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Daytime hypercapnia in adult patients with obstructive sleep apnea in China

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To the Editor: Obstructive sleep apnea (OSA) is a common sleep-disordered breathing. Previous studies reported that the incidence of daytime hypercapnia in patients with OSA was 26.2% in China[1] and 14% in Japan.[2] However, Weitzenblum *et al*[3] demonstrated that daytime hypercapnia in patients with OSA might not be secondary to sleep apneas/hypopneas, but might due to the comorbidities, such as chronic obstructive pulmonary disease or severe obesity. Obesity hypoventilation syndrome (OHS) is defined as a conjunction of obesity (body mass index [BMI] $\geq$30 kg/m^2), daytime hypercapnia (partial pressure of carbon dioxide in arterial blood [$PaCO_2$] $\geq$45 mmHg) and sleep disordered breathing, after excluding other causes for alveolar hypoventilation.[4] Since patients with OHS were not completely excluded in previous studies,[1,2] we assumed that the incidence of daytime hypercapnia in Chinese patients with OSA might be low.

Nearly 90% of patients with OHS have an associated OSA.[4] However, patients with OHS have higher rates of morbidity and mortality than patients with OSA.[4] Consequently, the differential diagnosis between OSA and OHS is very important, and daytime hypercapnia is the key index for that, especially for obese patients with OSA. Hence, it is necessary to analyze the clinical characters of OSA patients with daytime hypercapnia.

This retrospective study was performed from January 2013 to February 2021 in the sleep unit of our hospital. We included adult patients (age $\geq$18 years) with data on polysomnography, pulmonary function, and arterial blood analysis. We excluded participants if the apnea-hypopnea index (AHI) was <5/h, central/mixed apnea/hypopnea was the primary suspicion, or the ratio of forced expiratory volume in 1 s (FEV1) to the forced vital capacity (FVC) (FEV1/FVC) was <70% or percentages of predicted FEV1 and FVC were <80%, except due to obesity. Finally, we recruited 294 participants in this study [Supplementary Figure 1, http://links.lww.com/CM9/A640].

The study was conducted in accordance with the *Declaration of Helsinki* and was approved by the Research Ethics Committee of Peking Union Medical College Hospital (No. S-K567) (Trial registration: ChiCTR1800019159).

The full night polysomnography was performed with Embla N7000 (Natus Medical Incorporated, Broomfield, CO, USA) and was reviewed for analysis by an experienced sleep investigator. We scored respiratory events as stated in the 2017 American Academy of Sleep Medicine criteria. We determined nocturnal hypoxemia by oxygen desaturation index (ODI), minimum values of arterial oxygen saturation (SaO_2), mean values of SaO_2, and the percentage of time spent at oxygen saturation below 90% in total sleep time ($SIT_{90\%}$) during sleep. Pulmonary function tests were performed to determine the FEV1/FVC and the percentage of predicted FEV1 and FVC using a standard spirometer (MS-IOS, Jaeger, Hoechberg, Germany). Arterial blood was drawn when the patients were in the sitting position and breathed room air. The arterial blood gas analyzer (ABL800, Radiometer, Copenhagen, Denmark) was used to analyze potential of hydrogen, partial pressure of oxygen (PaO_2), $PaCO_2$, SaO_2, and bicarbonate. The data of arterial blood gas analysis that were closest to the time of polysomnography were collected. Hypercapnia was defined as $PaCO_2$ $\geq$45 mmHg.

The SPSS software (version 21.0, Chicago, IL, USA) was used. Quantitative data are expressed as mean ± standard

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Table 1: Comparison between eucapnic and hypercapnic patients with OSA.

Items	$PaCO_2$ <45 mmHg ($n = 270$)	$PaCO_2$ ≥45 mmHg ($n = 24$)	*P*
Male	224 (82.96)	23 (95.83)	0.174
Age, years	42.0 (34.0–53.3)	48.0 (41.0–53.8)	0.163
BMI, kg/m^2	28.73 (25.95–31.65)	30.75 (26.90–33.27)	0.188
FEV1 predicted	96.05 (88.18–103.03)	87.05 (81.05–100.65)	0.006
FVC, % predicted	98.50 (90.48–105.93)	90.80 (82.30–98.83)	0.004
FEV1/FVC	80.37 ± 4.56	80.38 ± 4.74	0.995
AHI, /h	33.35 (15.08–60.75)	55.70 (25.98–80.75)	0.056
ODI, /h	25.35 (11.63–54.90)	61.10 (16.45–83.28)	0.021
Nighttime minimum SaO_2	82.00 (74.00–87.00)	75.00 (58.00–86.75)	0.017
Nighttime mean SaO_2	96.00 (93.90–97.30)	92.70 (84.68–96.75)	0.003
$SIT_{90\%}$	2.10 (0.10–9.43)	14.70 (0.15–64.00)	0.018
PH	7.402 ± 0.020	7.384 ± 0.017	<0.001
PaO_2, mmHg	89.55 (83.23–96.73)	85.00 (71.53–93.00)	0.029
Daytime saO_2	97.10 (96.40–97.60)	96.30 (94.23–97.08)	<0.001
$PaCO_2$, mmHg	39.65 (38.00–41.25)	46.00 (45.55–47.00)	<0.001
Bicarbonate, mmol/L	24.084 ± 1.195	26.879 ± 1.298	<0.001

