiff values comparable with this paper (0.6–0.7 mL/kg).[2] However, different levels of leak in the study populations and different Pmax policies on different units make the comparison of ventilator performance in patients difficult.

In five SIMV cases the VTset was set at <3.5 mL/kg, sometimes as low as 2.1 mL/kg. During discussion with the clinical team, it emerged that their intention was to limit the ventilator contribution in babies with large spontaneous breathing effort to avoid hypocapnia. VG ventilation had been introduced during clinical care <1 year before this study and there was no explicit local guideline. These inappropriate settings highlight the importance of training and explicit clinical guidelines when a new ventilation mode is adopted.

There was weak correlation between VTe and capillary Pco_2 values. This is partially explained by the different ventilator rates at the time of different blood gases. However, the correlation between minute ventilation (that included both ventilator and spontaneous breaths) and Pco_2 was also weak and statistically not significant. One factor affecting the correlation between ventilator parameters and blood gases is that we used capillary blood gases, and capillary CO_2 levels may not accurately reflect the arterial partial pressure of CO_2 o_2 in all cases. However, several papers have reported no correlation or only poor inverse correlation of tidal volume or MV with Pco_2 values in ventilated infants even when only arterial blood gases were used.[16 18–20] This is not surprising, as alveolar ventilation is affected by anatomical and functional dead space and uneven lung perfusion. Finally, there is evidence that the current simple physical model of bulk gas flow during mechanical ventilation may not fully explain CO_2 elimination as very small infants can be ventilated using tidal volumes less than the dead space even during conventional ventilation and still have normal Pco_2.[18 21] Interestingly, only in half of the cases were the VTe within the generally accepted 4–6 mL/kg range even when Pco_2 was normal.

A strength of our study is that we used 0.5 Hz data sampling that captures most of the short-term variability of ventilator parameters due to patient–ventilator interactions. The use of Python computer language helped with the analysis of the obtained large data set and ensures reproducibility.

A limitation of our study is that almost all blood gases were capillary gases as most transferred infants did not have arterial lines in place. Another limitation is that we report the tidal volumes measured by the ventilator rather than by an independent method; however, these are the tidal volumes routinely available to clinicians.

In summary, the Fabian +NCPAP evolution ventilator delivers reasonably accurate and reliable tidal volumes during neonatal transport and ensures CO_2 elimination with similar tidal volumes as other ventilators, taking account of variation from babies' breathing and endotracheal tube leaks.

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Contributors GB designed the study, wrote the computer programs to analyse ventilator data, performed the data analysis and drafted the manuscript. AS, LL, GK, AB, MS, GL, FK and ZS performed the neonatal transfers and collected the clinical data. GS integrated the data downloading software and computer in the transport equipment. CJM helped with the interpretation of findings. All authors revised and approved the final manuscript.

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Competing interests CJM was a consultant to Acutronic Medical but not for Fabian ventilators.

Patient consent for publication Not required.

Ethics approval The study was approved by the Scientific and Medical Research Council Ethics Committee of Hungary (reference: 40158-2/2018/EKU).

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement Upon acceptance of the paper we will upload the Python code of the data analysis workflow to the GitHub code repository.

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