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# Introduction

Reproducibility of the respiratory dead space measurements in mechanically ventilated children using the  $CO_2SMO$  monitor

Abstract Objectives: To assess the reproducibility of respiratory dead space measurements in ventilated children. Design: Prospective study. Setting: University pediatric intensive care unit. Patients: Thirty-two mechanically ventilated children (0.13-15.4 years) who were clinically stable. Methods: The single-breath CO<sub>2</sub> test (SBT-CO<sub>2</sub>) was recorded using the CO<sub>2</sub>SMO Plus from the mean of 30 ventilatory cycles during 1 h (at T0, T15, T30, T45, and T60). Airway dead space was determined automatically (Novametrix Medical Systems, USA), and manually by Bohr- Enghoff equations using data obtained by SBT-CO<sub>2</sub>. At the end of the study period, arterial blood gas was sampled in order to calculate alveolar and physiologic dead space. Intrasubject reproducibility of measurements was evaluated by the intraclass correlation coefficient. Twoway analysis of variance was used to evaluate the relationships between time and measurements. The two methods for calculating airway dead

space were compared by using twotailed Student's t-test and Bland-Altman analysis. *Results:* Airway dead space measurement had a good reproducibility during the 1-h period, whatever the method used (intraclass correlation coefficient: 0.84 to 0.87). No significant difference was observed with time. Airway dead space values from the SBT-CO<sub>2</sub> method were smaller than those from Bohr-Enghoff equations. Physiologic dead space values from the SBT-CO2 method were similar to those from Bohr-Enghoff equations. Conclusion: The measurement of airway dead space by the CO<sub>2</sub>SMO Plus was reproducible over a 1-h period in children requiring mechanical ventilation, provided ventilatory parameters were constant throughout the study. SBT-CO<sub>2</sub> analysis may provide a bedside non-invasive monitoring of volumetric capnography.

**Keywords** Dead space · Mechanical ventilation · Children

Pulmonary dead space  $(V_D)$  represents the portion of the respiratory system not involved in gas exchange and includes both alveolar dead space and airway dead space. Airway (or anatomic) dead space  $(V_{Daw})$ , equals the volume of conducting airways. Alveolar dead space  $(V_{Dalv})$  is caused by ventilated but not perfused areas. In conditions without ventilation/perfusion inequalities, there would be no  $V_{Dalv}$  [1]. Physiologic dead space ( $V_{Dphysiol}$ ) equals  $V_{Dalv}$  plus  $V_{Daw}$ , and is often expressed as a ratio to tidal volume ( $V_D/VT$ ). During the past two decades, this ratio has been used to identify survivability of infants with congenital diaphragmatic hernia [2], detect pulmonary shunts in congenital heart children [3], determine pulmonary improvements in neonates with extracorporeal membrane oxygenation [4], and predict successful extubation in infants and children [5]. Initially,  $V_D/VT$  was

measured by collecting expired gas. Recent advances in computer and capnography technology have provided a simplified and automated method for calculating  $V_D/VT$  from single-breath CO<sub>2</sub> waveforms (SBT-CO<sub>2</sub>) [6, 7, 8, 9, 10]. Besides the above-mentioned conditions in which  $V_D/VT$  has been considered as useful, there is very little information concerning the reproducibility of  $V_D$  measurements in the pediatric ICU [11].

The main objective of this study was to evaluate in ventilated children the reproducibility of  $V_D$  measurements by SBT-CO<sub>2</sub> test using the CO<sub>2</sub>SMO Plus over a 1-h period (automatic measurement by the software and manual calculation according to Bohr-Enghoff equations).

The secondary objective was to compare calculation of  $V_D$  by SBT-CO<sub>2</sub> to that obtained by Bohr-Enghoff equations, since discrepancies between the two methods were previously reported [3].

