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Carbon dioxide monitoring during long-term noninvasive respiratory support in children

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Abstract *Introduction:* Routine monitoring of noninvasive respiratory support relies on nocturnal pulse oximetry and daytime arterial blood gases, without systematic nocturnal carbon dioxide recording. The aim of the study was to assess if overnight pulse oximetry and daytime blood gases are sufficiently accurate to detect nocturnal hypoventilation in children receiving long-term noninvasive respiratory support. *Materials and methods:* Pulse oximetry and carbon dioxide pressure measured by capillary arterialized blood gases and a combined transcutaneous carbon dioxide and pulse oximetry (PtcCO₂/SpO₂) monitor were compared in 65 patients (asthma, $n = 16$, recurrent bronchitis, $n = 8$, lung infection, $n = 8$, cystic fibrosis, $n = 15$, interstitial lung disease, $n = 6$, neuromuscular disease, $n = 12$). Daytime capillary arterialized blood gases and nocturnal recording of pulse oximetry and carbon dioxide by means of a combined PtcCO₂/SpO₂ monitor were performed in 50 other patients receiving nocturnal noninvasive respiratory support at home. *Results:* A correlation was observed between

pulse oximetry ($r = 0.832$, $P < 0.0001$) and carbon dioxide pressure ($r = 0.644$, $P < 0.0001$) measured by capillary arterialized blood gases and the combined PtcCO₂/SpO₂ monitor. Twenty-one of the 50 patients (42%) on long-term noninvasive respiratory support presented nocturnal hypercapnia, defined by a PtcCO₂ value >50 mmHg, without nocturnal hypoxemia. Daytime capillary arterialized carbon dioxide levels were normal in 18 of these 21 patients. *Conclusions:* Nocturnal hypercapnia may occur in children receiving nocturnal noninvasive respiratory support at home. Nocturnal pulse oximetry and daytime arterial blood gases are not sufficiently accurate to diagnose nocturnal hypercapnia, underlying the importance of a systematic carbon dioxide monitoring in children receiving noninvasive respiratory support.

Keywords Carbon dioxide · Noninvasive positive pressure ventilation · Child · Arterial blood gases

Introduction

Noninvasive respiratory support by means of positive pressure ventilation (NPPV) or continuous positive airway pressure (CPAP) has become a technique that is

increasingly used in infants and children for the treatment of chronic respiratory failure at home. Indeed, noninvasive respiratory support may correct nocturnal hypoventilation in children with neuromuscular or lung disease, disorders of ventilatory control, or abnormalities

of the upper airways [1–3]. Initiation and adaptation is generally performed in the hospital and ideally a sleep study with noninvasive respiratory support showing the normalization of the sleep pattern and the correction of nocturnal hypoxemia and hypercapnia is required before discharge. Polysomnography (PSG) represents the gold standard for assessing the correction of sleep and gas abnormalities with noninvasive respiratory support but this investigation is time consuming, expensive, technically demanding, and not feasible on a routine basis. As such, a consensus statement from the American College of Chest Physicians has recommended assessing diurnal gas exchange in order to confirm the efficacy of noninvasive respiratory support at initiation and during follow up [4]. However, it is well known that gas exchange during wakefulness does not reflect the situation during sleep. As the primary aim of noninvasive respiratory support is to correct alveolar hypoventilation, normalization of carbon dioxide (CO₂) during noninvasive respiratory support is a major objective. Noninvasive arterial oxygenation is routinely and satisfactorily monitored with transcutaneous pulse oximeters. However, noninvasive monitoring of CO₂ is more complex. End-tidal CO₂ is not appropriate for noninvasive respiratory support because of leaks. Traditional transcutaneous monitors require frequent repositioning because of heating and their accuracy is not always sufficient [5–7]. Most centers rely therefore on nocturnal pulse oximetry (SpO₂) and daytime arterial blood gases to monitor noninvasive respiratory support, without nocturnal CO₂ monitoring.

