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Original Article

The effect of CPAP on obstructive sleep apnea hypopnea syndrome during pregnancy

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Abstract: Objective: The study aimed to explore the curative effect of continuous positive airway pressure (CPAP) on obstructive sleep apnea hypopnea syndrome (OSAHS) in pregnant women. Method: Women diagnosed with OSAHS were recruited as the study cohort from June 2013 to May 2016 in our hospital. Their basic clinicopathological data were recorded, and polysomnography respiratory monitoring and CPAP therapy were performed. Serum samples were collected from the women and statistically analyzed. Results: According to the analysis of the cohort's clinicopathological data, there were more patients with severe diseases than there were with mild symptoms, with a significant difference. A further correlation analysis of various indexes including lactic acid and pH value showed that the levels of lactic acid in the patients were positively correlated with age and average SpO_2 (oxygen saturation) level, negatively correlated with neck circumference, their apnea-hypopnea index (AHI) classification, and the oxygen desaturation index (ODI) level, with significant differences ($P<0.05$). There was no significant correlation between the lactic acid content and body mass index (BMI), waist circumference, or LaO_2. In the correlation analysis between the pH values of the OSAHS patients and other indicators, it was found that the pH value of the OSAHS patients was positively correlated with age and neck circumference and negatively correlated with ODI, with a significant difference ($P<0.05$). The correlation between pH value and BMI, waist circumference, AHI classification, LaO_2, and average SpO_2 was not significant, and there was no significant difference. After the CPAP treatment, the AHI, ODI, and lactic acid levels were significantly reduced, with statistically significant differences compared with the levels before the CPAP treatment ($P<0.01$). After the CPAP treatment, the LaO_2, average SpO_2, pH value, and PaO_2 levels were significantly increased, with statistically significant differences compared with before the treatment ($P<0.01$). Conclusion: CPAP treatment for OSAHS patients can effectively improve blood lactic acid and pH levels.

Keywords: OSAHS, CPAP, gestation, blood lactic acid, polysomnography breathing monitor

Introduction

In people's daily life, with the continuous improvement of living standards, people pay special attention to their health. OSAHS, a common respiratory disease, is characterized by brief and repeated apnea or hypopnea during sleep, accompanied by decreased oxygen saturation and hypercapnia [1, 2]. This disease leads to sleep disorders. When they get up in the morning, they often feel dizzy, and during the day, they feel drowsy, leading to heart, brain, kidney, endocrine system, and other organ damage [3]. Survey data show that in the general population, the incidence of OSAHS is nearly 4%. However, after pregnancy, the incidence of OSAHS in pregnant women is significantly increased due to the aggravation of breathing and other phenomena. The gestational symptoms caused by this are also very significant, such as gestational hypertension, fetal growth retardation, etc. [4]. Therefore, in order to better control and prevent OSAHS, the disease has attracted the attention of scholars.

In the gestational period, because of the fetus, pregnant woman can't take medicine casually. As a result, some symptoms can only recover by themselves. OSAHS is one of the main causes of hypertension. Studies have shown that OSAHS can lead to multiple organ damage or hypertension, cardiovascular and cerebrovascular diseases, and stroke through some pathological mechanisms [5, 6]. There are many treatment methods for it. Basically, there are mainly two kinds of operative and nonoperative treatment methods. Surgical treatment, usually tonsillectomy or adenoidectomy, nasal surgery, glossoplasty, etc., is aimed at alleviating or eliminating airway obstruction and preventing airway tube tissue collapse. Anesthesia is often needed to reduce pain during surgery, which can be extremely dangerous for pregnant women, so non-surgical treatment is preferred [7]. Non-surgical treatment mainly includes trans-nasal CPAP therapy and oral orthodontic therapy. However, according to clinical manifestations, CPAP is the most effective treatment method at present, and most patients achieve a satisfactory therapeutic effect after CPAP therapy [8]. Gagnadoux et al. used oral instrument therapy (OAT) instead of CPAP as the preferred treatment for moderate OSAHS and found that at least 50% of OSAHS patients were affected by central obesity and related metabolic disorders but that there is no cure [9]. Wuttiumporn et al. evaluated the effect of CPAP therapy on improving oxidative stress and inflammation and found that CPAP therapy can gradually improve oxidative stress and the inflammatory response to produce clinical efficacy and that the severity of OSAHS is related to oxidative stress and the inflammatory response [10]. Ponce et al. evaluated the effect of CPAP on elderly patients with moderate OSAHS from the clinical, quality of life, neurocognition, and other aspects, and found that CPAP treatment can significantly improve daytime sleepiness, some sleep-related symptoms, and the quality of life of elderly patients with moderate obstructive sleep apnea (OSA) after relevant treatment [11].

