Disponible en ligne sur www.sciencedirect.com
ScienceDirect
ITBM-RBM 27 (2006) 227–232
ELSEVIER MASSON
ITBM RBM
http://france.elsevier.com/direct/RBMRET/

Original article

Air leakage during nocturnal mechanical ventilation in patients with neuromuscular disease

Fuites d'air durant la ventilation assistée nocturne chez des patients ayant une maladie neuromusculaire

A. Sabil[a], G. Mroue[b], H. Prigent[b], D. Orlikowski[b], M. Bohic[b], P. Baconnier[a,*], F. Lofaso[b,c], G. Benchetrit[a]

[a] *TIMC PRETA, faculté de médicine, université Joseph-Fourier, Grenoble, France*
[b] *Service de réanimation médicale, service de physiologie–explorations fonctionnelles et centre d'innovations technologiques, hôpital Raymond-Poincaré, APHP, 92380 Garches, France*
[c] *Inserm U 492, 94000 Créteil, France*

Received 31 August 2006; accepted 19 January 2007
Available online 22 February 2007

Abstract

Objective. – Air leakage is a major problem in long-term assisted ventilation both invasive and non-invasive that becomes even more important during sleep. The objective of this work was to provide a method for continuous estimation of tidal volume changes in patients under ventilatory support during sleep.

Materials and methods. – Recordings were from 14 patients with neuromuscular disorders admitted to hospital for a routine evaluation of assisted ventilation during sleep. Air leakage was continuously evaluated from: 1) the difference between the insufflated and expired volume using a flow meter; 2) the changes in lung volume using inductance plethysmography.

Results. – Both methods showed presence of air leaks in all patients and also variations in their amount throughout the night. However, inductance plethysmography provided more rigorous measurement of air leaks than flow meters as it measures the amount of air actually entering the lungs. The magnitude of leakage does not appear to be related to the method of assisted ventilation (invasive or non-invasive) or to the characteristic of the assistance mode (volume control or volume assist control).

Conclusion. – The proposed method offers a reliable, non-invasive, continuous, bedside evaluation of air leak changes in ventilated patients. On-line analysis can be performed to find optimal ventilator settings in order to compensate for leakage while providing patient comfort.

Résumé

Objectif. – Les fuites d'air au cours de la ventilation assistée constituent un problème majeur d'autant plus que leur quantité est accrue au cours du sommeil. Ces fuites existent quelle que soit la méthode d'assistance ventilatoire employée, invasive ou non invasive. L'objectif de ce travail a été de mettre au point une méthode d'estimation en continu du volume courant au cours du sommeil chez le patient ventilé.

Matériel et méthodes. – Chez 14 patients ayant une maladie neuromusculaire, hospitalisés pour une évaluation de leur assistance ventilatoire au cours du sommeil, l'estimation des fuites a été faite d'une part, en faisant la différence entre l'air insufflé et l'air expiré, et, d'autre part, en mesurant les variations de volume pulmonaire par pléthysmographie par inductance.

Résultats. – Les deux méthodes montrent l'existence de fuites chez tous les patients ainsi que des variations de l'importance de ces fuites au cours de la nuit. Cependant, la pléthysmographie par inductance permet une évaluation plus précise des fuites car elle mesure la quantité d'air atteignant effectivement les poumons. L'importance des fuites ne semble pas dépendre de la méthode d'assistance ventilatoire (invasive ou non invasive) ni du mode d'assistance (volume contrôlé ou volume assisté contrôlé).

* Corresponding author. Present address: Laboratoire TIMC, CNRS UMR 5525, faculté de médecine de Grenoble, université Joseph-Fourier, 38706 La-Tronche cedex, France.
E-mail address: Pierre.Baconnier@imag.fr (P. Baconnier).

1297-9562/$ - see front matter © 2007 Published by Elsevier Masson SAS.
doi:10.1016/j.rbmret.2007.01.003

Conclusions. – La méthode proposée offre une possibilité d'évaluation des fuites qui est continue, précise et non invasive. Elle peut ainsi être utilisée au lit du patient et une analyse en temps réel des données permettrait de trouver les réglages optimaux des ventilateurs : associer la diminution de la quantité de fuites et le meilleur confort du patient.