### **Patients and methods**

#### Patient population

During the study period (January 2002 to June 2002), of 105 children hospitalized in the pediatric ICU, 51 were mechanically ventilated and 32 fulfilled the protocol inclusion criteria: pressure-controlled mechanical ventilation (servo 900 or 300C ventilator, Siemens-Elema, Solna, Sweden), stable haemodynamic and respiratory conditions 1 h before and during the measurements, no suctioning and no changes in ventilator settings, sedation, and therapeutics during the study period. The local Ethics Committee approved this study.

Measurement of pulmonary dead space and respiratory mechanics

 $V_D$  and respiratory mechanics measurements were calculated from the mean of 30 ventilatory cycles, at each 15-min period, during 1 h (T0, T15, T30, T45, and T60). At the end of the study period, arterial blood gas was sampled. At each time period, haemodynamic parameters (heart rate, blood pressure, and SpO<sub>2</sub>) and ventilator settings [peak inspiratory pressure (PIP), positive end-expiratory pressure (PEEP), mean airway pressure (Paw), inspiratory time (Ti), expiratory time (Te), and inspired oxygen concentration (FiO<sub>2</sub>)] were obtained.

 $V_D$  measurements were performed using the CO<sub>2</sub>SMO Plus and its computer software. Among the different capnographs, the CO<sub>2</sub>SMO Plus (Novametrix Medical Systems, Wallingford, Conn., USA) is suitable for bedside  $V_D$  measurements in children and incorporates mainstream capnograph and gas flow monitor via a dual-purpose sensor in connection with a computer which enables automatic calculation of over 50 parameters on each breath (Analysis Plus! for Windows program, version 2.0, Novametrix Medical Systems). This device has been previously demonstrated to be accurate by Arnold et al., who measured V<sub>Daw</sub> in a lung model and quantified the bias and precision of V<sub>Dphysiol</sub> measurement in a surfactant-depleted animal model [9]. Its pediatric sensor (combined CO<sub>2</sub>/Flow sensor series 3, V<sub>D</sub> less than 4 ml) was inserted between the Y-piece and the endotracheal tube without any additional connector. Flow is measured with this device (flow range: 0.5–120 l/min, tracheal tube internal diameter: 3.5–6.0 mm, tidal volume: 30–400 ml). Airway and barometric pressure are measured with absolute pressure transducers and airway pressure is defined relative to the barometric pressure.  $CO_2$  is measured by a mainstream infrared absorption technique (response time less than 75 ms, accuracy: ±2 mmHg from 0 mmHg to 40 mmHg; 5% reading from 41 mmHg to 100 mmHg). The CO<sub>2</sub>SMO Plus provides a standard expired SBT-CO<sub>2</sub> waveform that can be divided in three phases [6]. In phase I, no  $CO_2$  is found. It corresponds to the "absolute  $V_D$ " from conducting airways. In phase II, the content of expired CO<sub>2</sub> increases because the expired gas contains mixed air from the alveoli and the airways. The third phase has a slightly increased CO<sub>2</sub> concentration which represents air from alveoli. By knowing the end-tidal (P<sub>ET</sub>CO<sub>2</sub>) and arterial (PaCO<sub>2</sub>) CO<sub>2</sub> concentrations and the expired volumes during the three phases, V<sub>Dphysiol</sub>, V<sub>Daw</sub>, and V<sub>Dalv</sub> can be calculated by using Aitken and Clarke-Kennedy's principle [6]. Briefly, the measurement offered by the software is based on an automatic recognition of the areas X, Y, Z generated by the shape of the PCO<sub>2</sub>/volume curve in phases I, II, and III. (Fig. 1):

$$\begin{split} &V_{Daw}/VT = Z/(X+Y+Z) \\ &V_{Dalv}/VT = Y/(X+Y+Z) \\ &V_{Dphysiol}/VT = (Y+Z)/(X+Y+Z) \end{split}$$

Area X is the volume of  $CO_2$  in the breath (VCO<sub>2</sub>), which allows us to calculate  $CO_2$  output (V'CO<sub>2</sub>=VCO<sub>2</sub> x respiratory rate). The slope of phase III is computed by linear regression of the points bounded by 30% to 70% of expired volume and is extrapolated to determine the end point of mixed air (phase II) and the beginning of alveolar volume exhalation (phase III). Then, a vertical line is set in the middle of phase II so that areas p and q are equal (Fig. 1).

