Adenotonsillectomy outcomes regarding bone age and osteocalcin in treatment of obstructive sleep apnea syndrome in children

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Original article

Background: **To investigate the effect of adenotonsillectomy (AT) on bone development, quality of life and polysomnography evaluation in children with obstructive sleep apnea syndrome (OSA).**

Methods: **Preoperative and postoperative (6 months) physical examination, PSG, bone age (BA) and osteocalcin (OC) evaluation were performed on the selected OSA children (*n*=92) and the healthy children (*n*=87). The OSA children were also scored based on the OSA 18-item questionnaire. A two-year follow-up was conducted to evaluate BA and OC changes.**

Results: **After AT, 81 (88.04%) OSA children recovered completely, eight (8.70%) achieved remarkable improvements, and three (3.26%) achieved moderate improvements. In the OSA children, postoperative OSA 18-item score and the scores of the five domains were significantly higher than preoperative ones. Compared with the preoperative, body mass index (BMI), weight for age *Z*-sores, height for age *Z*-sores, weight for height *Z*-sores and BMI *Z*-score in the OSA group 6 months after the operation were significantly increased, but no significant difference was detected between the OSA and the control group. The changes of BA and chronological age in the OSA group were significantly different from those in the control group. Two years after AT, BA between the two groups was no longer significantly different. Preoperative serum OC in the OSA group was lower than that in the control group, but increased to normal levels 6 months after AT. Correlation analysis showed serum OC levels were negatively correlated with apnea hyponea index, obstructive apnea index, arousal index, and lowest oxygen saturation.**

Conclusions: **After AT, bone growth and development in children with OSA recovered gradually, and the serum OC levels decreased to the normal level. Therefore, preventive measures and positive treatments should be applied to minimize the negative effects of OSA in children.**

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Key words: **obstructive sleep apnea syndrome;**
OSA-18 score;
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Introduction

The obstructive sleep apnea syndrome (OSA) is a condition characterized by the occurrence of various types of respiratory issues during sleep involving partial occlusion in or complete cessation of the airflow.[1] OSA happens as a result of the collapse of soft tissues in the upper respiratory tract during sleep.[2] In addition to the respiratory issues, there are also symptoms of daytime hypersomnolence, heavy snoring and cognitive dysfunction.[3] The risk factors for this disease include obesity, male, thick neck, upper respiratory tract abnormality, alcohol consumption, and snoring, while the underlying mechanisms remain unclear.[4] More than 10% of children are reported to have habitual snoring and the prevalence of this disease was higher among racial minorities, children with socioeconomic disadvantage, and premature children.[5] Adenotonsillectomy (AT) or adenoidectomy remains the commonest surgery to treat pediatric OSA.[6] Recent studies showed evidence that children with OSA had a higher risk of developing cardiovascular disorders

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based on the results of polysomnography (PSG) and continuous monitoring of blood glycose.[7] Moreover, airway obstruction may also result in ischemia and hypoxia which have an effect on bone metabolism.[8] Therefore, more studies are needed to verify the association between OSA and bone metabolism.

Bone age (BA), also known as skeletal maturity, is a measure of the maturation of bones, which is assessed by hand and wrist radiograph.[9] Along with chronological age, BA is also closely associated with growth and pubertal maturation.[9] The osteocalcin (OC) protein, encoded by the bone g-carbossiglutamate gene, is only secreted by osteoblasts and is thought to play an important role in the body's metabolic regulation.[10,11] As a non-collagenous protein, OC plays an essential role in the regulation of bone turnover and mineralization.[12] Increasing data have emerged to support that OSA is associated with abnormal bone mineral density (BMD), as well as abnormal bone metabolism in the older population.[13,14] High circulating OC level is positively correlated with insulin sensitivity and leptin concentration in children, while low serum level of uncarboxylated OC adversely influences the normal functions of beta-cells, especially in prediabetic children.[15] However, currently only a few studies have investigated the association between OSA and bone development.[8,16] Moreover, it remains controversial that in males with OSA, the serum level of OC was elevated after positive airway pressure treatment.[17] Therefore, we conducted this study to examine BA and OC changes in the OSA children, to explore the influence of AT on bone development and quality of life, thus providing suggestions for the early treatment of OSA.