New devices are available that allow a continuous noninvasive monitoring of CO₂. One of these devices is the SenTec Digital Monitor (SenTec Inc, Therwil, Switzerland) which measures SpO₂ and transcutaneous CO₂ (PtcCO₂). The main advantage of this device is that it can monitor SpO₂ and CO₂ over several hours by means of a disposable clip electrode applied on the ear with an excellent local tolerance. The experience with this combined PtcCO₂/SpO₂ monitor in adult patients is encouraging with an excellent correlation of the SpO₂ and PtcCO₂ with the arterial blood gases [8].

The aim of the present study was first, to validate the combined PtcCO₂/SpO₂ monitor in children and second, to assess the need for a systematic overnight CO₂ recording in children receiving long-term noninvasive respiratory support at home.

Materials and methods

Patients

For the first validation study, all consecutive patients referred to the lung function laboratory during one month for daytime assessment of gas exchange were enrolled.

These patients suffered from various respiratory diseases such as asthma, $n = 16$, recurrent bronchitis, $n = 8$, lung infection, $n = 8$, cystic fibrosis, $n = 15$, interstitial lung disease, $n = 6$, or neuromuscular disease, $n = 12$.

For the second study, consecutive patients using nocturnal noninvasive respiratory support at home were enrolled during their routine follow up if (1) they were in a stable condition, (2) were using nocturnal noninvasive respiratory support for at least one month, and (3) had no clinical symptoms of nocturnal hypoventilation such as frequent arousals, nocturnal agitation, or daytime fatigue and sleepiness.

For both studies, only children older than one year of age were included because the ear clip of the PtcCO₂/SpO₂ monitor is too large for small infants. Children with dark skin were also excluded because of inaccurate SpO₂ values, as has been observed with other devices [9].

All the parents, and if possible the patients, gave informed written consent for the two studies which were approved by the local ethical committee.

Validation of the combined PtcCO₂/SpO₂ monitor

Combined PtcCO₂/SpO₂ monitoring was performed with the SenTec Digital Monitor (software version SMB SW-V06.10; MPB SW-V04.03) and the V-Sign™ Sensor being applied to the second earlobe with a dedicated Ear Clip (SenTec AG, Therwil, Switzerland). This fully digital sensor combines the elements of an electrochemical Severinghaus-type CO₂ tension sensor with the optical elements of conventional SpO₂ sensors, thus providing noninvasive and continuous PtcCO₂ and SpO₂ monitoring. The sensor is warmed to a constant surface temperature of 42°C to improve local arterialization of the measurement site. Prior application of the sensor to the patient, the sensor was prepared and calibrated as per the manufacturer recommendations. The sensor was then applied to the patient's earlobe for 15 min, allowing a correct stabilization of the PtcCO₂ and SpO₂ values.

Thereafter, capillary arterialized blood gases, giving the results of SaO₂ and PaCO₂, were performed on the opposite ear according to a technique validated in our laboratory as previously described [10]. Briefly, arterialization of the earlobe was achieved by subjecting it to a 7 min heating by an infra red lamp (100 watts) placed at a distance of approximately 10 cm. The face was covered in order to protect it. A microlance was used to pierce the marginal edge of the middle portion of the ear to a depth of 2–3 mm. Three heparinized capillary tubes were filled successively by capillary action. The time taken for collection did not exceed 2 min. The tubes were immediately plugged with paste and placed in ice water. Before analysis, the capillary tubes were warmed to 37°C. The three capillary tubes were analyzed within the 3 min of collection (ABL810 Flex, Radiometer, Neuilly Plaisance,

France). For SaO_2 and partial arterial carbon dioxide (PaCO_2), the mean value of the three tubes was calculated.

During the punctures, SpO_2 and PtcCO_2 were read from the combined $\text{PtcCO}_2/\text{SpO}_2$ monitor. For this first study, the patients were classified into three age groups: <6 years, 7–12 years, and 13–18 years, in order to validate the monitor in the different age groups.

