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Calibration of Respiratory Inductance Plethysmograph in Preterm Infants With Different Respiratory Conditions

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Summary. Respiratory inductance plethysmography (RIP) is a method for respiratory measurements particularly attractive in infants because it is noninvasive and it does not interfere with the airway. RIP calibration remains controversial in neonates, and is particularly difficult in infants with thoraco-abdominal asynchrony or with ventilatory assist. The objective of this study was to evaluate a new RIP calibration method in preterm infants either without respiratory disease, with thoraco-abdominal asynchrony, or with ventilatory support. This method is based on (i) a specifically adapted RIP jacket, (ii) the least squares method to estimate the volume/motion ribcage and abdominal coefficients, and (iii) an individualized filtering method that takes into account individual breathing pattern. The reference flow was recorded with a pneumotachograph. The accuracy of flow reconstruction using the new method was compared to the accuracy of three other calibration methods, with arbitrary fixed RIP coefficients or with coefficients determined according to qualitative diagnostic calibration method principle. Fifteen preterm neonates have been studied; gestational age was (mean $\pm$ SD) 31.7 $\pm$ 0.8 weeks; birth weight was 1,470 $\pm$ 250 g. The respiratory flow determined with the new method had a goodness of fit at least equivalent to the other three methods in the entire group. Moreover, in unfavorable conditions—breathing asynchrony or ventilatory assist—the quality of fit was significantly higher than with the three other methods ($P < 0.05$, repeated measures ANOVA). Accuracy of tidal volume measurements was at least equivalent to the other methods, and the breath-by-breath differences with reference volumes were lower, although not significantly, than with the other methods. The goodness of fit of the reconstructed RIP flow with this new method—even in unfavorable respiratory conditions—provides a prerequisite for the study of flow pattern during the neonatal period. **Pediatr Pulmonol. 2008; 43:1135–1141.** © 2008 Wiley-Liss, Inc.

Key words: plethysmography; premature infant; artificial ventilation; dyspnea; asynchronism; neonatal respiratory distress syndrome.

INTRODUCTION

Objective assessment of respiratory function plays an important part in understanding the pathophysiology of the respiratory system, and in evaluating the effects of ventilatory support. Respiratory inductance plethysmography (RIP) is a widely accepted method for respiratory timing and volume measurements. RIP is particularly attractive in neonates because it is noninvasive and it does not require any interference with the airway, that could modify the breathing pattern.[1] This technique involves the subject wearing two inductance bands around the rib cage and the abdomen. Alterations in the inductance of the coils reflect the changes of thoracic and abdominal compartment volumes. It is assumed that the tidal volume (VT) can be estimated as the weighted sum of the ribcage (RC) and abdominal (AB) inductance signals:[2]

$$V_T = \alpha RC + \beta AB,$$

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where α and β are the volume/motion coefficients for RC and AB respectively. Various calibration methods have been used in adults to estimate these coefficients.[3–5] However, RIP calibration in infants and neonates remains controversial. The qualitative diagnostic calibration (QDC) described in adults by Sackner et al.[4] has been adapted for neonates or infants.[6] With this method, mean tidal volumes have been adequately estimated in term neonates,[6] whereas in other studies, the accuracy of QDC was found insufficient.[7,8] Other methods have been studied, with fixed coefficient ratio,[9] or coefficients estimated by the least squares technique,[9,10] but with inconsistent results. A specific difficulty in neonates is the high incidence of thoraco-abdominal asynchrony, that may alter RIP volume measurements.[7,9,11] RIP precision may also be altered by ventilatory assistance.[7] To overcome these problems, we hypothesized that RIP calibration should be adapted to each infant's breathing pattern. We have developed a new single posture RIP calibration method where both α and β calculation, and the filtering parameters are individualized.

The objective of this study is to evaluate the accuracy of this new calibration method as compared to three other frequently used calibration methods, in premature neonates with various respiratory conditions: infants breathing with synchrony, infants with thoraco-abdominal asynchrony, and infants with ventilatory support.

