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LETTER

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End-tidal and transcutaneous CO_2 monitoring during sleep in children aged under three with suspected sleep apnea

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To the Editor,

Obstructive sleep apnea (OSA) is increasingly being recognized in children, with an estimated prevalence between 1% and 5%. Untreated OSA in children is associated with neurobehavioral, cardiovascular, growth, and metabolic abnormalities. For these reasons, early and accurate diagnosis and management of OSA in children is acknowledged as essential, and children are being referred to sleep units at ever younger ages.

The findings of attended polysomnography (PSG), the gold standard method for establishing the presence and severity of OSA, differ in children and adults. In children, OSA frequently manifests as prolonged partial obstruction of the upper airway with associated hypercapnia.[1] As a consequence, the American Academy of Sleep Medicine (AASM)[2] recommends monitoring for hypoventilation as a standard of care in PSG in children, while in adults this practice is considered optional.

Although arterial blood gas analysis is the standard method for ventilation assessment, it is not used in routine PSG. Both end-tidal CO_2 ($PetCO_2$) using nasal sampling cannula or transcutaneous CO_2 ($PtcCO_2$) monitoring are recommended for the noninvasive detection and quantification of hypoventilation during sleep studies.[2] Both sensors are used interchangeably in sleep units during PSG for suspected OSA in children. Previous studies comparing the two methods[3,4] have shown comparable results. However, these studies have included very few patients under 3 years of age, a population with different characteristics and whose presence in sleep units is growing. The under-threes are less obese than older children with OSA and frequently have more severe sleep-disordered breathing, often associated with craniofacial malformations, neuromuscular, and respiratory comorbidities that could lead to a poor nasal cannula tolerance.[5] Furthermore, under-threes often have mouth breathing, nasal secretions, or rapid respiratory rates that compromise the quality of the nasal cannula signal.[5]

Based on these considerations, we assessed the adequacy of $PetCO_2$ and $PtcCO_2$ for detecting hypoventilation during sleep in children under 3 years of age with suspected OSA. We hypothesized that there would be discrepancies between the two methods in this population because of the lower reliability of the $PetCO_2$ sensor.

We conducted a prospective observational study of 109 consecutively recruited children aged <3 years referred to our Sleep Unit for suspected OSA. The study was approved by the Hospital's Ethical Committee, and written informed consent was obtained from the parents/legal caretaker of all participating children.

The evaluation protocol is described in the supplementary material. All children underwent an attended PSG using the E-Series system (Compumedics Inc.), during a daytime nap from 09:00am to 02:30 pm, after a night of partial sleep deprivation. No sedation was used. Neurophysiological and respiratory signals recorded, and the scoring criteria used are described in Online Supporting Information.

$PetCO_2$ was measured using a Microcap Micro-stream monitor (Oridion Capnography Inc.) via a nasal sampling cannula, and $PtcCO_2$ through a TCM4 monitor (Radiometer). The $PtcCO_2$ sensor was placed on the thorax or inner thigh area.

The quality of the $PetCO_2$ and $PtcCO_2$ data was assessed visually by an expert in sleep medicine. $PetCO_2$ data were defined as uninterpretable if the waveform signal was absent or did not have an expiratory plateau, and the nasal sampling cannula was repositioned if it had been displaced from its position or replaced if the probe was blocked by nasal secretions. Uninterpretable PtcCO2 data were defined as absent or artefactual numerical data, and the sensor was recalibrated and re-sited. Interventions during sleep were made during periods of slow-wave sleep to minimize patient disturbances or during spontaneous awakenings. All the uninterpretable $PetCO_2$ and $PtcCO_2$ data were removed from the analysis.

Sleep hypoventilation was defined as >25% of the total sleep time (TST) with $PetCO_2$ or $PtcCO_2$ > 50 mmHg.[2] OSA was defined as an obstructive apnea-hypopnea index (OAHI) ≥ 1 and was classified as mild when OAHI ≥ 1–4.9, moderate when OAHI ≥ 5–9.9 and severe when OAHI ≥ 10.

Data analysis was carried out using the software IBM SPSS Statistics 26.0 (SPSS Inc.). Statistical methods used are shown in Online Supporting Information.

Of the 109 children who met the inclusion criteria, six (5.5%) did not tolerate the placement of the $PetCO_2$ nasal cannula from the beginning of the PSG recording, and two (1.8%) did not tolerate $PtcCO_2$ sensor placement ($p = 0.125$). The characteristics and PSG findings of the sample finally included are summarized in Table 1. Sixty-eight children (66.0%) were diagnosed with OSA: 25 (24.3%) were mild, 9 (8.7%) moderate, and 34 (33.0%) severe.