Overnight SpO_2 and PtcCO_2 recording by the combined $\text{PtcCO}_2/\text{SpO}_2$ monitor

The overnight SpO_2 and PtcCO_2 recording was started at usual bedtime and care was taken to respect the patient's sleep. The monitoring lasted at least 6 h and sleep with noninvasive respiratory support as well as the correct positioning of the nasal mask and the ear clip was regularly checked by the attending nurse during the night. Capillary arterialized blood gases, with the analysis of PaO_2 , PaCO_2 , pH and bicarbonates, were performed on the following morning, between 11 and 12 am.

Analysis of the data

The validation of SpO_2 and PtcCO_2 values read on the combined $\text{PtcCO}_2/\text{SpO}_2$ monitor with the capillary arterialized blood gases was performed by calculating the Pearson correlation coefficient (r) between PaCO_2 and PtcCO_2 , and SaO_2 and SpO_2 . A concordance study was done by a Bland Altman analysis [11].

For the overnight sleep study, SpO_2 was considered abnormal if SpO_2 was $\leq 90\%$ for $\geq 10\%$ of nocturnal recording time or if SpO_2 was $\leq 90\%$ for at least 5 continuous minutes. PtcCO_2 was considered abnormal if PtcCO_2 was ≥ 50 mm Hg for $\geq 10\%$ of nocturnal recording time or if PtcCO_2 was ≥ 50 mm Hg for at least 5 continuous minutes. PaO_2 obtained by the capillary arterialized technique was considered normal when the value was within the normal value for age ± 2 standard deviation (± 10 mm Hg) and PaCO_2 was considered normal when the value was within 35 ± 2 standard deviation (± 10 mm Hg) [10, 12]. A secondary analysis was performed with a cut off value of nocturnal SpO_2 of 92 and 95%.

Results

Validation of the combined $\text{PtcCO}_2/\text{SpO}_2$ monitor

Sixty five consecutive patients referred to the lung function laboratory for capillary arterialized blood gases participated in the validation of the combined $\text{PtcCO}_2/\text{SpO}_2$

