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Volume-Targeted Ventilation and Arterial Carbon Dioxide in Neonates

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Abstract

Objectives: To review the arterial carbon dioxide tensions ($PaCO_2$) in newborn infants ventilated using synchronized intermittent mandatory ventilation (SIMV) in *volume guarantee* mode (using the Dräger Babylog 8000+) with a unit policy targeting tidal volumes of approximately 4 mL/kg.

Methods: Data on ventilator settings and arterial ($PaCO_2$ levels were collected on all arterial blood gases (ABG; *n* = 288) from 50 neonates (<33 weeks gestational age) ventilated using the Dräger Babylog 8000+ ventilator (Dräger Medizintechnik GmbH, Lübeck, Germany) in SIMV plus *volume guarantee* mode. Data were analysed for all blood gases done on the entire cohort in the first 48 h of life and a subanalysis was done on the first gas for each infant *(n* = 38) ventilated using *volume guarantee* from admission to the nursery. The number of ABG showing severe hypocapnoea (($PaCO_2$ < 25 mmHg) and/or severe hypercapnoea (($PaCO_2$ > 65 mmHg) were determined.

Results: The mean (SD) ($PaCO_2$ during the first 48 h was 46.6 (9.0) mmHg. The mean (SD) ($PaCO_2$ on the first blood gas of those infants commenced on *volume guarantee* from admission was 45.1 (12.5) mmHg. Severe hypo- or hypercapnoea occurred in 8% of infants at the time of their first blood gas measurement, and in <4% of blood gas measurements in the first 48 h.

Conclusions: Infants ventilated with *volume guarantee* ventilation targeting approximately 4 mL/kg (range: 2.9–5.1) have acceptable $PaCO_2$ levels at the first blood gas measurement and during the first 48 h of life; and avoid severe hypo- or hypercapnoea over 90% of the time.

Key words: artificial respiration; blood gas analysis; infant, newborn.

Volume-targeted ventilation strategies are increasingly used in the care of neonates.[1] *Volume guarantee* ventilation using the Dräger Babylog 8000+ ventilator (Dräger Medizintechnik GmbH, Lübeck, Germany) is a time-cycled, pressure-limited ventilation mode which targets a set expiratory volume of gas to be delivered to the patient with each inflation: peak inspiratory pressure (PIP) is altered by the ventilator to achieve the set tidal volume. Control of tidal volume and minute volume may help avoid hyper- and hypocapnoea,[2] and their consequences, such as volutrauma and lung injury[3–5] and alterations in cerebral blood flow.[6–10]

There are few studies on the correct tidal volume to target in neonates. A limited study by Davies *et al.*[11] showed that a tidal volume of 3.3 mL/kg (with a ventilator inflation rate of 60) leads to arterial carbon dioxide tensions ($PaCO_2$) of between 29 and 58 mmHg 95% of the time. The unit policy for very low-birthweight infants ventilated in the nursery at the Royal Women's Hospital, Brisbane, is to use the *volume guarantee* ventilation mode with the tidal volume set at 4 mL/kg: a compromise between the findings of Davies *et al.*[11] and tidal volumes of approximately 5-8 mL/kg. Tidal volumes from 5 to 8 mL/kg are those reported in the literature for ventilating preterm infants with hyaline membrane disease.[12–19] Despite the fact that volume-targeted ventilation is increasingly used both clinically and in randomized controlled trials, there exists no generally accepted tidal volume to target. There are also scant data on the $PaCO_2$ levels that result from such tidal volumes.

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The aim of this study was to quantify $PaCO_2$ levels achieved by ventilating neonates using the Dräger Babylog 8000+ ventilator in *volume guarantee* mode in the setting of a unit policy targeting tidal volumes of approximately 4 mL/kg. Specifically, we aimed to: determine the average first $PaCO_2$ in neonates, ventilated in *volume guarantee* mode from admission to the neonatal intensive care and the number of these infants with an unacceptable first $PaCO_2$; and the average $PaCO_2$ in neonates ventilated in *volume guarantee* mode during the first 48 h of life and the number of blood gas measurements in these infants with an unacceptable $PaCO_2$.