MATERIALS AND METHODS

Patient Population

We investigated premature newborn infants during their first 10 days of life in the neonatal intensive care unit of Grenoble University Hospital from March, 2005 to October, 2006. Inclusion criteria were: (1) gestational age from 30 to 33 weeks, (2) birth weight higher than 1,000 g, and (3) aged between 1 and 10 days. Patients were not eligible if they had one of the following conditions: hemodynamic impairment or need for inotropic treatment, cerebral haemorrhage, severe metabolic acidosis or alkalosis, or suspected neuromuscular disease. Patients were breathing either without any support or with assistance. Respiratory support included nasal CPAP (Infant Flow, EME Tricomed, Brighton, UK) or invasive ventilation (Babylog 8000, Draeger, Lubeck, Germany).

ABBREVIATIONS

AB	abdominal inductance signal
ACV	assisted controlled ventilation
TD	thoracic delay
GA	gestational age
HMD	hyaline membrane disease
NCPAP	nasal continuous positive airway pressure
QDC	qualitative diagnostic calibration
RC	ribcage inductance signal
RIP	respiratory inductance plethysmography
rmANOVA	repeated measures ANOVA
VT	tidal volume
VT_{RIP}	tidal volume determined from respiratory inductance plethysmography
VT_{PNT}	tidal volume determined from pneumotachography

Study Protocol

The protocol was approved by the local ethics committee. Written informed consent was obtained from the parents of all patients.

Immediately following morning nursing care, the RIP jacket was gently positioned. The infant was installed supine, with a 30° head elevation, and rested quietly for at least 5 min. RIP signals were then continuously recorded during 30 min. For the aim of calibration, RIP signals and airflow (pneumotachograph) were simultaneously recorded for 60 sec, when the infant was quiet. Oxygen saturation, heart rate, respiratory rate, and agitation episodes were monitored throughout the whole study.

RIP Signal Acquisition

The abdominal and ribcage RIP coils were coated in a sleeveless jacket allowing horizontal wiredrawing only (Fig. 1). This jacket was specially sized for preterm neonates, to prevent displacement of the classical separate bands. Lateral bonds allowed adaptation of the jacket size to the neonate's body, snugly, but not tightly. The RIP signals were digitized at a 40 Hz sampling rate (Visuresp®, RBI, Meylan, France).

Reference Airflow Measurements

In non-intubated infants, the reference respiratory flow was recorded for 60 sec by pneumotachography (PNT), with a flowmeter (dead space 1.9 ml. PN155500 Hamilton Medical, Rhäzüns, Switzerland) and a differential transducer (163PC01D36, Micro Switch) attached to a face mask (dead space 5 ml; Neonatal face mask, Ambu France, Le Haillan, France). The flowmeter was placed in the incubator and the transducer was turned on at least 30 min before the study, to minimize the temperature

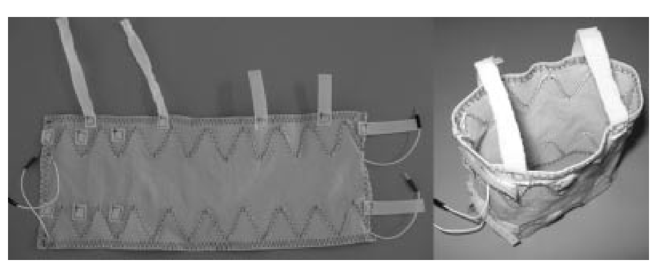

Fig. 1. The inductance plethysmographic jacket adapted for preterm neonates. Only horizontal wiredrawing is possible. Lateral bands permit to adapt the jacket size to the neonate's body.

changes during the measurements. Leaks from around the mask were detected and corrected before the recording was initiated using an end-tidal CO_2 analyser (N-1000; Nellcor, Inc., Hayward, CA). Immediately before the measurements, the pneumotachograph was calibrated with 3 injections of 10 ml air, after zero setting. In intubated patients, the flow signal was obtained from the ventilator (Babylog 8000, Draeger, Lubeck, Germany) and was recorded simultaneously with the RIP signal for 60 sec. The hot wire pneumotachograph of the ventilator was calibrated prior to the study, following the Babylog 8000 calibration procedure. Patients with air leak around tracheal tube (measured by the ventilator) higher than 10% were not eligible.