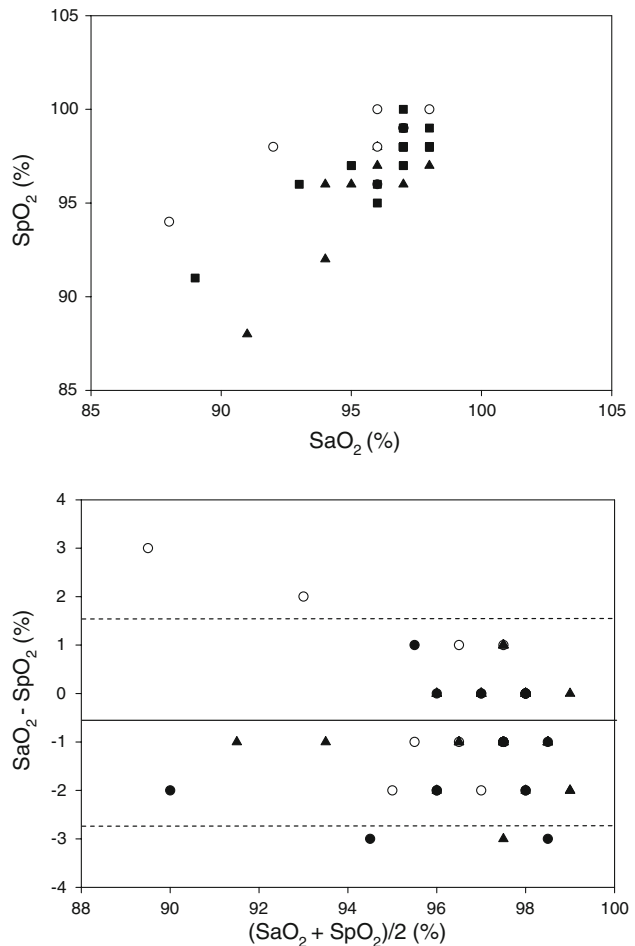


Fig. 1 Top Relationship between pulse oximetry measured during capillary arterialized blood gases (SaO_2 , %) and pulse oximetry measured by the combined $\text{PtcCO}_2/\text{SpO}_2$ monitor (SpO_2 , %) in children aged 0–6 years (open circles), 7–12 years (black triangles), and aged 13–18 years (black circles). Bottom Difference between pulse oximetry measured during capillary arterialized blood gases (SaO_2 , %) and pulse oximetry measured by the combined $\text{PtcCO}_2/\text{SpO}_2$ monitor (SpO_2 , %) against the mean of these two variables in children aged 0–6 years (open circles), 7–12 years (black triangles), and aged 13–18 years (black circles). The plain lines represent the mean values and the dotted lines the ± 2 standard deviation

SpO_2 monitor. None of the patients was excluded because of a technical problem or intolerance of the ear clip. Eight patients were aged 1–6 years, 35 were aged 7–12 years, and 22 were aged 13–18 years. SaO_2 correlated significantly with SpO_2 in the total population ($n = 65$), ($r = 0.832$, $P < 0.0001$) and in the 3 age groups (0–6 years: $r = 0.846$, $P = 0.03$; 7–12 years: $r = 0.814$, $P < 0.0001$, 13–18 years: $r = 0.855$, $P < 0.0001$) (Fig. 1). The Bland Altman analysis showed that SpO_2 moderately overestimated SaO_2 . PaCO_2 correlated also with PtcCO_2 in the total population ($r = 0.644$, $P < 0.0001$) and the 3 age groups (0–6 years: $r = 0.931$,

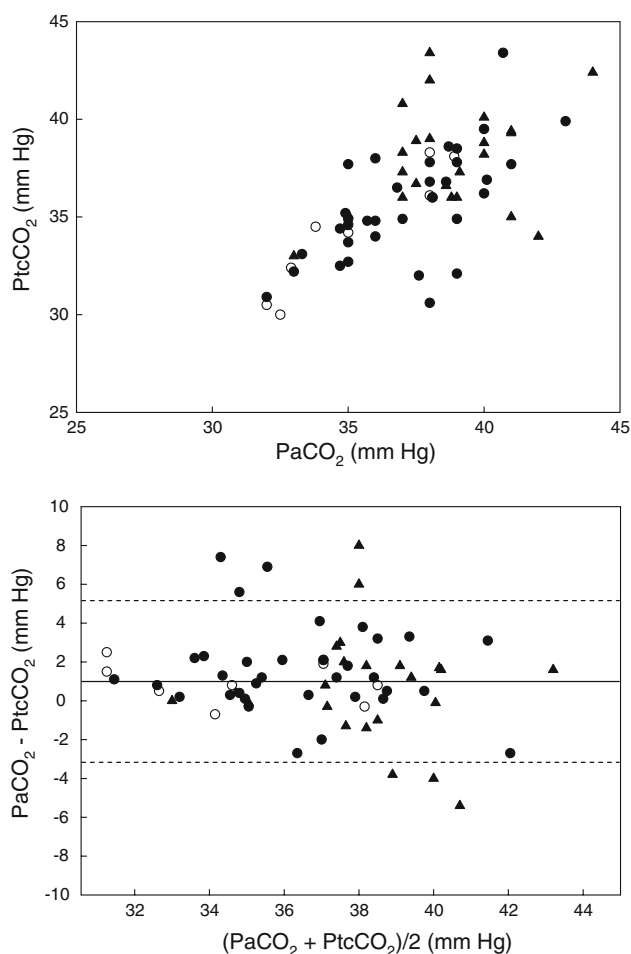


Fig. 2 Top Relationship between carbon dioxide measured during capillary arterialized blood gases (PaCO_2 , mm Hg) and carbon dioxide measured by the combined $\text{PtcCO}_2/\text{SpO}_2$ monitor (PtcCO_2 , mm Hg) in children aged 0–6 years (open circles), 7–12 years (black triangles), and aged 13–18 years (black circles). Bottom Difference between carbon dioxide measured during capillary arterialized blood gases (PaCO_2 , mm Hg) and carbon dioxide measured by the combined $\text{PtcCO}_2/\text{SpO}_2$ monitor (PtcCO_2 , mm Hg) against the mean of these two variables in children aged 0–6 years (open circles), 7–12 years (black triangles), and aged 13–18 years (black circles). The plain lines represent the mean values and the dotted lines the ± 2 standard deviation

$P = 0.007$; 7–12 years: $r = 0.630$, $P < 0.0001$, 13–18 years: $r = 0.505$, $P < 0.02$ (Fig. 2). The Bland Altman analysis showed that PtcCO_2 moderately underestimated PaCO_2 .