PATIENTS AND METHODS

This study was undertaken at the Royal Women's Hospital, Brisbane, Australia – a regional perinatal centre with level 3 neonatal intensive care. Patients were identified from the prospectively maintained database (NeoData) of all admissions to the nursery. A cohort of all babies that were managed with *volume guarantee* ventilation during the calendar year of 2002 was identified. Infants were included if they were ventilated using *volume guarantee* ventilation, with the Dräger Babylog 8000+ neonatal ventilator, at any time during the first 48 h of life and had at least one arterial blood gas sample taken. All infants were ventilated with synchronized intermittent mandatory ventilation (SIMV) mode while on *volume guarantee* ventilation. All blood gases were taken from indwelling arterial lines. Infants were excluded if they were only ever ventilated at a rate of <40 breaths/min during the study period: an attempt to minimize the influence of babies with significant spontaneous respirations.

Data from the infant's clinical records were recorded on arterial blood gases taken in the first 48 h of life on all the infants during the time they were ventilated with *volume guarantee* at a rate of >40 breaths/min (including $PaCO_2$ and pH). Data from the infant's clinical records were also recorded on the ventilator settings at the time the blood gas was done (including set tidal volume, ventilator rate, positive end expiratory pressure (PEEP), PIP, mean airway pressure (MAP) and fraction of inspired oxygen (FiO_2)). The mechanical minute volume was calculated by multiplying the set tidal volume with the set SIMV rate. A separate analysis was undertaken on the first arterial blood gas and ventilator settings of the subset of neonates who were commenced on *volume guarantee* ventilation from birth.

Neonatal units vary in what they consider an acceptable $PaCO_2$ for ventilated infants. There is good evidence that hypocapnoea is associated with poor outcomes and various cut-off values, for $PaCO_2$ have been used: <40 mmHg,[3] <29 mmHg,[4] <20 mmHg,[9] <17 mmHg.[7] Similarly, unacceptably high $PaCO_2$ levels are also variously defined. We determined the number of $PaCO_2$ measurements, in both the study groups mentioned above, for various $PaCO_2$ strata. Because of this wide disparity in defining limits for severe hypo- or hypercapnoea, we have arbitrarily defined severe hypocapnoea as <25 mmHg and severe hypercapnoea as >65 mmHg – using data from various studies and reviews.[2,20,21]

RESULTS

Fifty-five patients were identified from the database as having *volume guarantee* ventilation in the first 48 h. Three were excluded as they did not have an arterial blood gas while on *volume guarantee,* one because the ventilator rate was persistently <40 and one had no *volume guarantee* ventilation documented on subsequent chart review. Fifty patients were therefore included in the analysis, from whom 288 arterial blood gases were taken up to 48 h of life. The mean (SD) weight of the babies was 948 (301) g and mean (SD) gestation was 26.9 (2.1) weeks. All had a gestational age of <33 completed weeks. Reasons for ventilation were: 80% (40/50) hyaline membrane disease (all given at least one dose of surfactant), 16% (8/50) prematurity without lung disease, 2% (1/50) pulmonary hypoplasia and 2% (1/50) apnoea. The $PaCO_2$, pH levels and ventilatory settings for all blood gases in the first 48 h are shown in Table 1.

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Table 1. Summary of ventilation parameters and $PaCO_2$ levels for all infants up to 48 h old for 288 arterial blood gas measurements

	Mean	SD	Range
Ventilation parameter			
Set tidal volume (mL/kg)	3.93	0.35	2.9-5.1
MAP (cmH_2O)	10.2	2.1	5.4-22.0
PEEP (cmH_2O)	5.9	0.7	5.0-9.0
PIP (cmH_2O)	16.1	4.4	8.0-48.0
SIMV rate (breaths/min)	57.3	9.8	40.0-90.0
FiO_2	0.27	0.12	0.21-1.0
Measurements (*n* = 288)			
$PaCO_2$ (mmHg)	46.6	8.96	23.0-89.0
pH	7.29	0.07	7.05-7.54

FiO_2, fraction of inspired oxygen; MAP, mean airway pressure; $PaCO_2$, arterial carbon dioxide tension; PEEP, positive end expiratory pressure; PIP, peak inspiratory pressure; SIMV, synchronized intermittent mandatory ventilation.

Thirty-eight out of 50 infants were ventilated with *volume guarantee* from admission to the nursery. These infants had a mean (SD) weight of 955 (306) g and a mean (SD) gestation of 26.9 (2.1) weeks. The analysis of first arterial blood gas and corresponding ventilator settings on this subgroup of neonates are shown in Table 2.