RIP Calibration

Simultaneous PNT and RIP signals were analyzed with a specific software we developed under Matlab 7.1 (MathWorks, Inc., Natick, MA).[12] The 15 most regular (in duration) consecutive breaths of the PNT signal were automatically identified and formed the reference period. A least squares method was used over this 15 cycle reference period to estimate α and β coefficients allowing to obtain a RIP volume signal (V_{RIP}) by combination of RC and AB signals in comparison to the integrated simultaneously recorded flow signal (V_{PNT}):[12]

$$V_{RIP} = \alpha RC + \beta AB,$$

The derivative of V_{RIP} was then calculated by using centered divided differences.[12] In order to take out the individually adjusted filter, a transfer function was calculated over the reference period using the ratios of the moduli of the RIP derivative and airflow signal frequency spectra. The Fourier series development of this function permits computation of the filter, which was then applied to the entire recording, giving the RIP reconstructed flow.

Thoraco-abdominal asynchrony was quantified using the thoracic delay (TD). TD was calculated during the reference period, as the time delay between the inspiratory peaks of AB and RC signals, expressed as a percentage of the inspiratory time. Thoraco-abdominal asynchrony was defined as a TD higher than 40% of inspiratory time.[13]

Statistical Analysis

The accuracy of the new calibration method was compared to that of three other methods. In two methods, fixed coefficients were used, (i) with an equal weighting attributed to AB and RC ($\beta = \alpha$; method 1:1), or (ii) with a higher weighting attributed to AB ($\beta = 2\alpha$; method 1:2).[9] In the third method (*QDC-derived* method), the principle of calculation of α and β was derived from the QDC method. The coefficients were estimated from the standard deviations of the RIP signals[4] during the reference period:

$$\frac{\beta}{\alpha} = \frac{SD(AB)}{SD(RC)}$$

In these three methods, the RIP reconstructed flow was then calculated by the derivative of the RIP volume signal, using centered divided differences.

For each method, the goodness of fit (ρ) of the reconstructed RIP flow with regards to the reference PNT flow was calculated as $\rho = 1 -$ (mean square difference between normalized flows/variance of PNT);[12] that is, a ρ closer to one represents a better reconstruction of the signal. The goodness of fit was calculated during the 60 sec period where both simultaneous PNT and RIP flows were available, excluding the 15 cycles used for calibration. A mean goodness of fit for each method was evaluated in the entire population, as well as in the three pre-defined subgroups: patients breathing in synchronism, patients with thoraco-abdominal asynchrony, and patients with respiratory assist.

We also evaluated the accuracy of each method to estimate the mean tidal volume, by using a linear regression and the method described by Bland and Altman.[14] Individual breath results were also compared, by estimating the mean relative differences between tidal volume calculated from RIP (VT_{RIP}) and PNT (VT_{PNT}).

All data are provided as mean and standard deviation (mean ± SD). Statistical analysis was performed with commercially available software (Statview 5.0, SAS Institute, Inc., Cary, NC). One way repeated-measures ANOVA (rmANOVA) were used to determine differences between the results given by the four methods for goodness of fit, tidal volumes, and tidal volume differences. When a $P < 0.05$ was obtained with the rmANOVA, differences between two methods were estimated with a Tukey–Kramer test. A P-value < 0.05 was considered to be significant.