Overnight SpO_2 and PtcCO_2 recording by the combined $\text{PtcCO}_2/\text{SpO}_2$ monitor

During a 3-months period, 56 patients fulfilled the inclusion criteria and accepted to participate to the study. Six patients were excluded because of technical problems,

Table 1 Characteristics of the patients

	Patients $n = 50$
Age (years)	8.5 ± 5.2
Male/Female	29/21
Primary disease	
Neuromuscular disease	23
Lung disease	2
Upper airway obstruction	25
Duration of noninvasive respiratory support (months)	24 ± 20
Ventilatory mode	
AC/VT	21
PS	19
CPAP	10
Nasal mask	
Industrial	25
Custom made	25

Data are given as mean \pm standard deviation

Abbreviations: AC/VT: assist control/volume-targeted ventilation, PS: pressure support ventilation, CPAP: continuous positive airway pressure

such as displacement or removal of the ear clip during the night ($n = 4$), or a nocturnal recording time < 4 h ($n = 2$). The 50 patients who were included in the study were treated with nocturnal noninvasive respiratory support for alveolar hypoventilation due to neuromuscular disease ($n = 23$), lung disease ($n = 2$), or upper airway obstruction ($n = 25$) due to Pierre Robin syndrome, vocal cord paralysis, Goldenhar syndrome, laryngo or tracheomalacia, Prader Willi syndrome, achondroplasia, or facial hypoplasia (Table 1). Patients with neuromuscular disease or lung disease were treated with volume-targeted ventilation ($n = 21$) or pressure-targeted ventilation ($n = 4$), whereas the patients with upper airway obstruction were treated with pressure-targeted ventilation ($n = 15$) or CPAP ($n = 10$). All the patients were equipped with nasal masks, with older patients using industrial masks and younger patients using custom made masks [13].

Table 2 shows the results of the nocturnal SpO_2 and PtcCO_2 recording by the combined $\text{PtcCO}_2/\text{SpO}_2$ monitor. Nocturnal gas exchange was normal in 28 patients when considering a cut off value of 90% for SpO_2 . Only one patient had a nocturnal $\text{SpO}_2 \leq 90\%$ without hypercapnia. Most importantly, 21 patients (42%) had a high nocturnal PtcCO_2 without hypoxemia. The mean pH of the 21 hypercapnic patients was not significantly different from the mean pH of the 28 patients having a normal nocturnal PtcCO_2 (7.42 ± 0.03 vs. 7.41 ± 0.02), but the level of daytime bicarbonates was significantly higher in the hypercapnic group as compared to the normocapnic group (26 ± 2 vs. 24 ± 2 , $P < 0.0002$). The increase of the cut off for SpO_2 to 92% and 95% reduced the number of patients with nocturnal hypercapnia to 18 (36%) and 12 (24%) patients, respectively, but was not able to exclude the occurrence of hypercapnia.