 $V_D$  can be also manually determined by using Bohr-Enghoff equations [12, 13]:

$$\begin{split} V_{Daw} &= VT_E x((P_{ET}CO_2 - P_eCO_2)/(P_{ET}CO_2 - P_iCO_2))\\ V_{Dphysiol} &= VT_E x((P_aCO_2 - P_eCO_2)/(P_aCO_2 - P_iCO_2))\\ V_{Dalv} &= V_{Dphysiol} - V_{Daw} \end{split}$$

where  $VT_E$  represents the expired tidal volume,  $P_eCO_2$ mixed expired PCO<sub>2</sub>, and  $P_iCO_2$  mixed inspired PCO<sub>2</sub>. All these parameters, except  $P_aCO_2$ , were calculated by



**Fig. 1** Airway dead space ( $V_{Daw}$ ) as illustrated by a CO<sub>2</sub>-volume plot (SBT-CO<sub>2</sub>). Triangles p and q are of equal area. Area X is the volume of CO<sub>2</sub> in the breath (VCO<sub>2</sub>), while areas Z and Y are defects in CO<sub>2</sub> elimination which represent wasted ventilation due to  $V_{Daw}$  and alveolar dead space ( $VD_{alv}$ ) respectively. Alveolar tidal volume (VTalv) represents difference between tidal volume (VT) and airway dead space ( $V_{Daw}$ ) [8]

the  $CO_2SMO$  Plus. The apparatus  $V_D$  of the sensor was automatically subtracted from the measured  $V_D$ .  $CO_2$  sensor was systematically calibrated between each time period.

Respiratory mechanics data collection included Paw, PIP, PEEP, intrinsic positive end-expiratory pressure PEEPi, dynamic compliance of the respiratory system, inspiratory and expiratory airway resistance, and inspired tidal volume  $VT_I$  and  $VT_E$ . Airleak from around the endotracheal tube is computed as  $[(VT_E-VT_I)/VT_I]$ . VT and  $V_D$  are normalized to patient weight.

#### Statistical analysis

Statistical analysis was performed with SPSS 11.0 (SPSS, Chicago, Ill., USA). The results are expressed as mean±SD. Intrasubject reproducibility of measurements repeated over 1 h was evaluated by the intraclass correlation coefficient (ICC). Considering the ICC value, the reproducibility was qualified as excellent ( $\geq 0.81$ ), good (0.80–0.70) or bad ( $\leq 0.70$ ) [14]. Two-way analysis of variance was used to evaluate the relationships between time and measurements.

The two methods for calculating  $V_{Daw}$  from T0 to T60 and the three different components of  $V_D$  obtained by the two methods at T60 were compared by two-tailed Student's *t*-test and Bland and Altman analysis after modelling the variability in the SD of the differences as a function of the level of measurement when required [15]. Differences were considered significant with *P*<0.05.

# **Results**

# Patients

Thirty-two children ranging from 0.13 years to 15.4 years were enrolled (median age: 1.91 years; median weight: 13 kg). Fourteen patients had primary lung disease such as pneumonia (n = 11), sepsis (n = 2), and acute respiratory disease (n = 1). Twelve patients had neurologic disease such as encephalopathy (n = 4), status epilepticus (n = 3), meningitis (n = 2), neuromuscular disease (n = 2), and head trauma (n = 1). Six patients had cardiovascular disease. Ventilator settings, and respiratory and haemo-dynamic parameters remained unchanged during the study period (Table 1). No significant changes in SpO<sub>2</sub> or heart rate with time were observed.