Keywords: Respiratory inductance plethysmography; Respiratory failure; Long-term assisted ventilation

Mots clés : Pléthysmographie respiratoire par inductance ; Insuffisance respiratoire ; Ventilation assistée à long terme

1. Introduction

Mechanical ventilation efficacy depends upon adaptation of assisted ventilation to the patient's need. This is particularly crucial in patients with chronic respiratory failure because they not only require long-term ventilatory support but they are also conscious. One major problem in long-term assisted ventilation is the existence of air leakage from around the mask and through the mouth in patients receiving non-invasive ventilation and from around the cuffless tracheostomy tube in invasively ventilated patients.

The most frequent mechanism responsible for the increasing leaks during sleeping is air which escapes out of the mouth. Such leaking may not only create uncomfortable side effects for the patient, it can also lead to an incomplete response to therapy. Leakage of air out of the mouth has been shown to adversely affect sleep quality [1,2] and contribute to failure to fully correct nocturnal gas exchange [3], all of which may affect the patient's tolerance and long-term response to therapy.

The detrimental effect of leaks is not solely the reduction in alveolar ventilation [3]. During continuous positive airway pressure leakage has been shown to increase nasal resistance [4]. Large leaks may interfere with ventilator cycling and compromise minute ventilation [5]. However, the greater problem associated with air leakage is that it increases during sleep [6,7,1] leading to impairment of sleep quality despite no marked decrease in oxygenation. Sleep disorders associated with leaks have been observed in patients with COPD [8] as well as in patients with neuromuscular disease [1,2]. Reducing the amount of air leakage has been considered to be the principal means of improving efficacy of assisted ventilation [9]. This has been demonstrated in neuromuscular patients during wakefulness [3].

Leak measurement may be considered as a prerequisite to leak compensation. However, few studies have been devoted to leak measurement. Using a lung model Mehta et al. [5] tested leak-compensating capacity of various positive pressure ventilators. They found that the tidal volume differed between ventilators even in the absence of leakage. Their study also demonstrated that the ability to compensate for leakage varies considerably among ventilators. Respiratory inductance plethysmography (RIP) have been used by Meyer et al. [2] to measure air leaks in patients with symptoms of chronic hypoventilation. However, values of leaks were obtained by subtracting the volume obtained by calibrated RIP from the volume of air delivered through the nose.

The aim of the present study was to develop a non-invasive method of estimating tidal volume changes in patients on mechanical ventilation not only during wakefulness but also during sleep. Ventilator settings are generally adjusted only when awake while major detrimental effect of leakage is observed mainly during sleep leading to poor sleep quality. The method was developed using data obtained from patients with neuromuscular disease invasively or non-invasively ventilated during sleep. Non-calibrated RIP was used to evaluate breath-by-breath changes in tidal volume in proportion of their values during sleep latency time; decreases in tidal volume indicate increases in air leaks.

2. Methods and materials

2.1. Patients

The data analyzed in this study were obtained from 14 patients (Table 1) with neuromuscular disorders admitted to the Raymond-Poincaré Hospital in Garches (France) for a routine evaluation of assisted ventilation during sleep. Institutional review board approval was not necessary as no additional device or recording time to the routine protocol was used. Informed consent has been obtained from patients for anonymous analysis of their recording aimed at technical research as authorized by national ethical committee.

Seven patients were ventilated through a cufless tracheostomy and seven patients received non-invasive ventilation through a nasal mask.

Twelve patients were ventilated with an EOLE 3 ventilator (EOLE 3, ResMed, Saint-Priest, France) and the other two patients with an AIROX HOME 2 ventilator (Tyco, Elancourt, France). The ventilation mode was either volume control (five patients) or volume-assisted control (nine patients). The volume and frequency setting for each patient and the blood gas analysis during mechanical ventilation while awake are given in Table 2.