Although there are many studies on the application of CPAP therapy to the treatment of OSAHS symptoms in patients, there are not many studies on the application of CPAP therapy to the treatment of OSAHS symptoms in pregnant women. Therefore, we studied pregnant female patients diagnosed with OSAHS at The Third Affiliated Hospital of Guangzhou Medical University from June 2013 to May 2016. After polysomnography monitoring and CPAP treatment were performed, specimens were collected and statistically analyzed to provide new ideas for the diagnosis and treatment of obstructive sleep apnea hypopnea syndrome during pregnancy.

Materials and methods

Experimental subjects

The randomly selected subjects in this research were 108 pregnant women aged 21-45 who visited The Third Affiliated Hospital of Guangzhou Medical University from June 2013 to May 2016 with the symptoms of repeated night sleep snoring, apnea, choking and wakefulness, daytime sleepiness, etc. All the experimental operations conducted in this research were approved by the patients and their families and approved by our hospital's ethics committee.

Inclusion criteria: Subjects who signed the informed consent before the experiment. The subjects ranged from 21 to 63 years old. The subjects met the guidelines for the diagnosis and treatment of obstructive sleep apnea hypopnea [12] (revised 2011) for the diagnosis of OSAHS and the indications for CPAP treatment. All the subjects received their first diagnosis and had not had any OSAHS surgery or ventilator treatment.

Exclusion criteria: Patients who had previously undergone CPAP, oral orthotics, or uvula pharyngoplasty (uvulopalatopharyngoplasty, UPPP) treatment. Patients with diseases that affect lactic acid and blood gas analysis, such as severe infections, metabolic acidosis, and body mass, were excluded. Patients who took drugs that might affect their lactate metabolism, such as two armor pair of muscle, alcohol, acetaminophen, and amoxicillin, were excluded.

The diagnostic criteria and the prognosis of OSAHS

Diagnostic criteria: We mainly refer to the guidelines for the diagnosis and treatment of OSAHS (revised 2011) formulated by the sleep respiratory group of the Chinese society of respiratory medicine, which is mainly the diagnostic criteria related to OSAHS, and they monitor the polysomnography (PSG) results according to the medical history, signs and polysomnography (PSG). The typical clinical symptoms of OSAHS include snoring accompanied by apnea during night sleep, daytime sleepiness (ESS score $\geq$ 9) and other symptoms. OSAHS symptoms can be diagnosed if the AHI $\geq$ 5 times/h. OSAHS complications can also be diagnosed in patients who have no significant daytime sleepiness (ESS score <9), AHI ≥ 10/h or ≥ 5/h and who have one or more symptoms such as cognitive dysfunction, hypertension, coronary heart disease, cerebrovascular disease, diabetes, and insomnia.

Disease assessment: Patients suffering from OSAHS symptoms should be fully observed according to their symptoms, signs, AHI, SpO_2 and other indicators, and their symptoms should be classified into the three grades of mild, moderate, and severe according to their AHI and SpO_2 levels at night. Among them, AHI should be used as the main judgment standard when the AHI and SpO_2 indicators conflict.