Table 2. Summary of ventilation parameters and first $PaCO_2$ levels for all infants ventilated in *volume guarantee* mode from admission at the time of their first arterial blood gas (*n* = 38)

	Mean	SD	Range
Ventilation parameter			
Set tidal volume (mL/kg)	3.98	0.30	3.5-5.1
MAP (cmH_2O)	11.2	2.8	7.0-22.0
PEEP (cmH_2O)	5.9	0.9	5.0-8.0
PIP (cmH_2O)	18.8	6.2	10.0-48.0
SIMV rate (breaths/min)	62.0	8.2	40.0-83.0
FiO_2	0.31	0.13	0.21-0.75
Measurements (*n* = 38)			
$PaCO_2$ (mmHg)	45.1	12.45	23.0-89.0
pH	7.30	0.08	7.11-7.50

FiO_2, fraction of inspired oxygen; MAP, mean airway pressure; $PaCO_2$, arterial carbon dioxide tension; PEEP, positive end expiratory pressure; PIP, peak inspiratory pressure; SIMV, synchronized intermittent mandatory ventilation.

Scatter plots and linear trendlines (with regression equations) for $PaCO_2$ versus set tidal volume and $PaCO_2$ versus mechanical minute volume are shown in Figures 1 and 2. The scatter plots show that there is no apparent linear relationship between either the set tidal volume (range from 2.9 to 5.1 mL/kg) or mechanical minute ventilation and the observed $PaCO_2$ levels (Figs. 1 and 2).

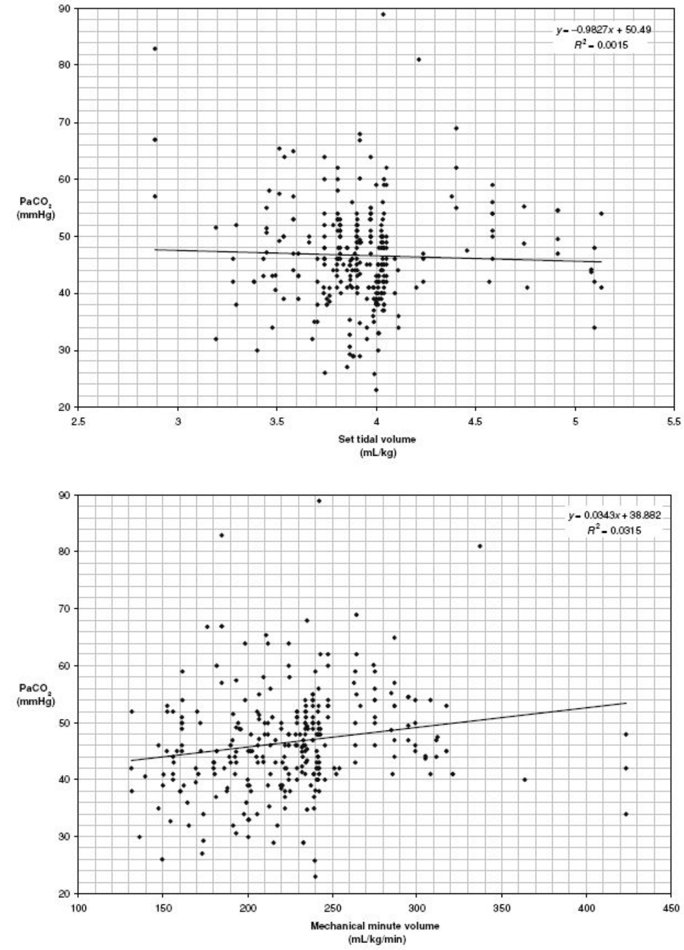

Fig. 1. Scatter plots and linear trendlines (with regression equations) for all infants blood gases up to 48 h old – $PaCO_2$ versus set tidal volume (top) and $PaCO_2$ versus mechanical minute volume (bottom).

The number of $PaCO_2$ values at various cut-off levels of hypo- and hypercapnoea are shown in Table 3 for both analysis groups.

DISCUSSION

In this study we show that if neonates are ventilated using the Dräger Babylog 8000+ ventilator in *volume guarantee* mode at a tidal volume setting of about 4 mL/kg (ranging from 2.9 to 5.1 mL/kg), the mean (SD) $PaCO_2$ in the first 48 h is 46.6 (9.0) mmHg. The mean (SD) $PaCO_2$ on the first arterial blood gas for infants ventilated in *volume guarantee* mode from admission to the nursery is 45.1 (12.5) mmHg. Severe hypo- or hypercapnoea is avoided in 92% of infants at the time of their first blood gas measurement when ventilated in *volume guarantee* mode from admission to the intensive care nursery.