Data are presented as mean ± standard deviation, median (interquartile range) or *n* (%). AHI: Apnea-hypopnea index; BMI: Body mass index; FEV1: Forced expiratory volume in 1 second; FVC: Forced vital capacity; FEV1/FVC: Ratio of FEV1 to FVC; AHI: Apnea-hypopnea index; ODI: Oxygen desaturation index; SaO_2: Oxygen saturation; $SIT_{90\%}$: The percentage of time spent at oxygen saturation below 90% in total sleep time; PaO_2: Partial pressure of oxygen; PH: Potential of hydrogen potential of hydrogen; $PaCO_2$: Partial pressure of carbon dioxide in arterial blood; OSA: Obstructive sleep apnea.

deviation or median (interquartile range), according to data distribution. Distribution of the variables was analyzed with the Shapiro-Wilk test. Qualitative data were expressed as counts and percentages. The statistical differences between two groups were tested with independent samples *t*-test or Mann-Whitney *U* test for whether the data were normally distributed, and Pearson χ^2 test for qualitative data. Univariate analyses and multiple forward stepwise logistic regression analyses (likelihood ratio) were applied to explore possible factors that were associated with daytime hypercapnia. $P < 0.05$ was considered statistically significant.

The prevalence of daytime hypercapnia was 8.16% (24/294) in the study population. OHS was diagnosed in 58.33% of hypercapnic patients (14/24). Thus, the incidence of daytime hypercapnia was 3.57% (10/280) in patients with OSA. As shown in Table 1, gender, age, BMI, FEV1/FVC ratio, and AHI were not significantly different between the two groups. Compared with eucapnic patients, hypercapnic patients had lower percentages of predicted FEV1 and FVC, lower daytime PaO_2 and SaO_2, higher bicarbonate level, and a worse degree of nocturnal hypoxia, expressed as higher ODI and $SIT_{90\%}$, and lower minimum SaO_2 and mean SaO_2. In the multivariable adjusted model, the bicarbonate and percentage of predicted FVC, adjusted by gender, BMI, ODI, minimum SaO_2, mean SaO_2, $SIT_{90\%}$, PaO_2, and percentage of predicted FEV1, were significantly associated with daytime hypercapnia [Supplementary Table 1, http://links.lww.com/CM9/A640].

In this study, the prevalence of daytime hypercapnia in Chinese patients with OSA was lower than that of patients in previous studies in Asia (3.57% *vs*. 14%–26.2%).[1,2] In patients with OSA, the daytime hypercapnia might be associated with impaired post-event ventilatory response during sleep and the increased bicarbonate level over time.[5] In this study, higher bicarbonate was the best predictor of daytime hypercapnia (odds ratio: 6.533, 95% confidence interval: 3.325–12.837). The incidence of daytime hypercapnia was 5.56% (10/180) in non-obese patients with OSA (BMI <30 kg/m^2) in this study. The prognosis of non-obese patients with OSA with daytime hypercapnia was unclear. Intermittent hypoxia, an important pathophysiological feature of OSA, is the key mechanism of metabolic and cardiovascular complications. Compared with eucapnic patients, hypercapnic patients had lower daytime PaO_2 and SaO_2 and a worse degree of nocturnal hypoxia. Hence, patients with OSA with daytime hypercapnia might have a poor prognosis.

Several limitations existed in this study. First, this retrospective study did not analyze the other pathophysiological features, complications, and prognosis of OSA. Thus, further studies are needed to explore the mechanisms and prognosis of patients with OSA with daytime hypercapnia. Second, the screening of pulmonary function and arterial blood analysis were not common for patients with OSA; therefore, a lot of patients were not included, which resulted in the small sample size. Hence, the large-scale, multicenter, prospective studies are needed to confirm these results.

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Conflicts of interest

None.

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