Subject basic indicators collection

A height measurement was performed for each subject who finally met the diagnostic criteria, that is, the subject took off her shoes and hat, stood at attention, and looked forward with her eyes. The measurement was repeated twice and the average value (accuracy: 0.01 m) was taken. Weight measurement: after calibrating the scale, removing their shoes and coat and with the patient on an empty stomach in the morning, we weighed the patient and repeated the measurement twice, taking the average value (accuracy: 0.1 kg). The blood pressure measurements were carried out by professional medical staff according to the unified standard. First, the patient was asked to rest quietly for no less than five minutes before the measurement. During the measurement, the patient took a sitting position, exposed the upper right arm and raised it to the same level as the heart. The formula is as follows: mean arterial pressure (MAP) = diastolic pressure + 1/3 (systolic - diastolic pressure). Neck circumference measurement: the subject took a standing position, the body remained upright, the eyes looked straight ahead, and the arms naturally drooped in a relaxed state. The tape measure was placed on the neck, the back was placed on the upper edge of the seventh cervical vertebra, and the test was repeated twice to get an average (accuracy: 0.01 m).

Polysomnography respiratory monitoring

All the subjects underwent sleep breathing monitoring at 10 o'clock on the night of their admission with a polysomnography monitor (Condi, Australia), and the monitoring duration was no less than seven h. During the monitoring period, we tried to make the patients have the same sleep quality as usual, and the sleep time could not be less than seven hours. If the sleep time was less than four hours, the patient was excluded. Preparation before patient monitoring: the patient was not allowed to sleep during the day on the monitoring day, and was not allowed to drink coffee, strong tea, or sedatives to prevent sleep disruptions. Before the monitoring, the patients were asked to take a shower and wash their hair and not to wear any accessories. They were asked to sleep according to their daily habits and to empty their bladder before going to bed.

Monitoring steps: the patient lay on the bed in a supine position and his blood pressure was measured before going to sleep. After that, all the lead wires and electrodes (electroencephalogram, electroencephalogram, electrocardiogram and electromyography, etc.) were connected, and then we checked to make sure the connection was correct. After the examination, the measuring instrument was turned on, the image was observed, the record button was pushed to start the monitoring, and we clicked the end button in the morning when the monitoring was finished. Then we removed the lead wires. The patient's blood pressure was measured again, and the monitoring results recorded in the instrument were interpreted. The interpretation results were read by specialized medical staff who were blinded to minimize the information bias caused by subjective factors, and the relevant polysomnography parameters were recorded. During the monitoring period, the relevant patient indicators mainly included mouth-nose airflow, pulse blood oxygen saturation, chest and abdominal movement, electroencephalogram, electrocardiogram, eye movement, lower collar electromyography, body position, familiar voice, leg movement, sleep structure analysis, such as sleep stages, the time percentage of each stage, and the number of awakenments. The sleep breathing parameters to be calculated included AHI, ODI, lowest O_2 saturation ($LaSO_2$), average SpO_2, and the percentage of total sleep time spent with SpO_2 <90% (ts90%) at night.

In the process of monitoring, the specific operation methods of each index were as follows.

Skin treatment: the first scrub was used to remove oil from the skin surface, and then alcohol was used to clean the local skin. Electrocardiogram monitoring: during the monitoring process, one of two electrocardiogram electrodes was placed in the front of the fourth intercostal axilla on the left and the other in the middle of the second intercostal clavicle on the right to record the changes in the center rate of the patient's sleep process at night. For eye movement and myoelectric monitoring of the mandibular muscle, the right eye movement electrode was placed at about LCM above the lateral canthus of the right eye, the left eye movement electrode was placed at about 1 cm below the lateral canthus of the left eye, and the reference electrode was placed at the middle of the forehead. Finally, electrical electrodes were placed in the mandibular region to help diagnose NREM and REM sleep stages. EEG monitoring: electrodes were placed at c4-a1 and c3-a2 to analyze and judge the sleep stages. Chest and abdominal respiratory movement monitoring: the chest band was put in place with a large amplitude of respiratory movement, roughly at the level of the nipple, and the abdominal band was placed at the level of the umbilicus. During the monitoring process, the chest and abdomen bands should be placed in the most suitable way for the patients to feel comfortable, which is mainly to judge the type of sleep apnea. Pulse oxygen saturation during the monitoring and a finger touch pulse oxygen saturation meter were used to observe the decrease of pulse oxygen saturation during sleep, specifically the amount and duration of the decrease. The monitoring of the oral and nasal airflow is done mainly to feel the changes in the oral and nasal airflow by connecting the tube of oral and nasal airflow to the thermal sensor, so as to judge the number and duration of apnea and hypopnea incidents during sleep. Snoring was monitored by placing a tiny microphone on the side of the patient's neck.