RESULTS

Patients

Seventeen premature newborn infants were included in the study. Two infants were excluded from the analysis because of the difficulty in obtaining a stable PNT signal lasting longer than 30 sec, secondary to agitation. Fifteen infants 5 ± 3 days of age were therefore investigated. Eight patients were studied twice, 23 recordings were then analyzed. The mean gestational age was 31.7 ± 0.8 weeks with a birth weight of $1,470 \pm 250$ g (range: 1,060–1,870 g). Characteristics of the patients are reported in Table 1. The mean respiratory frequency was 70 breaths per minute (range: 47–92). Recordings were well tolerated by all investigated infants, according to continuous observation,

TABLE 1— Patient Characteristics

Patient	Age (days)	GA (weeks)	Birth weight (g)	Respiratory diagnosis at admission	Respiratory status (TD/T I, %)	Antenatal steroids	Exogenous surfactant (doses)	Ongoing sedation
1	9	31	1,780	—	Synchrone (23%)	Yes	0	No
2	9	32	1,850	HMD	Ventilatory assist (ACV)	Yes	3	Yes
3	6	30	1,190	—	Synchrone (38%)	Yes	0	No
4	10	31	1,600	HMD	TAA (98%)	No	1	No
5	5	31	1,210	HMD	TAA (99%)	Yes	0	No
6	4	32	1,980	HMD	TAA (61%)	Yes	1	No
7	3	31	1,440	—	Synchrone (12%)	No	0	No
8	3	32	2,040	Wet lung	Synchrone (14%)	Yes	0	No
9	3	32	1,470	—	Synchrone (11%)	Yes	0	No
10	7	32	1,580	HMD	TAA (113%)	Yes	0	No
11	8	30	1,700	HMD	Ventilatory assist (NCPAP)	Yes	1	No
12	8	31	1,410	HMD	Synchrone (12%)	Yes	0	No
13	2	31	1,310	HMD, pneumothorax	Ventilatory assist (ACV)	Yes	1	Yes
14	1	31	1,175	HMD	Ventilatory assist (ACV)	No	1	No
15	1	30	1,570	HMD	Ventilatory assist (ACV)	Yes	1	No

TD/T I, thoracic delay expressed as a percentage of inspiratory time; ACV, assisted controlled ventilation; GA, gestational age; HMD, hyaline membrane disease; NCPAP, nasal continuous positive airway pressure; TAA, thoraco-abdominal asynchrony.

and monitoring of heart and respiratory rates and oxygen saturation.

Goodness of Fit

Figure 2 shows the mean goodness of fit ρ for each method in the entire population, ρ was 0.57 ± 0.26 with method 1:1, 0.47 ± 0.37 with method 1:2, 0.55 ± 0.28 with *QDC-derived* method, and 0.66 ± 0.20 with the new method ($P < 0.01$; rmANOVA, with significant differences between method 1:2 and the new method). In the four patients (eight recordings) with thoraco-abdominal asynchrony, ρ was higher with the new method in comparison to the other three methods ($P < 0.05$; rmANOVA; significant difference between the new method and every other method). In the six patients spontaneously breathing with synchrony (10 recordings), there was a significant difference between method 1:2 and the new one. In patients with ventilatory assist (five patients, 5 recordings), the rmANOVA also shows a difference ($P < 0.05$) and a significant difference was established between *QDC-derived* method and the new method.

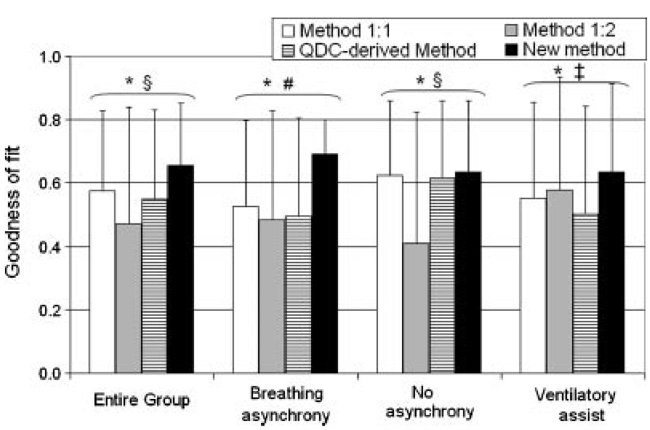

Fig. 2. Goodness of fit of the respiratory flow reconstructed with the different methods in the entire group, and in the three predefined subgroups. *$P < 0.05$, repeated measure ANOVA; (§) significant difference between method 1:2 and new method; (#) significant difference between the new method and every other method; (‡) significant difference between *QDC-derived* method and new method.