Reproducibility of primary parameters and airway dead space measurements obtained with the SBT-CO<sub>2</sub> and the Bohr-Enghoff equations over a 1-h period

Table 2 shows that PiCO<sub>2</sub> increased significantly with time (P=0.02; ICC=0.77). Interestingly, PiCO<sub>2</sub> values were significantly higher (P < 0.03) in infants weighting less than 5 kg (n = 8) compared to those in infants weighting more than 15 kg (n = 11) whatever the time period (1.24±3.03 mmHg, 2.67±5.31 mmHg, 3.22± 4.24 mmHg, 4.15±3.70 mmHg, 4.04±4.64 mmHg vs 0±0 mmHg, 1.79±3.77 mmHg, 2.18±4.61 mmHg, 2.64± 6.00 mmHg, and 3.00±6.86 mmHg, respectively, at T0, T15, T30, T45, and T60). Consequently,  $P_{ET}CO_2$ values were corrected according to this PiCO<sub>2</sub> increase with time, such as  $P_{ET}CO_2$  corr = ( $P_{ET}CO_2$ -PiCO<sub>2</sub>).  $V_{Daw}$ obtained from Bohr equation after correction for the increase in PiCO<sub>2</sub> with time were significantly smaller than non-corrected V<sub>Daw</sub> (mean difference: 0.187± 0.363 ml/ kg, or 5.01% of mean value, P<0.001). The 95% confidence interval (CI) for this bias was -0.126 ml/kg to 0.250 ml/kg. The limits of agreement were -0.539 ml/kg to 0.915 ml/kg. Table 2 shows that  $V_{Daw}$  measurement had a good reproducibility during the 1-h period, whatever the method used [ICC ranged from 0.84 to 0.87, within-subject coefficient of variation (CV) for V<sub>Daw</sub> and V<sub>Daw</sub>/VT was, respectively, for SBT-CO<sub>2</sub> test: 9.9 and 11.4%, and for Bohr-Enghoff equations: 8.4 and 6.2%]. No significant differences in measurement were observed with time. No significant relation was observed between age or weight and  $V_D$  values (r=0.4).

**Table 1** Ventilator settings, and respiratory and haemodynamic parameters expressed as means $\pm$ standard deviations, at each 15-min period, during 1 h (T0, T15, T30, T45, and T60). Intrasubject reproducibility of measurements repeated over 1 h was evaluated by the intraclass correlation coefficient (ICC). Two-way analysis of variance (*P*) was used to evaluate the relationships between time

and measurement (*PIP* peak inspiratory pressure, *PEEPt* ventilator positive end-expiratory pressure, *PEEPi* intrinsic positive end-expiratory pressure, *VT* expiratory tidal volume,  $FiO_2$  inspiratory oxygen fraction, *Re* and *Ri* expiratory and inspiratory dynamic airway resistances, *Crs,dyn* dynamic compliance, *HR* heart rate, *SBP* systolic blood pressure)

Parameters	T0	T15	T30	T45	T60	ICC	Р
Ventilator settings							
PIP $(cmH_2O)$	22.1±7.7	22.6±7.6	22.4±7.7	21.4±6.8	22.3±7.8	0.97	0.972
PEEPt $(cmH_2O)$	$2.6 \pm 3.5$	$2.6 \pm 3.5$	2.7±3.5	2.7±3.5	$2.7\pm3.5$	0.99	0.999
PEEPi $(cmH_2O)$	$2.8 \pm 4.2$	3.1±4.4	3.2±4.3	$3.0 \pm 4.5$	3.3±5.3	0.91	0.994
VT (ml/kg)	7.0±2.3	7.1±2.7	7.2±2.3	7.3±2.4	7.3±2.7	0.93	0.984
$FiO_2(\%)$	27.4±7.8	26.4±7.5	28.5±7.6	28.5±8.4	28.5±8.4	0.87	0.918
Air leaks (%)	17.7±19.7	18.1±22.3	15.2±18.5	15.4±19.5	15.9±19.7	0.92	0.969
Respiratory mechanics							
Re, dyn (cmH <sub>2</sub> O· $l\cdot$ s)	51±24	47±23	49±24	47±21	45±21	0.86	0.917
Ri,dyn (cmH <sub>2</sub> O·l·s)	48±22	45±22	46±21	47±20	45±22	0.88	0.991
Crs,dyn (ml·cmH <sub>2</sub> O·kg)	$0.79 \pm 0.34$	$0.82 \pm 0.39$	0.77±0.27	$0.96 \pm 0.91$	$0.90 \pm 0.66$	0.86	0.945
Haemodynamic parameters							
HR (c/min)	133±28	127±26	128±29	132±31	133±31	0.87	0.917
SBP (mmHg)	102±17	103±17	103±17	102±18	102±19	0.99	0.999
Body temp (°C)	37.4±0.9	37.4±0.9	37.5±1.0	37.7±1.0	37.6±1.1	0.97	0.984