CPAP treatment

OSAHS patients diagnosed through polysomnography breathing monitoring were subjected to an auto-CPAP ventilator for pressure measurement for one continuous night, with memory CARDS set in the ventilator, and the next morning, the ventilator data were read by specialized medical personnel, including ventilator use time, AHI, ODI, $LaSO_2$, and average SpO_2, etc. The patients who had been on ventilator for less than four hours per night were excluded.

Serum collection, preparation and monitoring

All the subjects signed the informed consent when the serum samples were collected, and on the premise of the consent of the patients, in the early morning of the next day after the polysomnography breathing monitoring was done (usually between 6:30 and 7:30 am, and with at least 10 h on an empty stomach). During the blood draw, the patient was kept awake and asked to breathe in a supine position. After that, 10 mL peripheral venous blood was extracted from the patient and was injected into the anticoagulant tube of EDTA for mixing, and 2 mL radial artery blood was extracted from the patient with a syringe for blood gas analysis and sealed for preservation. The stored blood samples were immediately sent to the laboratory for analysis, such as blood lactic acid and arterial blood gas, etc. The review process was the same as above.

The sampling process of the specimens was aseptic, and the testing personnel were double-blinded. Glycerides (TG) were determined using the GPO-PAP method, the total cholesterol (TC) using the COD-PAP method, and high density lipoprotein-cholesterol (HDL-C) using phosphor-tungstic magnesium precipitation method. The low density lipoprotein-cholesterol (LDL-C) was determined using a polyethylene sulfur acid precipitation. All the indexes measured above were measured on a semi-automatic biochemical analyzer. Platelet detection was performed using an ADVIA 2120 system, the blood lactic acid content was quantified using a Vitros5.1FS analyzer and analyzed using the dry chemical method. The blood gas analysis was done using an ABL500 automatic analyzer and measured using the electrode method. The steps were carried out according to the instructions of the corresponding kit.

Statistical analysis

In this study, SPSS 21.0 statistical software was used for the statistical analysis. The normal distribution count data were expressed in the form of "mean ± standard deviation" ($\overline{x}$ ±

Table 1. Criteria for determining the severity of OSAHS and AHI and/or hypoxemia in pregnant women

Symptom classification	AHI (time/h)	Least at nighttime SpO_2 (%)
Mild	5~15	85~90
Moderate	15~30	80~85
Severe	>30	<80