Table 2 Results of the nocturnal recording by the combined PtcCO₂/SpO₂ monitor

	Normal PtcCO ₂ recording	Abnormal PtcCO ₂ recording	Total number of patients N = 50
SpO ₂ cut off of 90%			
SpO ₂ > 90%	28 (56%)	21 (42%)	49 (98%)
SpO ₂ ≤ 90%	1 (2%)	0 (0%)	1 (2%)
SpO ₂ cut off of 92%			
SpO ₂ > 92%	28 (46%)	18 (36%)	46 (92%)
SpO ₂ ≤ 92%	3 (6%)	1 (2%)	4 (8%)
SpO ₂ cut off of 95%			
SpO ₂ > 95%	18 (36%)	12 (24%)	30 (60%)
SpO ₂ ≤ 95%	13 (26%)	7 (14%)	20 (40%)

Abbreviations: PtcCO₂: transcutaneous carbon dioxide, SpO₂: pulse oximetry

PtcCO₂ was considered abnormal if PtcCO₂ was ≥50 mm Hg for ≥10% of nocturnal recording time, or for at least 5 continuous minutes

For the overnight sleep study, SpO₂ was considered abnormal if SpO₂ was ≤90%, ≤92% or ≤95% for ≥10% of nocturnal recording time, or for at least 5 continuous minutes

Table 3 Daytime partial arterial carbon dioxide pressure (PaCO₂) and nocturnal transcutaneous carbon dioxide (PtcCO₂) recording with the combined PtcCO₂/SpO₂ monitor in the 50 patients

	Patients with normal overnight PtcCO ₂ n = 29 (%)	Patients with abnormal overnight PtcCO ₂ n = 21 (%)
PaCO ₂ < 45 mm Hg	29 (48%)	18 (36%)
PaCO ₂ ≥ 45 mm Hg	0 (0%)	3 (6%)

In order to assess if nocturnal hypercapnia was associated with daytime hypercapnia, we compared PtcCO₂ and PaCO₂ for each patient (Table 3). Of the 21 patients who were hypercapnic during noninvasive respiratory support, 18 had a normal daytime PaCO₂.

We then compared the patients with a normal or an abnormal nocturnal PtcCO₂ recording. The two groups were comparable with regard to age, underlying disease, ventilatory mode, and type of nasal masks. The only difference was a shorter duration of noninvasive respiratory support in the hypercapnic group as compared to the non-hypercapnic group (15 ± 16 months vs. 28 + 21 months, respectively, P < 0.05).

Table 4 shows the interventions that were performed to improve nocturnal hypercapnia. The most frequent interventions were the change of the ventilatory settings or mode, the addition of an abdominal girdle or a chin strap, and/or the change of the interface. A control nocturnal SpO₂ and PtcCO₂ recording with daytime blood gases was available for 13 patients. After the intervention, the mean percentage of time spent with a PtcCO₂ ≥ 50 mm Hg decreased from 41 ± 32% to 10 ± 19%, P < 0.001. The mean daytime PaO₂, PaCO₂ and bicarbonates did not

Table 4 Interventions (not exclusive) in the patients who had nocturnal hypercapnia during noninvasive positive pressure ventilation (NPPV)

	Patients, n = 21
Change of the settings of noninvasive respiratory support	7
Change of interface	6
Addition of a chin strap	4
Addition of an abdominal girdle	3
Change of NPPV mode	2
Adaptation of brace	2
Other intervention*	3
No change	3
Tracheostomy	1

*The other interventions were: use of an insufflator-exsufflator, re-assessment by polysomnography, and nutritional support

change but the mean pH decreased after the intervention, from 7.42 ± 0.03 to 7.40 ± 0.02, P = 0.005.

Discussion

The present study shows first, that the values for SpO₂ and PtcCO₂ measured by a combined PtcCO₂/SpO₂ monitor are reliable in children, and second, that nocturnal hypercapnia is observed in a significant number of children treated at home with nocturnal long-term noninvasive respiratory support. This nocturnal hypoventilation is not associated with clinical symptoms of sleep disordered breathing, nocturnal desaturation, or daytime hypercapnia on capillary arterialized blood gases, underscoring the value of a systematic nocturnal PCO₂ monitoring in children treated by noninvasive respiratory support at home.