2.2. Measurements

In addition to the polysomnographic recording, thorax and abdomen section surface area changes were recorded using a computer-assisted respiratory inductance plethysmograph the Visuresp® (RBI, Meylan, France) system. A flow signal, measured by a pneumotachograph (PNT) inserted between the ventilator and the patient's interface device (tracheal tube or nasal mask), was also recorded, using the Visuresp® system.

2.3. Signal processing and analysis

The Visuresp® system includes specific signal processing software that provides cycle delimitation on a flow signal

Table 1
Patients characteristics

Patients	Age (years)	Sex	Diagnosis	Weight (kg)	Height (cm)	VC (%)	MIP (cmH_2O)
#1	21	M	Myotonic dystrophy	50	160	43	14
#2 ***T***	37	M	Myasthenia gravis	63	182	36	24
#3	69	M	Acid maltase deficiency	65	170	51	17
#4	53	M	Acid maltase deficiency	76	168	50	36
#5 ***T***	52	M	Poliomyelitis	65	170	NA	NA
#6	65	M	Poliomyelitis	43	165	36	32
#7	38	M	Limb girdle muscular dystrophy	30	170	12	16
#8 ***T***	68	M	Amyotrophic lateral sclerosis	60	191	49	32
#9	53	F	Myasthenia gravis	62	162	40	30
#10 ***T***	31	M	Duchenne muscular dystrophy	43	163	9	20
#11	19	M	Duchenne muscular dystrophy	24	164	8	11
#12 ***T***	71	M	Poliomyelitis	43	156	28	40
#13 ***T***	47	F	Inclusion body myositis	59	162	16	19
#14 ***T***	41	M	Lipid myopathy	80	180	34	20

T: tracheostomized patients; VC: vital capacity; %: percentage of predicted values according to the guideline (ref = ERJ 93); MIP: maximal inspiratory pressure.

Table 2
Mechanical ventilation settings, blood gases when awake and SaO_2 during sleep

Patients	VT (ml)	*F* (min^{-1})	PaO_2 (kPa)	$PaCO_2$ (kPa)	pH	HCO_3^- ($meql^{-1}$)	SaO_2		
							Mean (%)	Min (%)	< 90% (%TST)
#1	1100	15	14.60	4.30	7.47	23.30	94.1	83	3.2
#2 ***T***	600	16	12.90	4.60	7.43	23.90	95.6	NA	0
#3	560	20	11.30	3.90	7.49	23.10	96.5	96	0
#4	800	16	11.10	4.80	7.45	26.10	91.2	85	35.6
#5 ***T***	700	15	13.10	2.80	7.49	16.30	95.4	NA	1
#6	800	16	9.50	6.10	7.46	33.00	94.0	84	5
#7	750	17	14.30	3.30	7.53	21.60	96.0	85	< 1
#8 ***T***	700	18	16.20	3.90	7.45	22.70	96.1	NA	0
#9	780	15	9.10	5.60	7.42	26.60	87.9	71	49.9
#10 ***T***	420	17	12.50	5.10	7.41	24.70	95.3	NA	0
#11	530	15	14.50	4.30	7.39	20.20	95.2	NA	0
#12 ***T***	550	20	12.10	3.60	7.53	23.50	97.3	NA	0
#13 ***T***	600	17	13.00	3.70	7.43	18.60	93.3	86	4.6
#14 ***T***	440	22	11.60	3.40	7.50	19.70	93.9	89	1

T: tracheostomized patients; VT: volume delivered by the ventilator; *F*: ventilator back up rate; TST: total sleep time.

obtained from either PNT or RIP derivative. A breath-by-breath analysis of the PNT and RIP signals was then performed. The positive area of the flow signal recorded by PNT for each cycle is the insufflated volume (Vin) whereas the negative area corresponds to the expiratory volume (Vex). For a given cycle, an expiratory volume less than the insufflated volume indicates the presence of leaks. Each insufflation causes an increase in both thoracic and abdominal RIP signals. For each breath, thoracic (Vtho) and abdominal (Vabd) tidal volumes can be estimated from the difference between the maximum and minimum value of the thoracic signal and the abdominal signal, respectively.