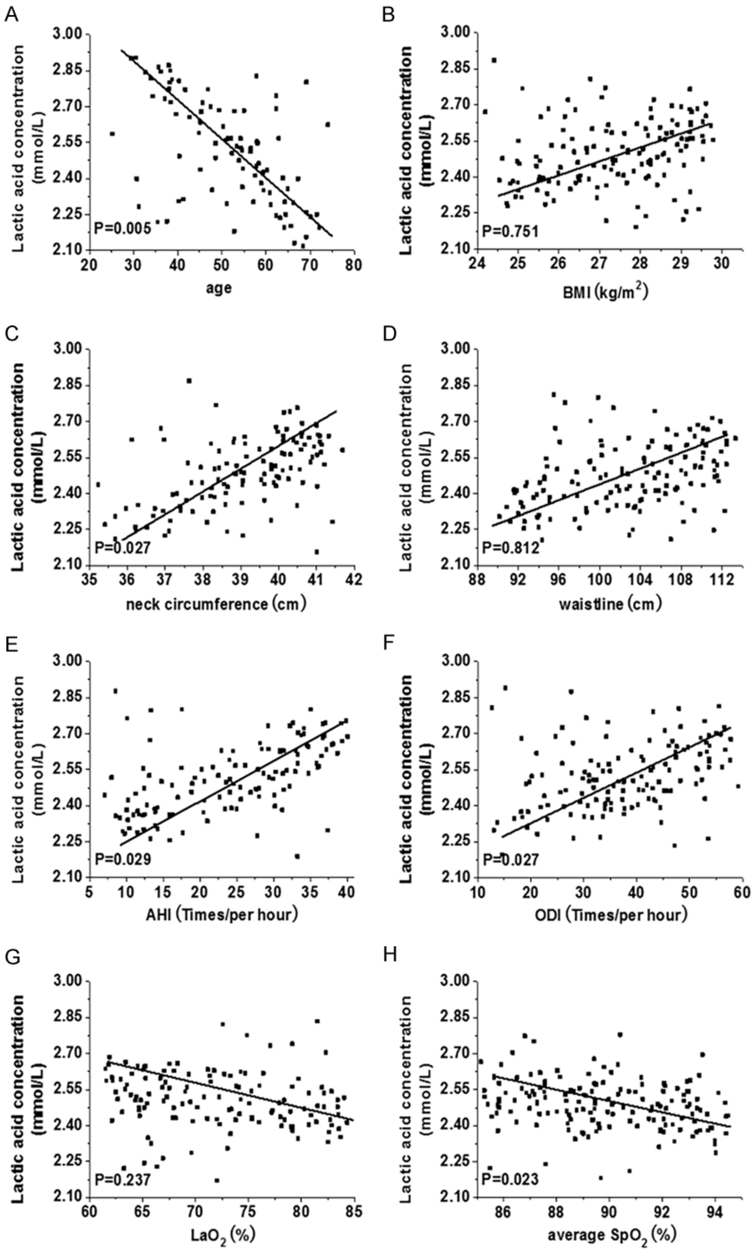

Figure 1. The correlation analysis between lactic acid content and other indexes of the OSAHS patients (A. Correlation with age; B. Correlation with BMI; C. Correlation with neck circumference; D. Correlation with waist circumference; E. Relevance to AHI; F. Correlation with IDO; G. Correlation with LaO_2; H. Correlation with average SpO_2).

s), and the skewed distribution measurement data were expressed in the form of median and interquartile. We used percentage or a percentage representation for the enumeration data. The changes in lactic acid, pH, SpO_2, PaO_2, and $PaCO_2$ before and after the CPAP treatment were tested using paired t tests. Spearman's rank correlation coefficient was used to analyze the correlation between two variables, and the test level was P<0.05, indicating that a difference was statistically significant.

Results

Basic information analysis

As shown in **Table 1**, we recorded the ages, the body mass indexes, neck circumferences, waist circumferences, ESS scores, blood pressure levels, cholesterol levels , triglyceride of liver oil levels, apnea level index classifications, and disease differentiations of the 108 OSAHS patients included in the study. In terms of the differentiation of the patients' conditions, there were significantly more severe patients than mild patients.

Correlation analysis between lactic acid, pH, and other OSAHS patient indexes

A further correlation analysis was conducted between each index and the lactic acid and pH values, and the results are shown in **Figures 1** and **2** below. In **Figure 1**, the correlation analysis of lactic acid content and other indicators in the OSAHS patients showed that the patients' lactic acid levels were positively correlat-