Validation of the combined PtcCO₂/SpO₂ monitor

In the first part of the study, we showed that values for SpO₂ and PtcCO₂ measured by the combined PtcCO₂/SpO₂ monitor were reliable in children of various age groups, as demonstrated previously in adult patients and healthy controls [8]. We excluded patients with dark skin because of inaccurate SpO₂ values results, as has been observed with other devices [9]. Also, patients with a too small ear lobe or ear rings were excluded. The skin tolerance of the combined PtcCO₂/SpO₂ monitor ear clip was excellent in all the patients, even during a whole night, without need for replacement because the electrode works with a low temperature (between 39°C and 42°C). Finally, the memory capability and easy analysis of the data are very convenient for the use of the combined PtcCO₂/SpO₂ monitor in clinical practice.

Overnight SpO₂ and PtcCO₂ recording by the combined PtcCO₂/SpO₂ monitor

This study is the first to show the results of an overnight gas exchange recording in a large group of children treated at home with nocturnal noninvasive respiratory support for various disorders. The conclusions of the present study are of major clinical importance. Indeed, 42% of the patients who were well acclimatized to non-invasive respiratory support, without evidence of symptoms of sleep disordered breathing, were hypercapnic during sleep. Most importantly, this nocturnal hypercapnia was not associated with nocturnal hypoxemia or abnormal daytime blood gases in approximately one third of the patients. Our results are not surprising. Indeed, persistent hypercapnia is common in both invasively and noninvasively ventilated neuromuscular adult patients [14]. A striking observation is that this persistent alveolar hypoventilation during sleep was not associated with overt symptoms of sleep disordered breathing and/or nocturnal desaturation and/or abnormal daytime blood gases, underscoring the need of a systematic overnight CO₂ monitoring in these patients. Importantly, the increase of the cut off value of nocturnal SpO₂ to 92% or 95% was associated with a reduction but not a suppression of the number of hypercapnic patients.

Interventions aiming at reducing or normalizing nocturnal hypercapnia were performed in all hypercapnic patients. As shown in other studies, simple practical measures such as changing the mask, using a chin strap, increasing minute ventilation and changing the type of the ventilator, were able to reduce the volume of air leaks and improve the efficacy of ventilation [14]. However, for these interventions to be effective, the pathophysiology of persistent nocturnal hypoventilation has to be fully understood. Within this context, polysomnography with recording of CO₂ and leaks remains the gold standard.

Limitations of the study

Our criteria to define nocturnal hypoxemia or hypercapnia are arbitrary and have not been validated in pediatric

patients. Indeed, the cut off values of SpO₂ and PtcCO₂ that are associated with significant side effects in children are not known. The cut off value of 50 mm Hg for PtcCO₂ retained in the present study is in agreement with the values defined by experts and consensus conferences [4]. It has been suggested that nocturnal hypoventilation is defined by a rise in overnight PCO₂ of >10 mm Hg or a PaCO₂ >49 mm Hg for more than 50% of sleep time [15]. However, more recently, some authors would consider lower peak values to adapt noninvasive ventilatory support, especially during rapid eye movement (REM) sleep [16, 17]. With regard to the lower limit of SpO₂, we analyzed the data with different cut offs. But, even when higher cut off levels of SpO₂ are considered, it is not possible to exclude nocturnal hypercapnia on the basis of a normal nocturnal SpO₂ monitoring in children treated with noninvasive respiratory support.

Capillary arterialized blood gases were performed in the morning. It is possible that the performance of blood gases in the afternoon would have shown different results. Indeed, in patients with cystic fibrosis, evening PaO₂ and morning PaCO₂ were correlated to nadir SaO₂ during sleep [18]. Also, evening PaO₂ was predictive of the increase in PtcCO₂ from non REM to REM sleep.

In conclusion, the present study shows that the combined PtcCO₂/SpO₂ monitor enables a valid and accurate recording of SpO₂ and PtcCO₂ in children. Systematic overnight SaO₂ and PtcCO₂ monitoring is recommended in children receiving long term nocturnal noninvasive respiratory support at home because asymptomatic hypercapnia may be observed in as much as one third of the patients.

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Conflict of interest All the authors certify that they do not have any conflict of interest to declare in relation to this work (such as employment, consultancies, stock ownership, honoraria, paid expert testimony, patent applications/registrations, and grants or other funding).

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