Methods

Ethical statement

The study design was reviewed and approved by the ethics committee of our hospital, and informed consent was obtained from the guardian of each subject. All procedures of this study were in compliance with the Declaration of Helsinki.[18]

Subjects

Between January 2011 and July 2013, 92 children of Han population diagnosed with OSA in our hospital were enrolled in this study as the OSA group, including 57 boys and 35 girls. The mean age of the OSA group was 7.57±2.31 years (ranged from 3-12 years), and the duration of disease ranged from 0.5 to 6 years. The OSA group had a mean weight of 22.32±6.70 kg and a mean height of 1.24±0.17 m. All the children in the OSA group were diagnosed based on the criteria proposed by American Academy of Sleep Medicine (AASM) in 2007[19] and presented one of the following symptoms: snoring; labored respiration, paradoxical movement on thoracoabdominal motion and obstructed respiration during sleep; sleepy, hyperactivity, behavior problems and learning problems. The polysomnography (PSG) monitoring found that all the OSA children had obstructive apnea index (OAI) ≥1 time/h or apnea hyponea index (AHI) >5 time/h. Each child was given a physical examination and an electro epipharyngoscope examination, and was found to have different degrees of tonsil hypertrophy and adenoidal hypertrophy. The exclusion criteria were: 1) subjects with abnormal anatomic structure in the mouth, nose or pharynx; 2) subjects diagnosed with severe asphyxia in newborn or neonatal hypoxic ischemic encephalopathy (HIE); 3) subjects with central sleep apnea (CSA), liver-kidney disease, fracture, rickets, metabolic bone disease, asthma, infectious diseases, tumors, peripheral vascular disease, rheumatic and immunologic disease or chronic renal failure; 4) subjects with severe mental retardation or schizophrenia that might influence PSG evaluation; 5) subjects with a history of glucocorticoid, growth hormone or vitamin D use within six months that could affect the measurement of serum OC; 6) children who recently had surgery. During the same period, a total of 87 healthy children of Han population were enrolled as the control group, containing 51 boys and 36 girls. All subjects in the control group didn't have snoring, sleep disorders or endocrine diseases, and all passed the PSG evaluation. The mean age of the control group was 7.75±1.98 years. There was no significant difference in sex or mean age between the OSA group and the control group (both $P>0.05$). The blood samples from all the subjects must be free from hemolysis.

AT surgery

All the OSA children were under general anesthesia with endotracheal intubation prior to AT. The mouth was held open with a Boyle-Davis mouth gag and then a urethral catheter was inserted to lift the soft palate. Then a nasal endoscope was inserted in 70° to distinguish the adenoid from its surrounding tissues. During the AT surgery, an adenoid curette was used to ensphere the adenoid and keep it away from the torus. The adenoid was then gently and rapidly pushed to the retropharyngeal. After the curette reached the boundary between the retropharyngeal and the top of nasopharynx, the curette was adjusted into an arc shape. Meanwhile, cotton pledgets were used to inhibit bleeding. Dissection method was used to remove the tonsil. Mucous membranes were separated to reach the top of tonsil. Then the top of tonsil was pulled to

plica triangularis, and a snare was applied to remove the tonsil, followed by compression hemostasis. The wound was stitched once the active bleeding appeared. Subsequently, the cotton pledgets were removed, and a nasal endoscope was inserted in 70° to check for adenoid residue and bleeding. Once adenoid residue or bleeding was found, coblation was used. After AT, each child in the OSA group was given antibiotics for three consecutive days and kept under close observation for wound bleeding and respiration.