**Table 2** CO<sub>2</sub>SMO Plus data, expressed as means±standard deviations, at each 15-min period, during 1 h (T0, T15, T30, T45, and T60). Intrasubject reproducibility of measurements repeated over 1 h was evaluated by the intraclass correlation coefficient (ICC). Two-way analysis of variance (P) was used to evaluate the relationships between time and measurement. The two methods for calculating airway dead space (SBT-CO<sub>2</sub> and Bohr equation after

correction for PiCO<sub>2</sub>) were compared by using two-tailed Student's *t*-test. (*PiCO*<sub>2</sub> and *PeCO*<sub>2</sub> mean inspiratory and expiratory CO<sub>2</sub> partial pressure, *PETCO*<sub>2</sub> expiratory end-tidal CO<sub>2</sub> partial pressure, *V'CO*<sub>2</sub> expiratory CO<sub>2</sub> production, airway dead space (V<sub>Daw</sub>) and ratio of airway dead space to tidal volume (V<sub>Daw</sub>/VT) automatically calculated by CO<sub>2</sub>SMO Plus (SBT-CO<sub>2</sub>) and manually calculated by Bohr equation)

Parameters	Т0	T15	T30	T45	T60	ICC	Р
$CO_2$ parameters							
$PiCO_2$ (mmHg)	$1.0 \pm 2.5$	4.1±5.9	5.5±7.9	6.3±8.9	6.5±9.2	0.77	0.019
PeCO <sub>2</sub> (mmHg)	17.2±7.1	17.7±6.4	16.9±7.2	17.7±6.5	15.9±7.5	0.82	0.844
PETCO <sub>2</sub> (mmHg)	40.6±11.9	43.1±15.7	44.6±17.5	46.5±17.4	45.7±18.5	0.91	0.657
$PETCO_2$ corr (mmHg)	39.6±11.0	39.1±11.8	39.1±11.7	38.6±12.9	39.1±11.4	0.94	0.999
V'CO <sub>2</sub> (ml/min/kg)	4.6±2.5	$5.2 \pm 2.9$	4.5±2.4	$4.9 \pm 2.7$	4.6±2.7	0.82	0.831
SBT-CO <sub>2</sub>							
V <sub>Daw</sub> (ml/kg)	1.58±0.68	1.61±0.69	1.49±0.65	1.52±0.66	1.60±0.74	0.87	0.953
V <sub>Daw</sub> /VT	$0.24 \pm 0.10$	$0.24 \pm 0.10$	$0.22 \pm 0.08$	0.21±0.09	0.23±0.08	0.84	0.623
Bohr equation							
V <sub>Daw</sub> (ml/kg)	3.63±1.25*	3.66±1.30*	3.74±2.14*	3.6±1.04*	3.63±1.27*	0.86	0.995
V <sub>Daw</sub> /VT	0.54±0.18*	0.52±0.16*	0.55±0.19*	0.51±0.16*	0.56±0.26*	0.87	0.856

\*P<0.01

Comparison of the dead space components calculation using SBT-CO<sub>2</sub> test and that using Bohr-Enghoff equations.