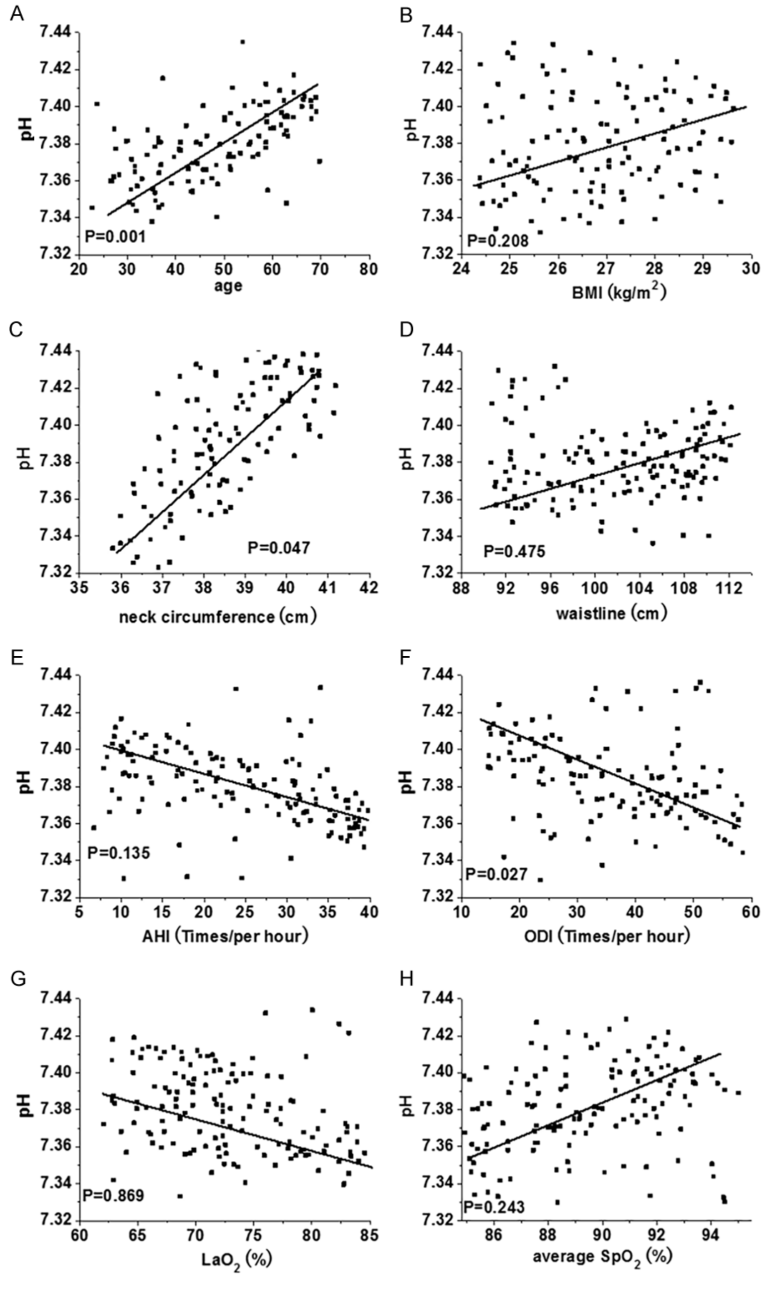

Figure 2. The correlation analysis between PH value and other indexes of the OSAHS patients (A. Correlation with age; B. Correlation with BMI; C. Correlation with neck circumference; D. Correlation with waist circumference; E. Relevance to AHI; F. Correlation with IDO; G. Correlation with LaO_2; H. Correlation with average SpO_2).

ed with age and average SpO_2 and negatively correlated with neck circumference, AHI grade, and ODI, with significant differences (P<0.05). There was no significant correlation between the lactic acid content and BMI, waist circumference, or LaO_2.

In **Figure 2**, the correlation analysis between the pH value of the OSAHS patients and other indicators showed that the pH value of the OSAHS patients was positively correlated with age and neck circumference and negatively correlated with ODI, with a significant difference (P<0.05). The correlation between pH value and BMI, waist circumference, AHI classification, LaO_2 and average SpO_2 was not significant, and there was no significant difference (**Table 2**).

Analysis of the blood gas and lactic acid levels before and after the CPAP treatment

As shown in **Table 3** and **Figure 3**, the changes in AHI and ODI before and after CPAP treatment were analyzed. It was found that both the AHI and ODI values were significantly decreased after the treatment, with a statistically significant difference compared with the levels before the treatment (P<0.01). In the analysis of the change of LaO_2 or average SpO_2 before and after the CPAP treatment in **Figure 4**, it was found that the LaO_2 or average SpO_2 ratio increased significantly after the CPAP treatment, with a statistically significant difference compared with before the treatment (P<0.01). In the analysis of the pH value and PaO_2 levels before and after the CPAP treatment, it was found that there was a significant increase after the treatment, with a statistically significant difference compared with before the treatment (P<0.01). In the analysis of the change of lactic acid before and after the CPAP treatment, it was found that the level of lactic acid decreased

Table 2. Basic information and indicators of the subjects

Index		OSAHS patients
Age (years)		42.08±6.09
Body mass index (BMI) (kg/m^2)		27.53±3.17
Neck circumference (cm)		38.97±3.51
Waist circumference (cm)		96.59±6.37
ESS score		9.27±3.52
Blood pressure	Systolic Blood Pressure (SBP) (mmHg)	139.65±18.06
	Diastolic blood pressure (DBP) (mmHg)	85.37±13.26
Cholesterol (mmol/L)		4.52±0.86
Triglyceride (mmol/L)		2.51±0.93
Apnea hypopnea index (AHI) classification		
Symptom classification	Mild (%)	9 (8.33%)
	Moderate (%)	20 (18.52%)
	Severe (%)	79 (73.15%)