During the sleep study, a higher proportion of children required the intervention of the sleep laboratory technician to replace the PetCO2 nasal sampling cannula than for the $PtcCO_2$ sensor, 85 children (82.5%) versus 16 (15.5%), respectively ($p < 0.001$). The number of interventions per child was also higher in the case of $PetCO_2$, 2 (0–12) versus 0 (0–3) for $PtcCO_2$ ($p < 0.001$). The problems detected using the $PetCO_2$ nasal sampling cannula have been reported in previous work studying nasal cannula as a flow sensor in this population.[5] The intervention of the technician to improve the PetCO2 signal was mainly due to a poor tolerance with voluntary removal of the nasal cannula during wakefulness (36.9%), or to a poor signal due to mouth breathing (34%). Other causes of the poor $PetCO_2$ signal were obstruction of the nasal cannula due to secretions, tachypnea, nasal cannula displaced by involuntary movements during sleep and equipment failure during the study. The $PtcCO_2$ sensor required to be re-sited due to poor tolerance in

TABLE 1 Demographic and clinical characteristics and polysomnographic data of the study population ($n = 103$)

Variables	
Age, years	2.3 (1.1)
Sex, male/female	53 (51.5)/50 (48.5)
Ethnicity	
White	83 (80.6)
Hispanic	16 (15.5)
Black	1 (1.0)
Asian	3 (2.9)
Prematurity	18 (17.5)
BMI z-score	0.0 (1.7)
Obesity	10 (9.7)
Gastroesophageal reflux	9 (8.7)
Tonsils and adenoid grade	
No hypertrophy	26 (25.2)
Mild-moderate	27 (26.2)
Severe	50 (48.5)
Neurological comorbidity[a]	26 (25.2)
Respiratory comorbidity[b]	54 (52.4)
TRT, min	257.8 (226.2–301.1)
TST, min	178.5 (138.0–216.5)
Sleep efficiency, %	77.8 (62.3–86.7)
Stage NREM, %TST	84.9 (79.3–88.8)
Stage REM, %TST	15.2 (11.1–20.9)
Patients without REM sleep	6 (5.8)
Arousal index, No./h	16.6 (11.7–22.2)
Respiratory arousal index, No./h	4.3 (1.0–14.2)
OAHI, events/h	2.5 (0.3–18.1)
Minimal SpO2, %	90.0 (86.0–93.0)
CT90, %	0.0 (0.0–0.2)
ODI3, No./h	2.5 (0.7–8.3)
Baseline PetCO2, mmHg	35.0 (32.0–35.0)
Baseline PtcCO2, mmHg	38.0 (36.0–40.0)

Note: Continuous variables are expressed as mean ± standard deviation, or median (interquartile range). Categorical variables are expressed as *n* (percentage).

Abbreviations: BMI z-score, body mass index standard deviation; CT90, percentage of total sleep time with saturation under 90%; NREM, non-rapid eye movement; OAHI, obstructive apnea-hypopnea index; ODI3, 3% oxygen desaturation index; $PetCO_2$, end-tidal carbon dioxide; $PtcCO_2$, transcutaneous carbon dioxide; REM, rapid eye movement; SpO_2, oxygen saturation; TRT, total recording time; TST, total sleep time.

[a]Neurological comorbidity: global developmental delay ($n = 6$), Prader-Willi syndrome ($n = 5$), Arnold-Chiari malformation ($n = 5$), spinal muscular atrophy ($n = 2$), brainstem dysgenesis ($n = 2$), Down syndrome ($n = 2$), congenital myopathy ($n = 1$), mitochondrial disease ($n = 1$), metabolic disease ($n = 1$), autism spectrum disorder ($n = 1$).

[b]Respiratory comorbidity: recurrent upper respiratory infections ($n = 52$), laryngomalacia ($n = 1$), bronchopulmonary dysplasia ($n = 1$).

one child (1.0%) and due to the absence $PetCO_2$ values or artifacts in 15 (14.5%).

Overall, the percentage of total recording time (TRT) with uninterpretable signal was higher for $PetCO_2$ than for $PtcCO_2$: 48.6% (23.9–75.6) and 0.0% (0.0–9.0), respectively ($p < 0.001$). Differences were also observed in the percentages of TST: 31.2% (10–82.2) with $PetCO_2$ and 0.0% (0.0–0.0) with $PtcCO_2$ ($p < 0.001$). $PetCO_2$ signal was uninterpretable for >50% of TRT in 48 (46.6%) of the PSG studies compared to 5 (4.90%) with $PtcCO_2$ ($p < 0.001$). The percentage of time without an interpretable $PetCO_2$ signal was higher than that previously reported in older children by Paruthi et al.[6] and similar to that found by Kirk et al.[4] Our study is the first to focus on children under 3 years of age. We found that the loss of the $PetCO_2$ signal was associated with the presence of severe adenotonsillar hypertrophy, severe OSA, and lower sleep efficiency (Table 2). Conversely, the presence of respiratory or neurological comorbidity was not associated with a longer time of poor $PetCO_2$ signal.