For each recording, samples of 25–30 breaths in steady state were taken at intervals of 20 min throughout the night. Mean values of Vin, Vex, Vtho and Vabd were calculated for each sample.

2.4. Leak estimation during sleep

The method proposed in this study is based on:

- the evaluation of breath-by-breath changes in tidal volume. The tidal volume received during each breath by the subject is distributed between Vtho and Vabd and may be theoretically denoted as: (Gain factor) × [α Vtho + (1 – α) Vabd] with $0 \le \alpha \le 1$.
  Any leaks during insufflation would result in decrease in tidal volume and thus a decrease in both Vtho and Vabd. However, the amount of the decrease in tidal volume (or increase in leakage) will be at most equal to the maximum decrease in either Vtho or Vabd and at least equal to the minimum decrease in either Vtho or Vabd. Accordingly, changes in the amount of leaks can be estimated as being comprised in the limits of the decreases in Vtho and Vabd. As α is not calculated, only relative changes in Vtho and Vabd are expressed for each recording;
- the fact that leaks increase during sleep compared to during sleep latency time. Values of Vtho and Vabd during sleep latency time were thus considered to be a maximum and were given the value 100% and all subsequent samples were expressed in %age of these values: *Vtho* is given in %age of Vtho during sleep latency time and *Vabd* in %age of Vabd during sleep latency time.

To compare leaks estimated by the proposed method to leaks evaluated by Vin – Vex, this difference during sleep was also expressed in %age of its value during sleep latency time.

Vex less than Vin indicates the presence of air leaks, which may take place during insufflation (in-leaks), expiration (ex-leaks) or both.

$$\text{Vin} = \text{in} - \text{leaks} + \text{Vex} + \text{ex} - \text{leaks}$$

Air leaks during insufflation result in decrease in tidal volume.

3. Results

Fig. 1 shows the mean values of *Vtho* and *Vabd* for the 27 samples taken throughout the night in subject #1. The first column for both *Vtho* and *Vabd* is considered as the reference taken from the sample recorded during sleep latency time and is given the value 100%. All other samples recorded during sleep are expressed in proportion of these values. It can be seen that all *Vtho* and *Vabd* for the other samples are smaller than the reference value.

Vtho and *Vabd* vary throughout the night. Although these variations for most samples are in the same direction they are not always parallel. These variations indicate changes in the tidal volume and following in the amount of leakage.

In order to show the variation in the leaks, (100 – *Vtho*) and (100 – *Vabd*) for each sample of Fig. 1 were plotted in Fig. 2. The amount of leaks for each sample is comprised between these two values: at most equal to the highest value of either (100 – *Vtho*) or (100 – *Vabd*) and at least equal to the lowest value of either (100 – *Vtho*) and (100 – *Vabd*). The zone delimited by (100 – *Vtho*) and (100 – *Vabd*) may be considered as the leakage zone for this recording. To compare this leak estimation to leaks measured by Vin – Vex, for each sample *Vin – Vex* in proportion of its value during the sleep latency time was calculated and plotted as the solid line on the same figure. For this subject, *Vin – Vex* line follows closely the leakage zone, although slightly higher.

Similar graphs for all subjects are given in Fig. 3, where they are classified according to the use of tracheal tube (T) or mask (M) and the ventilatory mode: volume controlled (VC) or volume assist control (VAC).

For subjects #2 and 8 with cufless tracheostomy and subject #9 ventilated with mask, the *Vin – Vex* line is markedly higher than the leakage zone suggesting that the Vin – Vex difference overestimates the amount of leaks. For the other subjects the *Vin – Vex* line is above the leakage zone apart for subject #10.

However, no obvious difference appears between these graphs related to the use of tracheal tube or mask as well as the ventilatory mode.

4. Discussion

The important finding of this study is that RIP may be used for a continuous evaluation of changes in tidal volume throughout sleep period in mechanical ventilation. They could be due to the occurrence of leakage, and in a less degree to a change of patient–ventilator coordination.