Evaluation of quality of life

Quality of life for children with OSA was evaluated based on OSA 18-item quality of life survey containing five domains that were sleep disturbance, physical suffering, emotional distress, daytime problems and caregiver concerns.[20,21] A point scale was used ranging from 1 (never) to 7 (all the time) to grade the severity of the problem mentioned in the item. The total score, which could range from 18 to 126, was used to categorize the severity of OSA into mild (<60), moderate (60-80) and severe (>80). Children were scored before and after the surgery; the difference between the preoperative average score (preoperative OSA-18 total score/18) and postoperative average score (postoperative OSA-18 total score/18) was used to measure the change of the quality of life due to AT. The difference between the two average scores could range from -7.0 to +7.0; a negative score indicated deterioration, while a positive score indicated improvement in quality of life. The improvement of quality of life was further categorized into four groups based on the average score difference: slightly improved (<0.5), mildly improved (0.50-0.99), moderately improved (1.00-1.49), and remarkably improved (>1.5).

Physical examination

Height, weight, body mass index (BMI), height standard deviation score (HtSDS) and weight standard deviation score (WtSDS) of each child were recorded and used to evaluate physical condition. Height and weight were measured using gauge-height measurements when the subject stood still on the machine in light clothes. The children were asked to stand straight with the occipital bone, the top of buttock and the heels touching the measure ruler, and then weight and height were recorded to 0.01 kg and 0.01 m. The assessment of BMI growth was conducted by *Z*-score method (standard deviation method) using height, weight, BMI, weight age, height for age, height for age *z*-score as well as BMI *Z*-score for indicators. *Z*-score was calculated by the formula *Z*-score=(measured value-median of reference value)/standard deviation of reference value. The standards for assessment were: 1) low body weight: weight for age *Z*-sores (WAZ) <-2; overweight: WAZ >2; 2) growth retardation: height for age *Z*-sores (HAZ) <-2; 3) slim: weight for height *Z*-sores (WHZ) <-2; obesity: WHZ >2; 4) slim: BMI *Z*-score <-0; obesity: BMI Z -score >2.[22]

PSG

A PSG (Embla RemLogic, Embla Systems LLC, USA) measurement was performed for more than 7 hours. The data, including electroencephalogram, electrocardiogram, electronystagmogram, oxygen saturation, scoring, oral and nasal respiration, oral and nasal respiration, leg movement and sleep position, were recorded. The results of PSG were auto-analyzed by computer software and were manually checked. Sedative, drinks that may influence the central nervous system, or exciting activities were prohibited within 24 hours prior to PSG. The OSA children were accompanied by their own parents and urinated before PSG. The sleep related indexes, including AHI, OAI, arousal index (AI), and lowest oxygen saturation ($LSaO_2$), were calculated according to the results of PSG. AHI was an index used to indicate the severity of sleep apnea, represented by the number of apnea and hypopnea events per hour during sleep (apneas for more than or equal to two respiratory cycles). Hypopnea is defined as a decreased amount of air movement into the lungs and could cause decreased oxygen level in the blood (airflow reduced 50%). AI was the number of times of arousal in the cerebral cortex. PSG monitoring was conducted every night. Abnormal phenomena were defined as OAI >1 time/h or AHI >5 time/h. Hyoxemia was diagnosed if the lowest oxygen saturation was less than 0.90. The subjects who had the abnormal phenomena or hyoxemia were diagnosed with OSA.

Examination of BA and OC

The BA of each child with OSA was determined by *X*-ray on the wrist of the left hand in the anteroposterior position. The film was evaluated using TW2 score randomly and blindly by experienced professional radiologists. According to the score by gender, the stage of the bone development was assessed, based on which the corresponding BA was decided by referring to the Children's bone age standard table.[23] Each film was double assessed and the second assessment should be at least 90% consistent with the original assessment.