Tidal Volumes

The median number of cycles per patient included in the analysis was 69 (ranges: 26–91). The mean tidal volumes estimated by each method are presented in Table 2. A significant correlation was obtained between VT_{PNT} and VT_{RIP} calculated with each method, with a coefficient of determination of 0.87, 0.89, 0.90, and 0.91 for methods 1:1, 1:2, *QDC-derived*, and the new method respectively. The Bland-Altman graphical representation in Figure 3 shows the agreement between VT_{PNT} and VT_{RIP} calculated with the 4 methods. The 95% confidence interval of agreement was [−1.6–3.3 ml] between PNT and method 1:1, [−1.4–2.9 ml] between PNT and method 1:2, [−1.4–2.7 ml] between PNT and *QDC-derived* method, and [−1.2–2.5 ml] between PNT and the new method. The relative breath-by-breath differences between VT_{RIP} and VT_{PNT} were lower with the new method than with the three other methods, although not significantly (Table 2).

DISCUSSION

This study was undertaken to evaluate the accuracy of a new individualized calibration method of RIP in premature infants with different respiratory conditions. The respiratory flow determined with this new method had a

TABLE 2— Tidal Volumes Determined by the Reference Method and by Plethysmography With the Four Calibration Methods

	Reference method (PNT)	Method 1:1	Method 1:2	QDC-derived Method	New method	*P*
Mean tidal volume (ml/kg)	4.7 ± 2.1	5.3 ± 2.2	5.2 ± 2.2	5.1 ± 2.2	5.1 ± 2.3	<0.05*
Cycle-by-cycle differences between VT_{PNT} and VT_{RIP} (% VT_{PNT})		14 ± 26	22 ± 40	12 ± 19	10 ± 19	0.31

Data are presented as mean ± SD.
*The four RIP methods are different from PNT; no significant difference between the RIP methods.

goodness of fit at least equivalent to the three other methods in the entire population. Contrary to the other methods, the quality of fit remained good even in presence of thoraco-abdominal asynchrony. The accuracy of tidal volume measurements was at least equivalent to the other methods.

During the neonatal period, different respiratory patterns may be observed and one particular difficulty is the high incidence of thoraco-abdominal asynchrony. Asynchrony has been reported as a factor of RIP imprecision.[9,11,15] We developed this new method in order to adapt the RIP calibration to individual respiratory pattern. The identification of coefficients is based on the least-squares method to obtain the best fit between the combination of RC and AB signals and the integrated PNT flow signal,[12] and not only between tidal volumes as sometimes reported.[10] The objective is to optimize not only the tidal volume measurement, but also the determination of the flow pattern.[12,16] The filter calculation was also individualized, which is of critical importance for taking into account each patient's respiratory rhythm, heart rate, or thoraco-abdominal synchrony. Filter calculation is not individualized in most RIP studies.[4,6,7,17] Finally, we tried to minimize the displacement artefacts of the RIP bands with the specially adapted jacket.

An important difficulty inherent to studies attempting to validate a method that determines the respiratory flow is the absence of a gold standard. In the current study, a pneumotachometer signal was used as a reference due to it being the most reliable available.[18] We tried to avoid the