Time-cycled, pressure-regulated modes have traditionally been used to ventilate neonates. In the last few years, volume-controlled and volume-targeted techniques have increasingly been used, although there are little clinical data to suggest the correct tidal volume setting. There have been four randomized controlled trials investigating the feasibility of volume-targeted or volume-controlled ventilation in newborns.[22–25] A randomized crossover trial by Cheema and Ahluwalia[22] studied 40 neonates ventilated in *volume guarantee* mode with *assist control* ventilation on the Dräger Babylog 8000+ ventilator. A mean tidal volume of 5 mL/kg was used and there was a significant reduction in PIP and MAP using *volume guarantee* ventilation when compared with pressure-controlled ventilation. Only transcutaneous $PaCO_2$ was measured with mean values from 45 to 48 mmHg, and ventilator rates were not reported. A small randomized crossover trial by Herrera *et al.*[23] studied 17 infants using *volume guarantee* with SIMV. Two tidal volume settings were used (3 and 4.5 mL/kg) and resulting mean $PaCO_2$ values varied from 48 to 52 mmHg. Again, only transcutaneous $PaCO_2$ monitoring was done. Neither study showed a significant difference in $PaCO_2$ levels between pressure-controlled and volume-targeted modes. Two earlier studies examining volume-controlled ventilation in neonates showed a significant reduction in the incidence of intraventricular haemorrhage when compared with pressure-regulated ventilation.[24,25] Tidal volume settings varied from 5 to 8 mL/kg, and $PaCO_2$ values were not reported. None of these four studies assessed arterial carbon dioxide levels.

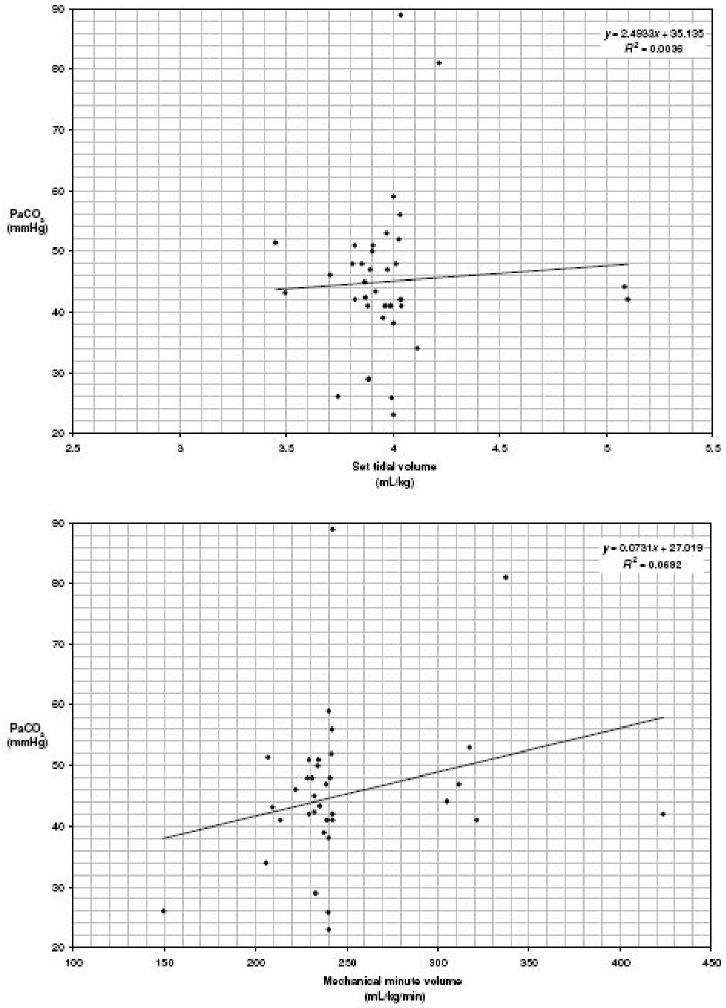

Fig. 2. Scatter plots and linear trendlines (with regression equations) for all infants ventilated in *volume guarantee* mode from admission at the time of their first arterial blood gas *(n* = 38) – $PaCO_2$ versus set tidal volume (top) and $PaCO_2$ versus mechanical minute volume (bottom).