Venous blood sample in the ulnar vein (5 mL) was collected from each OSA child with overnight fasting and stored in sterile tubes. Blood sample was centrifuged at 3000 r/min for 15 min at the room temperature, and then the supernatant was obtained

and stored at -70°C for later use. Enzyme-linked immunosorbent assay (ELISA) was conducted with MultiskanMK3 Enzyme-labelled meter (Thermo Lab systems, Franklin, MA) based on the instructions from the manufacturer to measure the OC level. The ELISA assay kit was provided by Blue Gene Biotechnology, Shanghai, China.

Routine monitoring was conducted 2 hours after surgery including blood pressure, oxygen saturation and heart rate. The OSA children were administered hemostatic drug for one day and anti-infection treatment for five days, after which they were discharged from hospital.

Follow-up

Within four weeks prior to AT, the OSA 18-item survey was taken by the guardian of each OSA child, and physical examination and PSG evaluation were conducted on each OSA child as well. Six months after AT, each OSA child was given the OSA 18-item survey, physical examination and PSG again to assess the efficacy of AT. Data collection and follow-up were conducted by the same physician. The BA and OC were examined for three times during the follow-up, 6 months, 12 months and 14 months after surgery. All the OSA children were followed up for 2 years.

Therapeutic evaluation

Treatment outcomes were defined as follows. Complete recovery: no signs of clinical symptoms, AHI <5 times per hour, and $LSaO_2$ >90%; remarkable improvement: significantly relieved clinical symptoms, reduction of AHI >50%, and increase of $LSaO_2$ >50%; moderate improvement: slightly relieved clinical symptoms, reduction of AHI ranging 25%-50%, and increase of $LSaO_2$ ranging 25%-50%; no improvement: constant or deteriorated clinical symptoms, reduction of AHI <25%, and increase of $LSaO_2$ <25%.

Statistical analysis

SPSS 21.0 software (SPSS Inc, Chicago, IL, USA) was used for data analysis. Continuous data were presented as mean±standard deviation (mean±SD), and were compared by *t* test or variance analysis. Pairwise comparisons among three groups were conducted by *q* test (Newman-Keuls method). Categorical data were presented as frequencies and proportions, and compared by χ^2 test. Categorical data with $n<40$ or $T<5$ were assessed by Fisher's exact test. The comparisons on the score of quality of life were conducted with Wilcoxon signed rank sum test. The associations between OC and the other indicators were assessed by correlation analysis. *P* value <0.05 was considered statistically significant.

Results

Comparisons of qualify of life before and after AT

Table 1 shows the OSA 18-item scores before and after AT in the OSA children. Compared with preoperative OSA 18-item total scores and the scores of the five domains, the post-operation evaluation on the quality of life showed remarkable improvement (all $P<0.01$). More specifically, the preoperative OSA 18-item total score was 81.9±6.3, while the postoperative score was 42.1±4.6. The average domain difference before and after AT was 5.68±0.54. Among the five domains of the OSA 18-item survey, sleep disturbance (change=1.73±0.25) showed remarkable improvement after AT (change ≥1.50); physical suffering (change=1.23±0.34) and caregiver concerns (change=1.38±0.24) were both moderately improved (change=1.00-1.49); daytime problems (change=0.97±0.15) and emotional distress (change=0.51±0.16) were only mildly improved (change=0.50-0.99).

Comparisons of growth parameters before and after AT

Preoperative BMI, WAZ, HAZ, WHZ and BMI Z-score of the two groups all showed significant difference (all $P<0.05$), but no significant difference in preoperative height or weight between the control group and the OSA group was observed (both $P>0.05$, Table 2). Six months after surgery, the differences in height, weight, BMI between the control and OSA group were not statistically significant (all $P>0.05$). In the control group, the preoperative WAZ, HAZ and WHZ were not significantly different from those after AT (all $P>0.05$); the differences of postoperative WAZ, HAZ and WHZ between the OSA group and the control group were not significant (all $P>0.05$). However, the preoperative WAZ, HAZ, WHZ and BMI *Z*-score in the OSA group were significantly different from those in the control group (all $P<0.05$); and the comparisons between the preoperative and postoperative WAZ, HAZ WHZ and BMI *z*-score in the OSA group also showed significant results (all $P<0.05$).