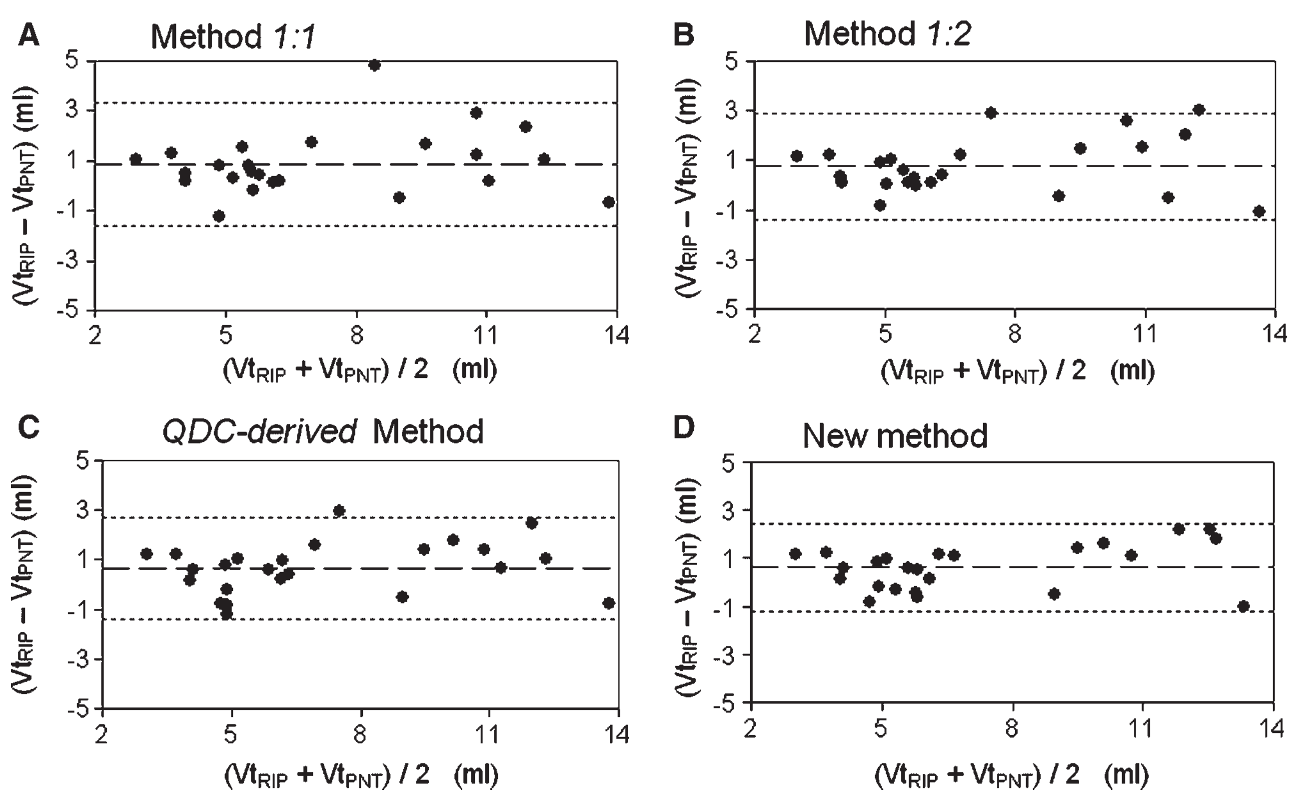

Fig. 3. Bland-Altman plots of the differences between mean VT_{PNT} and mean VT_{RIP} calculated with method 1:1 (A), method 1:2 (B), *QDC-derived* method (C), and the new method (D). Central and lateral dotted lines represent mean differences and the limits of agreement respectively.

potential limitations of this technique. The air leaks were detected and corrected, temperature changes were prevented, and flowmeters appropriate for neonates were used.[18] The face mask was applied for brief periods (less than 1 min) to avoid breathing perturbation.[1]

We used the thoracic delay to evaluate thoraco-abdominal asynchrony to classify the spontaneously breathing patients. This simple method permits accurate quantification of asynchrony.[13] Our choice of a TD of 40% as a definition of thoraco-abdominal asynchrony is in line with previous reports.[13,19] Noteworthy, striking differences in breathing synchrony were observed between the two groups (Table 1), coinciding well with this threshold.