Table 2 shows that, from T0 to T60,  $V_{Daw}$  calculated from SBT-CO<sub>2</sub> method were always smaller than those obtained from Bohr-Enghoff equations. The mean percent difference for the  $V_{Daw}$  calculated from the SBT-CO<sub>2</sub> analysis was 81.1% of mean value (the mean percent difference was calculated from the following formula: percent difference (%) = 100 × (difference between the methods)/mean dead space measurement). Bland and Altman analysis revealed a non-uniform relationship between the  $V_{Daw}$  difference and the magnitude. The dif-

ference between the V<sub>Daw</sub> obtained by the two methods was regressed on their average (x). The regression equation was y = -0.101-0.790x. The variability of the differences increased as the magnitude of the differences increased. The SD of the residuals was modeled as a function of the magnitude of VTE to obtain the limits of agreement [15].

Table 3 shows that  $V_{Daw}$  and  $V_{Dalv}$  calculated at T60 from the two methods appeared different even after correction for the PiCO<sub>2</sub> (*P*<0.01). Bland and Altman analysis revealed a non-uniform relationship between the  $V_{Daw}$  difference and the magnitude as shown in Fig. 2. The difference between the  $V_{Daw}$  obtained by the two methods was regressed on their average (x). The regression

**Table 3** Comparison of dead space (V<sub>D</sub>) components and ratio of dead space to tidal volume (V<sub>D</sub>/VT) automatically calculated by CO<sub>2</sub>SMO Plus (SBT-CO<sub>2</sub>) and manually calculated By Bohr-Enghoff equations at T60. Data are expressed as means±standard deviations. The two methods for calculating dead space components (SBT-CO<sub>2</sub> and Bohr-Enghoff equation) were compared by using two-tailed Student's *t*-test. V<sub>D</sub> obtained by Bohr-Enghoff equations was corrected for the increase of PiCO<sub>2</sub> with time. (V<sub>Daw</sub> airway dead space, V<sub>Dalv</sub> alveolar dead space, V<sub>Dphysiol</sub> physiologic dead space)

Parameters	SBT-CO <sub>2</sub>	Bohr-Enghoff equations			
		Not corrected	Corrected		
	$\begin{array}{c} 1.60{\pm}0.74\\ 0.23{\pm}0.08\\ 2.86{\pm}1.14\\ 0.42{\pm}0.13\\ 4.46{\pm}1.64\\ 0.65{\pm}0.16\end{array}$	$\begin{array}{c} 3.86{\pm}1.36^{**}\\ 0.60{\pm}0.21^{**}\\ 0.40{\pm}1.52^{**}\\ 0.03{\pm}0.12^{**}\\ 3.91{\pm}2.66^{*}\\ 0.60{\pm}0.22^{*} \end{array}$	3.63±1.27** 0.56±0.26** 0.67±1.99** 0.05±0.16** 4.06±1.66 0.62±0.25	NS NS	

\*P< 0.01; \*\*P<0.001

sion equation was y = -0.203-0.760x. The variability of the differences increased as the magnitude of the differences increased. The SD of the residuals was modeled as a function of the magnitude of VTE to obtain the limits of agreement [15].

 $V_{Dphysiol}$  obtained from SBT-CO<sub>2</sub> method was quite similar to  $V_{Dphysiol}$  calculated from Bohr-Enghoff equations as shown in Fig. 2, (mean difference:  $-0.287\pm$ 1.046 ml/kg, or 6.8% of mean value, NS). The 95% CI for the bias was -0.690 ml/kg to 0.116 ml/kg. The limits of agreement were -1.806 ml/kg to 2.380 ml/kg.

#### Discussion

This study demonstrated that the measurement of  $V_{Daw}$ by the CO<sub>2</sub>SMO Plus was reproducible over a 1-h period, in ventilated children, provided ventilatory parameters were kept constant throughout the study. To our knowledge, this is the first clinical study evaluating in children the reproducibility of SBT-CO<sub>2</sub> analysis. In adults too, the data seem very scarce: Koulouris et al. [16] found that the mean within-study, within-day, and day per day CV for V<sub>Daw</sub>/VT calculated from Bohr's equation was 6.5%, 6.8%, and 7.25% in three normal adults in whom measurements were repeated three times per day for three consecutive days. In our study, the within-subject CV for V<sub>Daw</sub> and V<sub>Daw</sub>/VT was comparable (SBT-CO<sub>2</sub>: 9.9% and 11.4%, Bohr-Enghoff equations: 8.4% and 6.2%).