The proposed method is easy to use and does not require RIP calibration. In these patients with neuromuscular disease

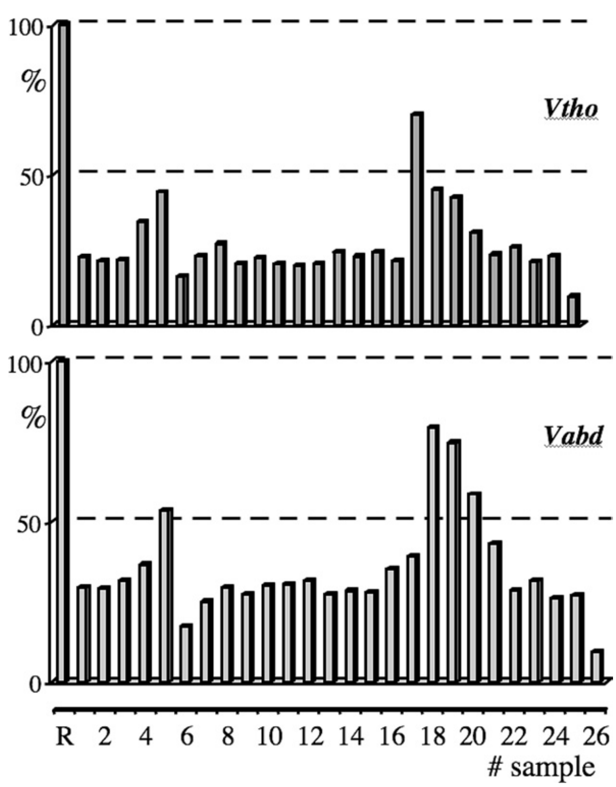

Fig. 1. Variations in *Vtho* and *Vabd* throughout sleep period in subject # 1. Each column is a mean value calculated over 25–30 breaths of either Vtho or Vabd from RIP signals. *Vtho* or *Vabd* are expressed in percentage of the values during sleep latency time.

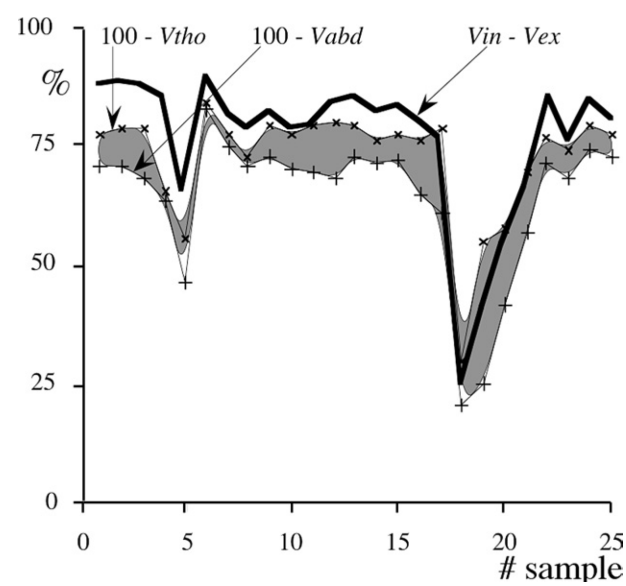

Fig. 2. Estimation of changes in leaks from the samples of Fig. 1. These changes are compared to those obtained from flow meter (Vin – Vex).
Each line was traced between 100 – *Vtho* (x) and 100 – *Vabd* (+) samples; the zone delimited by these two lines is the leakage zone; the thick line is *Vin – Vex* in percentage of its value during sleep latency time.
Note changes in the amount of leakage throughout the night, almost parallel changes in 100 – *Vtho* (x) and 100 – *Vabd* (+) and finally, parallel changes in *Vin – Vex* with however higher values; the thick line is always above the gray zone.