Table 3. Analysis of the blood gas and lactic acid before and after CPAP treatment

Index	Before treatment	After treatment	*P* value
AHI (time/hour)	48.32±11.09	5.53±4.32	0.000
ODI (time/hour)	37.28±5.08	3.73±0.36	0.000
LaO_2 (%)	71.47±14.08	89.05±1.08	0.000
average SpO_2 (%)	88.49±7.97	98.23±1.38	0.001
pH	7.389±0.25	7.401±0.15	0.005
PaO_2 (mmHg)	89.52±6.53	94.67±1.94	0.004
$PaCO_2$ (mmHg)	38.79±4.13	38.05±4.08	0.112
Lactic acid (mmol/L)	2.25±0.37	2.11±0.29	0.002

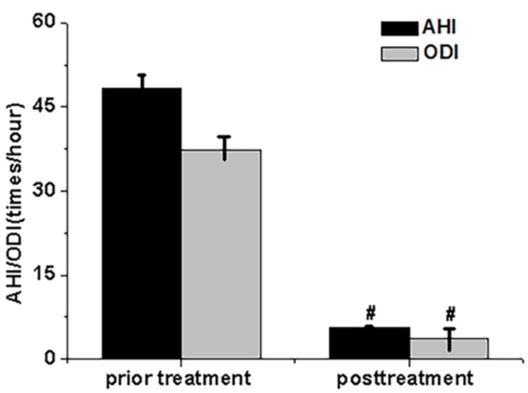

Figure 3. Change of AHI or ODI before and after the CPAP treatment (compared with before the treatment, #P<0.01 indicated a statistically significant difference).

significantly after the treatment, and there was a significant statistical difference compared with the level before the treatment (P<0.01).

Discussion

OSAHS is a series of chronic diseases caused by partial or complete upper respiratory tract obstruction occurring repeatedly during sleep, including snoring at night, repeated apnea or hypopnea, hypoxemia, hypercapnia, sleep structure disorder, and daytime sleepiness [13]. OSAHS affects a number of systems, such as the cardiovascular system, the respiratory system, the nervous system, and the secretory system, etc., especially in pregnant patients [14]. Through the analysis of the basic information of the subjects in this research, it was found that in terms of the differentiation of the patients' conditions, severe patients were significantly more common than patients with mild symptoms, with a statistical difference. A further correlation analysis was conducted between each index and the lactic acid and pH values, and it was found that the patients' lactic acid levels were positively correlated with age and mean SpO_2 and negatively correlated with neck circumference, AHI grade, and ODI, with significant differences (P<0.05). There was no significant correlation between lactic acid content and BMI, waist circumference, or LaO_2. In the correlation analysis between the pH value of the OSAHS patients and other indicators, it was found that the pH value of the OSAHS patients was positively correlated with age and neck circumference and negatively correlated with ODI, with a significant difference (P<0.05). The correlation between pH value and BMI,