A wide range of  $V_{Daw}$  values was observed in our patients, whatever the method used (SBT-CO<sub>2</sub>: 0.81–4.20 ml/kg; Bohr equation: 1.48–5.90 ml/kg). These results can be compared to data from the literature in ventilated infants ( $V_{Daw}$  ranges from 1.6 ml/kg to 3.2 ml/kg) [10]. In our patients, variability could be explained by the heterogeneity of the population and the wide range of



VDaw difference (SBT CO2-Bohr) ml/kg

0

-1

-2

-3

-4

-5 -6 -7

6



Fig. 2 The difference between the CO<sub>2</sub>SMO Plus dead space (V<sub>D</sub>) components and the Bohr V<sub>D</sub> components plotted against the average of the two measurements with regression-based limits of agreement, at T60 (V<sub>Daw</sub>: airway dead space, V<sub>Dalv</sub>: alveolar dead space, V<sub>Dphysiol</sub>: physiologic dead space)

ages (0.13–15.4 years). In fact, Numa et al. demonstrated in 40 patients aged 7 days to 14.2 years who were intubated with cuffed endotracheal tubes, that extrathoracic  $V_{Daw}$  decreased exponentially with increasing age, ranging from 2.3 ml/kg in early infancy to 0.8 ml/kg in children older than 6 years. Mean intrathoracic  $V_{Daw}$  was 1.03 ml/kg and was not related to age [17]. However, in our study, no significant relation was observed between age or weight and dead space values.

Although major difficulties of this technique are eliminated when applied to intubated infants, a zeroing of the PCO<sub>2</sub>-volume plot at the starting point of expiration and an alveolar plateau of the PCO<sub>2</sub>-volume plots are necessary to apply SBT-CO<sub>2</sub> [18]. In our study, P<sub>i</sub>CO<sub>2</sub> slightly increased with time and this was probably due to rebreathing of expired gas, because of the pediatric sensor  $V_D$ . In fact, PiCO<sub>2</sub> values were significantly higher in small infants. This was also observed by Wenzel et al. who tested the applicability of Ventrak 1550/Capnogard 265 for  $V_D$  measurement in 22 ventilated neonates: after inserting the combined sensor of the device, transcutaneous PCO<sub>2</sub> rose within 5 min by 3.2% in newborns of  $\geq$ 2,500 g and by 5.7% in those of <2,500 g [10]. Rebreathing of expired gas detected by an increased endinspiratory CO<sub>2</sub> impairs alveolar gas exchange [19] which can lead to an overestimation of  $P_{ET}CO_2$  and  $P_eCO_2$ . SBT-CO<sub>2</sub> enables the calculation of  $P_iCO_2$ , defined as the minimum value of the moving-average of the CO<sub>2</sub> sample over the last 20 s, and the correction of  $CO_2$  elimination and P<sub>e</sub>CO<sub>2</sub> (calculated by dividing VCO<sub>2</sub> by VT) for rebreathed P<sub>i</sub>CO<sub>2</sub>. Conversely, simplified Bohr-Enghoff equations do not take into account rebreathed P<sub>i</sub>CO<sub>2</sub> and may overestimate V<sub>Daw</sub> values [20]. Fletcher et al. estimated that rebreathing was the most important source of error in the measurement of  $CO_2$  elimination. By using a 3-1 rubber bag containing radioactive xenon and connected to a ventilator, they demonstrated that the calculated rebreathed volume corresponded to about 24 ml of end-expiratory gas per breath with a standard Y-piece and tubing, at a frequency of 10 bpm and an overestimation of  $F_eCO_2$  by 5–12% [19]. These results were similar to those of our study in which the mean percent difference for the corrected V<sub>Daw</sub> calculated from the Bohr equation was 5%. The present results suggest that the difference, although statistically significant, is small  $(0.19\pm0.24 \text{ ml/kg})$ and thus can be neglected under most conditions prevailing during mechanical ventilation. P<sub>a</sub>CO<sub>2</sub> values were never over 51 mmHg (mean: 39.9±11.8 mmHg, range: 25–51 mmHg, except in one case: 63 mmHg in a 13.8-kg child), suggesting that rebreathing was not an important phenomenon in our patients. The other effects of insertion of the sensor were not measured in this study but Castle et al., studying accuracy of displayed values of VT in the pediatric ICU, by using CO<sub>2</sub>SMO Plus, demonstrated that this insertion had minimal effect on either VT or PIP, the average change being <1%, provided the appropriate sensor is used over a designated flow range [21]. However, these authors described some underestimations of recorded volumes at low flows with the pediatric pneumotachometer and did not recommend using this sensor in children with mean flows less than 4 l/min. This last study was not published when we started ours.