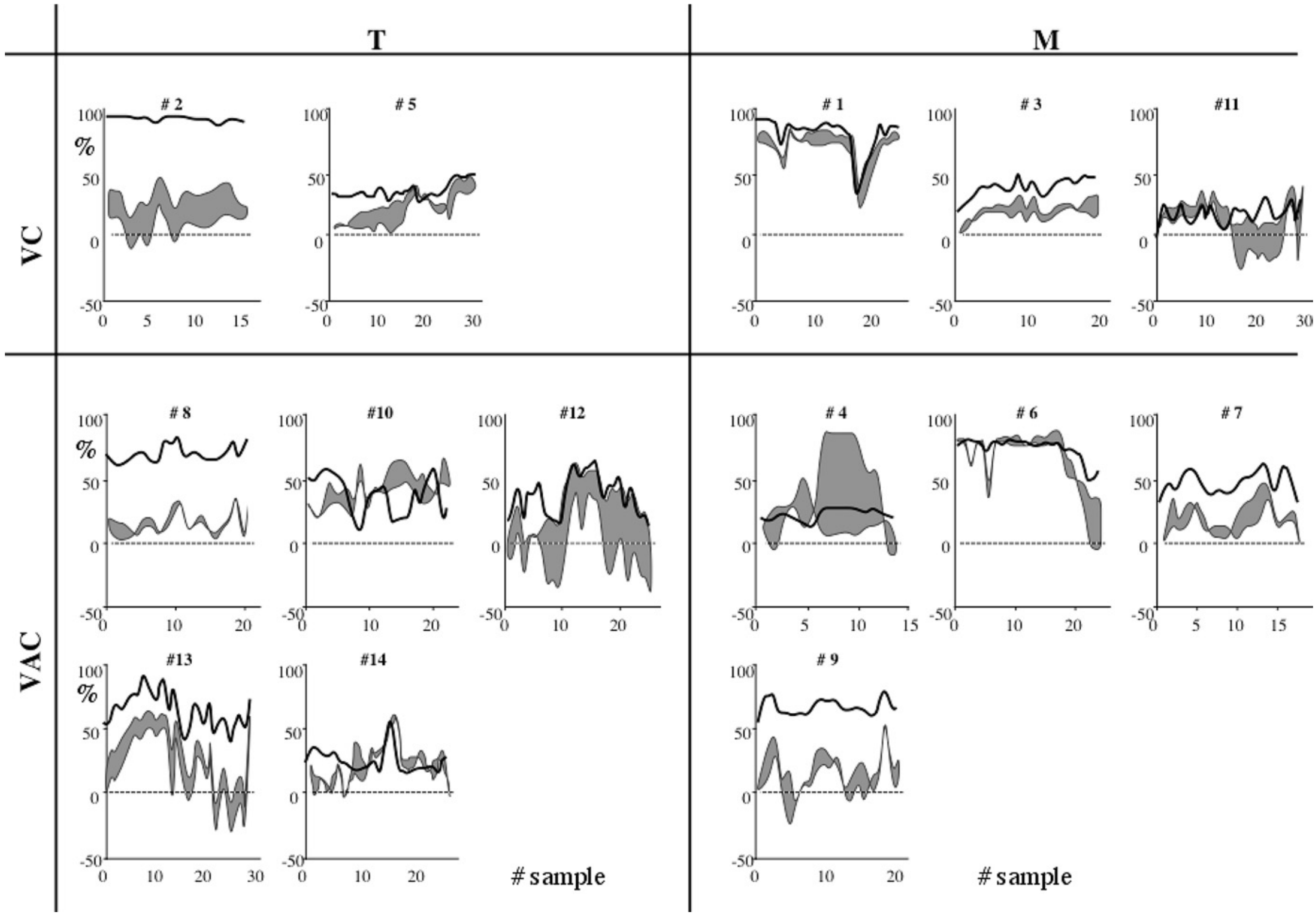

Fig. 3. Plots as in Fig. 2 for all subjects.
Plots are classified according to the use of tracheal tube (T) or mask (M) and the ventilatory mode: VC or VAC.

no obstructive event occurred under mechanical ventilation and so there was no noteworthy phase difference between Abd and Tho signals. In addition, the Visuresp® software provides breath-by-breath Abd – Tho phase difference and thus, leak calculation may be performed on those breaths free of obstructive events.