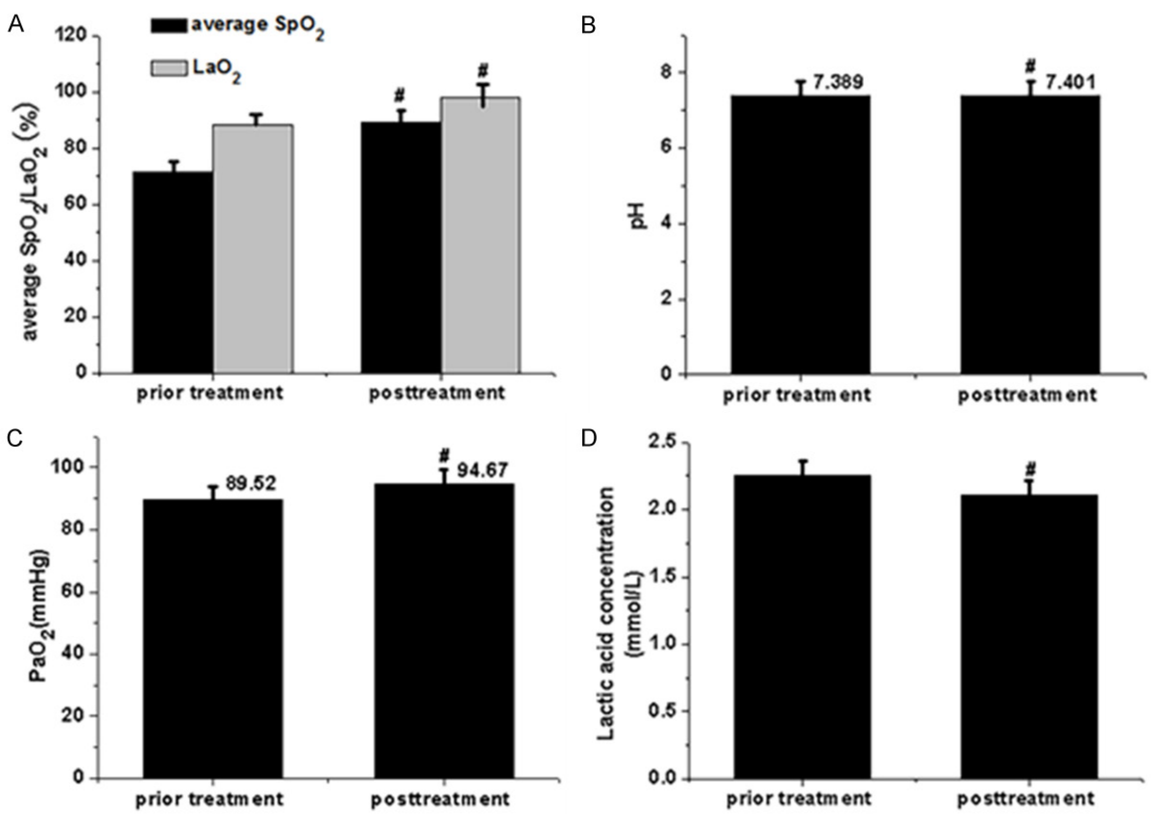

Figure 4. All indexes before and after the CPAP treatment (A. Changes in the LaO_2 or SpO_2 levels before and after the CPAP treatment. B. Change in the pH values before and after the CPAP treatment. C. Change in the PaO_2 level before and after the CPAP treatment. D. Changes in the lactic acid levels before and after the CPAP treatment) (compared with before the treatment, #P<0.01 indicates a statistically significant difference).

waist circumference, AHI classification, LaO_2, and average SpO_2 was not significant, and there was no significant difference.

OSAHS is closely related to the occurrence of hypertension, coronary heart disease, severe arrhythmia, and chronic congestive heart failure. Moreover, the hormone levels and physiological factors of women during pregnancy all undergo special changes. Studies have shown that the prevalence of women in pregnancy is significantly higher than that in non-pregnancy, and as the pregnancy progresses, the prevalence of OSAHS in women also increases, and especially the prevalence of OSAHS in high-risk women is significantly increased [15]. In this study, the changes in blood gas and lactic acid before and after CPAP treatment were analyzed, and it was found that AHI, ODI and lactic acid were significantly decreased after the treatment, with statistically significant differences compared with the levels before the treatment (P<0.01). However, the changes in LaO_2, average SpO_2, the pH values, and the PaO_2 levels before and after the CPAP treatment were found to be significantly increased after the treatment, with statistically significant differences compared with before the treatment (P<0.01).

In conclusion, by studying the therapeutic effect of CPAP on obstructive sleep apnea hypopnea syndrome in pregnant women during pregnancy, it was found that CPAP treatment can effectively improve blood lactic acid and pH levels in OSAHS patients, providing an experimental basis for the diagnosis and treatment of obstructive sleep apnea hypopnea syndrome during pregnancy. However, there are some deficiencies in the experimental process, such as the too small sample size. Therefore, the sample size will be increased in a follow-up study to provide more evidence for follow-up clinical treatment.

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Disclosure of conflict of interest

None.

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