Many studies have investigated the link between early carbon dioxide levels and neurodevelopmental and respiratory outcomes of premature infants. Hypocapnoea, particularly at $PaCO_2$ levels <25–30 mmHg, has been shown to be associated with periventricular echodensities,[7] periventricular leucomalacia,[8,9] cerebral palsy,[7] neurodevelopmental deficits[10] and bronchopulmonary dysplasia.[3,4] For this reason, many centres have moved towards allowing higher $PaCO_2$ levels in neonates: a practice known as permissive hypercapnoea. Permissive hypercapnoea may decrease the incidence of lung injury, particularly in the most vulnerable extremely lowbirthweight infants but the long-term neurodevelopmental effects are unknown.[26] Severe hypercapnoea will increase cerebral blood flow, which is associated with increased incidence of intraventricular haemorrhage.[6] The definition of an ideal range for $PaCO_2$ is still unknown, but it would seem prudent to avoid $PaCO_2$ levels <25 mmHg and

>65 mmHg. In our study, 96.5% of all $PaCO_2$ values in the first 48 h were between 25 and 65 mmHg, with only 0.3% of values <25 mmHg. This would indicate that planning to use a set tidal volume of approximately 4 mL/kg is useful in avoiding an undesirable $PaCO_2$.

Table 3. Numbers of $PaCO_2$ levels at various cut-off levels of hypo-and hypercapnoea

$PaCO_2$ cut-off (mmHg)	*n (%)*	
	All infants (*n* = 288)	VG from admission (*n* = 38)
<20	0(0)	0(0)
20–24.9	1(0.3)	1(2.6)
25–29.9	8(2.8)	5(13.1)
30–50	138(48.0)	15(39.5)
50.1–55	81(28.1)	9(23.7)
55.1–60	34(11.8)	4(10.5)
60.1–65	17(5.9)	2(5.3)
>65	9(3.1)	2(5.3)

$PaCO_2$, arterial carbon dioxide tension; VG, *volume guarantee* ventilation.

We have made no attempt in this study to compare *volume guarantee* ventilation with any other mode of ventilation: we have not included a comparison group. Also, we did not aim to determine, out of a myriad of factors, which factors had specific influence on $PaCO_2$ levels. We merely wanted to show the $PaCO_2$ levels achieved with *volume guarantee* ventilation at set tidal volumes of approximately 4 mL/kg (as was the policy in our unit at the time).

The lack of relationship between either the set tidal volume or mechanical minute ventilation and the observed $PaCO_2$ level may be related to the fact that the majority of tidal volume values are distributed approximately 4 mL/kg. It may also be because of the influence of biological variability between individuals or the influence of spontaneous respirations. We attempted to negate the influence of spontaneous respirations on $PaCO_2$ by only including infants on an SIMV rate of >40 breaths/min. Unfortunately, we did not seem to remove the influence of spontaneous respirations, and we were unable to determine their relative influence as we do not record the actual minute ventilation (spontaneous and mechanical) as part of the nursing observations. Recent data from Mishra *et al.*[27] show that ventilated low-birthweight infants do seem to vary their own respiratory rate to normalize $PaCO_2$ levels when tidal volume is lowered.

Although the general policy in our neonatal unit at the time was to set the target tidal volume at 4 mL/kg, the actual tidal volume varied between 2.9 and 5.1 mL/kg (overall mean set tidal volume was 3.93 mL/kg, SD = 0.35). Variation occurred because of the baby's weight being estimated before weighing, rounding error and clinician preference. However, almost 90% of infants were started on set tidal volumes of between 3.7 and 4.3 mL/kg on admission. It would be useful to look at a larger population of neonates with respiratory distress, with tidal volumes more strictly adherent to the setting of 4 mL/kg to ascertain whether this volume is the most appropriate for control of $PaCO_2$. Only once appropriate tidal volumes are known can we progress to making valid comparisons between *volume guarantee* ventilation and more traditional modes of ventilation with randomized controlled trials looking at long-term respiratory and neuro-developmental outcomes.

In summary, limiting tidal volume seems like a good idea to limit mechanical stretch and, therefore, limit volutrauma. Modern neonatal ventilators allow targeting of tidal volume (but not minute ventilation). The literature offers little guidance on what tidal volume to use with volume-targeted ventilation. Our unit policy is to set the target tidal volume at 4 mL/kg. As a result we achieve acceptable arterial carbon dioxide levels for the overwhelming majority of blood gas measurements.

CONCLUSIONS

Newborn infants ventilated with *volume guarantee* ventilation targeting approximately 4 mL/kg (range: 2.9–5.1) at ventilator rates >40/min, using the Dräger Babylog 8000+ ventilator, have acceptable $PaCO_2$ levels at the first blood gas measurement and during the first 48 h of life. They also avoid severe hypo- or hypercapnoea over 90% of the time.

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