The study was carried out using data from patients with neuromuscular disease because reducing leaks for such patients is a major clinical objective [10]. Indeed, neuromuscular disorders often involve respiratory muscles and respiratory failure is the principal cause of morbidity and mortality [11–13]. Thus ventilatory assistance constitutes an important part of disease management. Furthermore, once initiated, ventilatory assistance is rarely discontinued and most patients are being treated at home. Non-invasive ventilation through a nasal mask therefore represents the most suitable treatment and is proposed for patients with stable or slowly progressing neuromuscular diseases [14]. However, air leaks through the mouth are common in this type of ventilation, especially during sleep. As the neuromuscular disease progresses, hypoventilation starts to occurs during the daytime, and additional daytime ventilation is offered [17]. When non-invasive ventilation is inadequately effective, poorly tolerated or not feasible owing to severe upper airway dysfunction, invasive ventilation via a tracheostomy may be considered [17].

Air leaks are usually measured using a calibrated flow meter placed between the ventilator and the patient, so that the tidal volume delivered by the ventilator (Vin) and the expired volume (Vex) can be measured. However, this measurement may be inaccurate [15]. Leaks are considered to be present if Vex is less than Vin [3,4], but if leaks also take place during expiration then the Vin – Vex difference will overestimate the magnitude of leaks during insufflation. RIP provides signals proportional to the changes in volume of the thorax and the abdomen during breathing. It can thus provide a measurement of the air actually entering the lungs and possibly estimate changes in the amount of those leaks with significant respiratory effects.

The method proposed here was designed to estimate changes in the amount of leakage during sleep. It relies simply on the assumption that the values of RIP signals during sleep latency time are systematically greater than those recorded during sleep. This assumption is based on the observation that there is an increase in leaks during sleep in neuromuscular disease patients with nasal masks [7] as well as in those with cuffless tracheostomy [4] and also on the fact that optimal mechanical ventilation was adjusted during wakefulness following polysomnography [16].

It can be seen in Fig. 1 that of all samples the sleep latency sample had the highest value, suggesting that the values measured during sleep latency may serve as satisfactory reference values.

In Fig. 3, for few samples, usually successive samples, either *100 – Vtho* or *100 – Vabd* were below zero. This indicates that the thoracic and/or abdominal volume of these samples are higher than their value during sleep latency time. This may be due to changes in body position so that the sleep latency time sample, if not recorded in the same position, can no more be considered as a reference. Another possibility could be that leakage, which was present during wakefulness for some patients, was less severe during this short night period.

Although the patients in this study show little movement during sleep a further development of the method could include simultaneous recording of the body position, in order to discard those samples not obtained in the sleep latency position.

In Fig. 2 the zone delimited by *100 – Vtho* and *100 – Vabd* is the leakage zone, the thick line obtained from *Vin – Vex* is above the leakage zone indicating an overestimation of the leaks when measured by *Vin – Vex*. More important is the observation that all variations are parallel attesting the existence of changes in the amount of leakage throughout the sleep period. Such variations in leakage have been observed also by Meyer et al. [2] and Bach and Alba [1] and were associated to episodes of arousal. Various factors have been put forward to explain the mechanism by which air leakage may contribute to arousals, oxygen desaturation [4], end tidal CO_2, sensation of airflow or noise [7].

Variations in the amount of leakage were observed in all subjects as shown in Fig. 3. Large differences between *Vtho* and *Vabd*, entailing large leakage zone such as in subject #12 or #4 may be due to measurement error mainly explained by changes in body position.

Despite the existence of leakage it can be seen in Table 2 that only one patient had a $SaO_2 < 90\%$ and five patients a $SaO_2 < 95\%$. However, the values of ventilation setting in most patients are very high and this may explain the fact that notwithstanding leaks, the amount of air that reached the lungs provided satisfactory SaO_2. Furthermore, well-maintained oxygenation despite prevalent leaking has been reported by several authors [7,4]. On the other hand, for those patients with low values of SaO_2 (for example patient # 9) the values of PaO_2 and $PaCO_2$ suggest that there were leaks even when the patients were awake as this has been observed by Gonzalez et al. [3].