In order to evaluate the new method, it has been compared to three other calibration methods. The QDC method remains controversial for the small infant population,[7–9,20] but it is frequently used even in this setting.[21–24] The *QDC-derived* method used in the present study relies on the principle of QDC concerning the calculation of α and β.[4] Both methods however are not equivalent because the coefficients were estimated during a shorter reference period (15 cycles) in the present study. Nevertheless, the hypothesis of quasi-constant ventilation required with QDC has most likely been respected, the reference period being identified as the most regular cycles. The fixed coefficients method has been evaluated in infants with acceptable results as compared to QDC,[9] and its main advantage is its simplicity. The fixed coefficients of method 1:1 and method 1:2 were chosen from a previous study[9] and from clinical observations of the importance of abdominal contribution to breathing.[25]

Efforts have been made for years attempting to provide non-invasive measurements of respiratory flow in neonates. Direct airflow recording with a pneumotachograph is not clinically usable for longer than a few seconds, as the interaction with the airway induces a perturbation of the breathing pattern.[1,26] Whole-body volume displacement plethysmography permits prolonged measurements, however this technique remains complex and is not easily accessible for small patients in clinical practice. Indirect measurements have therefore been studied, such as impedance pneumography, strain gauges, and RIP. The first two methods however have been proven to be inaccurate,[27,28] and RIP is the most widely used method for respiratory volumes measurements in infants.

A quantitative determination of respiratory flow with RIP requires a calibration, which remains challenging in infants. A few studies have been conducted in neonates without respiratory distress, using the two-posture calibration method,[15,29] the least-squares method,[10,11] or the QDC method,[6,7,9,17,27] showing the accuracy of RIP for determination of the mean tidal volume from a large number of breaths. Accuracy of RIP seems to be much more limited for a breath-by-breath volume quantification,[7,8,10,15] with large individual breath differences between VT determined from RIP compared to the reference method.

In the present work, the main outcome measure was the goodness of fit of the RIP flow in comparison to the reference PNT flow. It has been chosen rather than a volume-derived measure because the reference used (PNT) is indeed a flow recording. This parameter best reflects the global accuracy of a method, and permits comparison between methods.[12] To our knowledge, RIP goodness of fit quantification has not been previously reported in neonates, and does not permit comparison. As compared to the results in adults,[12,30] the goodness of fit in our study are lower. However, in studies conducted in neonates, the differences between RIP parameters and reference values are nearly always greater than in adults, reflecting the complexity of monitoring in this population. In contrast to the other three calibration methods, a higher goodness of fit is obtained using the new method, particularly in patients with thoraco-abdominal asynchrony. Ventilatory assistance has also been described as a condition that lowers RIP accuracy.[7] In the present work, RIP accuracy in assisted patients was similar to the other conditions. The improvement of the goodness of fit may result from the coefficient determination method and/or from the filtering method. It has been shown that similar volume determination could be obtained with a wide range of thoracic/abdominal RIP coefficient ratio in healthy infants.[9] This may suggest that the accuracy difference between the calibration methods is mainly due to the individualized filtering method. However, determination of RIP coefficients is more critical in patients breathing in asynchrony [9,11] and the coefficient calculation method probably contributes to the goodness of fit observed.

The mean tidal volume determination in the present study was similar to previous reports,[7,9,15,27] with mean differences below 0.5 ml/kg, which can be considered acceptable in clinical practice. The cycle-by-cycle difference in tidal volume was also relatively low (10%), comparable to other studies.[7,9,15] The new method tended to give lower cycle-by-cycle tidal volume differences with the reference method, as well as narrower limits of agreement, although these differences were not statistically significant.

Some studies have shown that RIP precision decreases with time,[7] especially if the sleep status changes.[9,11,15] Conversely, similar tidal volume accuracy was found a few hours after the calibration period in 8 infants.[17] In the present study, the patients were monitored during less than 1 hr, in order to avoid changes in calibration coefficients.

CONCLUSION

This new single posture RIP calibration method permits to accurately reconstruct the respiratory flow in neonatal period. Moreover, the goodness of fit was greater than with classical methods in presence of thoraco-abdominal asynchrony or ventilatory assist. This provides a flow signal which may be used to study flow pattern changes during the neonatal period.

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