Like Fletcher et al. [3, 18], we found wide significant differences between  $V_{\text{Daw}}$  and  $V_{\text{Dalv}}$  values by the two methods. The V<sub>Daw</sub> SBT-CO<sub>2</sub>/V<sub>Daw</sub> Bohr relation is affected by the slope of phase III. V<sub>Daw</sub> Bohr consists of V<sub>Daw</sub> plus part of V<sub>Dalv</sub>. The magnitude of the alveolar part of V<sub>Daw</sub> Bohr is proportional to phase III. Thus, in children with normal slopes, Fletcher found that V<sub>Daw</sub> SBT-CO<sub>2</sub> was 67% of V<sub>Daw</sub> Bohr. In children in whom phase III slope was increased, V<sub>Daw</sub> SBT-CO<sub>2</sub> was only 51% of V<sub>Daw</sub> Bohr [3]. In contrast, Wenzel et al. found no significant difference between  $VD_{Daw}$  and  $V_{Dalv}$  calculated by the two methods in 22 ventilated neonates [10]; nevertheless, in their study V<sub>Daw</sub> SBT-CO<sub>2</sub> values were smaller than those by Bohr-Enghoff equations (V<sub>Daw</sub> SBT-CO<sub>2</sub>: 3.65±1.59 ml, V<sub>Daw</sub> Bohr: 5.27±2.44 ml). We observed no significant difference between V<sub>Dphysiol</sub> calculated by the two methods, after correction was made for rebreathing of expired gas. Only when arterial-end tidal  $CO_2$  gradient is zero will the two methods give the same V<sub>Dpysiol</sub> values. In our patients, the small gradient (0.81±3.4 mmHg) explains that V<sub>Dphysiol</sub> values were quite similar with the two methods.  $\hat{V}_{Dalv}$  cannot be estimated by using Bohr-Enghoff equations in contrast to SBT-CO<sub>2</sub> analysis which enables V<sub>Dalv</sub> calculation. However, determination of V<sub>Dalv</sub> may be of importance because previous data suggest that quantification of the V<sub>Daly</sub> may be directly related to effective pulmonary perfusion [22] and that changes in phase III slope may reflect alveolar development and lung growth in infants [23].

Despite its pitfalls, volumetric capnography and  $V_D/VT$  determination might be useful in many clinical situations: it could serve as a useful device to monitor adequacy of mechanical ventilation and help in evaluating ventilatory disturbances in patients with acute respiratory distress syndrome [2, 4, 5, 9, 11, 24]. Finally,  $V_D/VT$  measurement could be used to evaluate the consistency of breathing before extubation [5].

### Conclusion

Measurement of  $V_{Daw}$  by the CO<sub>2</sub>SMO Plus was reproducible over a 1-h period, in ventilated children, provided ventilatory parameters were kept constant throughout the study. A more prolonged use will have to take into account the pitfalls of the method (damage by water condensate, alteration of end-tidal CO<sub>2</sub> readings by deposition of secretions) [25, 26, 27, 28, 29]. Furthermore, to minimize the risk of hypercapnia, we recommend choosing the sensor with the minimal dead space, i.e., the neonatal one up to a mean flow of 5 l/min as suggested by Castle et al. [22].

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