In conclusion, RIP method offers a reliable, non-invasive, bedside evaluation of tidal volume changes in ventilated patients who are not expected not trigger their ventilator. RIP method can also underestimate the leaks when using pressure limited ventilation, considering that compensatory systems exists with these devices. Nevertheless, if the RIP system cannot measure the leaks when using pressure limited ventilation, it is able to approximate volume inflation changes induced by leakage. Recording of the signals can be easily carried out and repeated as often as required on ventilated patients treated at home. In a care environment, on-line analysis can also be carried out with various ventilator setting in order to compensate for leakage [18,5] and find the optimal ventilator settings to assure proper ventilation and improve the quality of sleep. This method can easily be adapted for the children.

References

[1] Bach JR, Alba AS. Tracheostomy ventilation. A study of efficacy with deflated cuffs and cuffless tubes. Chest 1990;97:679–83.

[2] Meyer TJ, Pressman MR, Benditt J, McCool FD, Millman RP, Natarajan R, et al. Air leaking through the mouth during nocturnal nasal ventilation: effect on sleep quality. Sleep 1997;20:561–9.

[3] Gonzalez J, Sharshar T, Hart N, Chadda K, Raphaël JC, Lofaso F. Air leaks during mechanical ventilation as a cause of persistent hypercapnia in neuromuscular disorders. Intensive Care Med 2003;29:596–602.

[4] Richards GN, Cistulli PA, Ungar G, Berthon-Jones M, Sullivan CE. Mouth leak with nasal continuous positive airway pressure increases nasal airways resistance. Am J Respir Crit Care Med 1996;154:182–6.

[5] Mehta S, McCool FD, Hill NS. Leak compensation in positive pressure ventilators: a lung model study. Eur Respir J 2001;17:259–67.

[6] Rodenstein DO, Levy P. To sleep, perchance to leak. Eur Respir J 1999; 14:1241–3.

[7] Bourke SC, Gibson GJ. Sleep and breathing in neuromuscular disease. Eur Respir J 2002;19:1120–94.

[8] Teschler H, Stampa J, Ragette R, Konietzko N, Berthon-Jones M. Effect of mouth leak on effectiveness of nasal bilevel ventilatory assistance and sleep architecture. Eur Respir J 1999;14:1251–7.

[9] Elliott MW. The interface: crucial for successful non-invasive ventilation. Eur Respir J 2004;23:7–8.

[10] Tzeng AC, Bach JR. Prevention of pulmonary morbidity for patients with neuromuscular disease. Chest 2000;118:1390–6.

[11] Raphaël JC, Chevret S, Chastang C, Bouvet F. Randomised trial of preventive nasal ventilation in Duchenne muscular dystrophy. French Multicentre Cooperative Group on home mechanical ventilation assistance in Duchenne de boulogne muscular dystrophy. Lancet 1994;25:1600–4.

[12] Raphael JC, Chevret S, Auriant I, Clair B, Gajdos P. Ventilation à domicile au long cours dans les maladies neurologiques de l'adulte. Rev Mal Respir 1998;15:495–505.

[13] Anonymous. Clinical indications for non-invasive positive pressure ventilation in chronic respiratory failure due to restrictive lung disease, COPD and nocturnal hypoventilation—a consensus conference report. Chest 1999;116:521–34.

[14] Hill NS. Ventilator management for neuromuscular disease. Am J Respir Crit Care Med 2002;23:293–305.

[15] Lofaso F, Fodil R, Lorino H, Leroux K, Quintel A, Leroy A, et al. Inaccuracy of tidal volume delivered by home mechanical ventilators. Eur Respir J 2000;15:338–41.

[16] Lofaso F, Quera-Salva MA. Polysomnography for the management of progressive neuromuscular disorders. Eur Respir J 2002;19:989–90.

[17] Lofaso F, Orlikowski D, Raphael JC. Ventilatory assistance in patients with Duchenne muscular dystrophy. Eur Respir J 2006;28:468–9.

[18] Parreira VF, Jounieaux V, Delguste P, Aubert G, Dury M, Rodenstein DO. Determinants of effective ventilation during nasal intermittent positive pressure ventilation. Eur Respir J 1997;10:1975–82.