During PSG, median and maximum $PetCO_2$ values were lower than $PtcCO_2$ values: 36.0 mmHg (31.5–37.7) versus 43.3 mmHg (39.4–45.2), respectively ($p < 0.001$) and 40 mmHg (37.4–42.3) versus 46.9 mmHg (42.5–50.2), respectively ($p < 0.001$). According to the Bland–Altman method the bias and limits of agreement were 9.80 mmHg (95% confidence interval [CI]: 7.77–11.84) ($p < 0.001$) for the median values and 7.83 mmHg (95% CI: 6.12–9.54) ($p < 0.001$) for the maximum values. Previously a better agreement was reported with both techniques[4] but with wider 95% CI limits than those observed in our patients. Our finding of higher values for $PtcCO_2$ than for $PetCO_2$ is as expected with these techniques[7] and is in agreement with what was described during PSG in children.[3] We think that the difference in interpretable time between the two sensors has determined this lack of concordance detected in our patients during the sleep study. However, although the periods of poor $PetCO_2$ signal quality were eliminated from the analysis, we cannot rule out the presence of false low values due to undetected mouth breathing, small tidal volumes, or partial obstruction of the nasal sampling line.

The detection of sleep hypoventilation according to AASM criteria differed according to the sensor used: it was observed in eight children (7.8%) with $PtcCO_2$ but in none (0.0%) with $PetCO_2$ ($p = 0.008$). It did not differ between children with and without neurological co-morbidities ($p = 0.230$). The prevalence of hypoventilation in children under 3 years of age with suspected OSA had not previously been the subject of specific study, and the rate detected in our patients is lower than that reported in older children.[4,6] According to the other definitions of hypoventilation published in the literature (maximum CO_2 value >50 mmHg, CO_2 > 50 mmHg for >2% of TST and CO_2 value >10 mmHg during sleep above baseline level), the percentages obtained with the two sensors, $PtcCO_2$ and $PetCO_2$, were 26.2% vs 1.9% respectively ($p < 0.001$), 19.4% versus 0.0% ($p < 0.001$) and 2.9% versus 1.0% ($p = 0.625$).

In summary, in our study in children under the age of three with suspected OSA, the ability of PetCO2 to detect sleep

TABLE 2 Clinical and PSG variables with uninterpretable signal for $PetCO_2$

Variables	TRT with uninterpretable $PetCO_2$ signal		p
	<50% (n = 55)	≥50% (n = 48)	
Age, years	2.4 (1.2)	2.2 (1.1)	0.623
Sex, female	30 (54.5)	20 (41.7)	0.192
Obesity	7 (12.7)	3 (6.3)	0.337
Severe adenotonsillar hypertrophy	19 (34.5)	31 (64.5)	0.002
Respiratory comorbidity	25 (45.5)	29 (60.4)	0.129
Neurological comorbidity	19 (34.5)	7 (14.6)	0.020
TST, min	189 (173.5–238.0)	152.7 (105.7–198.1)	<0.001
Sleep efficiency, %	81.1 (71.3–89.3)	68.4 (48.8–83.7)	<0.001
Arousal index, No./h	13.8 (11.1–19.0)	18.6 (14.2–30.0)	0.002
OSA severity			<0.001
No OSA	25 (45.5)	10 (20.8)	
Mild	15 (27.3)	10 (20.8)	
Moderate	6 (10.9)	3 (6.3)	
Severe	9 (16.4)	25 (52.1)	

Note: Continuous variables are expressed as mean ± standard deviation, or median (interquartile range). Categorical variables are expressed as *n* (percentage).

Abbreviations: OAHI, obstructive apnea-hypopnea index; OSA, obstructive sleep apnea; $PetCO_2$, end-tidal carbon dioxide; TRT, total recording time; TST, total sleep time.

hypoventilation was inferior to that of $PtcCO_2$, due to the presence of a longer recording time with an uninterpretable signal. The factors underlying this limitation were the poorer tolerance of the $PetCO_2$ sensor, and the presence of severe adenotonsillar hypertrophy, severe OSA, and poorer sleep efficiency, which occur frequently in this age group. Although the simultaneous use of both sensors has been recommended, this practice entails an increase in costs, and our results suggest that its value in children under 3 years of age is limited.

AUTHOR CONTRIBUTIONS

María José Jurado: Conceptualization; methodology; data curation; investigation; validation; formal analysis; supervision; writing – original draft; writing – review and editing. **Júlia Sampol**: Conceptualization; methodology; investigation; validation; data curation; writing – review and editing. **Manuel Quintana**: Investigation; Formal analysis; validation; writing – review and editing. **Odile Romero**: Investigation; validation; writing – review and editing. **Roser Cambrodí**: Data curation; Investigation; validation; writing – review and editing. **Alex Ferré**: Data curation; Investigation; validation; writing – review and editing. **Gabriel Sampol**: Conceptualization; methodology; investigation; validation; formal analysis; supervision; writing – original draft; writing – review and editing.

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CONFLICT OF INTERESTS

The authors declare that no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data is available upon request to the corresponding author.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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