Table 1. Comparisons of quality of life in the OSA children preoperatively and postoperatively (mean±SD, $n=92$)

OSA-18 items	Preoperative score	Postoperative score (6th month)	Change values	*P*
Sleep disturbance	20.2±2.6	8.1±2.1	1.73±0.27	<0.01
Physical suffering	17.5±3.4	8.2±2.4	1.32±0.35	<0.01
Emotional distress	10.9±2.0	7.4±1.4	0.51±0.16	<0.01
Daytime problems	14.7±2.1	8.0±1.6	0.97±0.15	<0.01
Caregiver concerns	18.8±3.2	9.1±2.2	1.38±0.24	<0.01
OSA-18 total score	82.2±5.9	40.7±4.2	5.92±0.53	<0.01

OSA: obstructive sleep apnea syndrome. Change values=(Preoperative score-Postoperative score)/7.

Comparisons of PSG before and after AT

In the OSA group, 81 children (88.04%) showed complete recovery after AT. Eight children (8.70%) showed significant improvements, and three children (3.26%) achieved moderate improvements. Preoperative AHI, AI and $LaSO_2$ were significantly different between the OSA and control groups (all $P<0.01$). In the OSA group, postoperative AHI, OAI and AI were significantly lower than preoperative ones (both $P<0.01$), while postoperative $LSaO_2$ was significantly higher than preoperative $LSaO_2$ ($P<0.01$). No significant difference was found in any sleep-related index between the two groups six months after AT (all $P>0.05$) (Table 3).

BA and OC analysis before and after AT

According to our records, four children in the control group and five children in the OSA group were lost to follow-up by the end of the first year of the follow-up. In the second year of the follow-up, nine children in the control group and 12 children in the OSA group were lost to follow-up. The overall follow-up rate of our study was 88.27%. The data obtained in the follow-up are presented in Table 4. BA in the OSA group was 7.37±2.18, which was slightly younger than that of the control group (7.67±1.99, $P>0.05$). Similarly, chronological age of the OSA group was 7.59±2.30, which was slightly younger than that of the control group (7.75±1.98, $P>0.05$). Our data showed that BA of the control group was 0.4 years older than that of the OSA group, and the chronological age in control group was 0.16 years older than in OSA group. The differences in BA and chronological age were considered as indexes to measure the differences between the control and the OSA group. Completely randomized pairwise t tests found that the difference between BA and chronological age was statistically significant ($P<0.01$). The OSA group had greater changes in BA and chronological age compared with the control group. The OSA group had a smaller mean BA compared with control group adjusted by age. One year after surgery, the difference in BA between the OSA and control group was significantly narrowed, and after followed up for 24 months, the difference in BA between the two groups was no longer significant ($P>0.05$). Moreover, before surgery, the OSA group had a significantly lower OC level than the control group

Table 2. Comparisons of the growth parameter between the control group and OSA group (mean±SD)

Items	Preoperative		Follow-up (6th month)	
	Control group (n=87)	OSA group (n=92)	Control group (n=87)	OSA group (n=92)
Height (m)	1.28±0.13	1.24±0.17	1.36±0.17†	1.31±0.17‡
Weight (kg)	23.42±6.21	25.32±6.70	25.86±6.45†	26.21±6.70‡
BMI (kg/m^2)	18.11±3.08	20.22±3.41*	18.53±3.21†	19.82±3.65‡
WAZ	0.54±0.08	0.22±0.18*	0.56±0.11	0.50±0.17‡
HAZ	1.14±0.31	0.67±0.36*	1.10±0.26	1.02±0.30‡
WHZ	0.45±0.09	0.07±0.16*	0.46±0.10	0.42±0.14‡
BMI-Z-score	0.82±0.29	0.59±0.35*	0.79±0.26	0.83±0.28‡

OSA: obstructive sleep apnea syndrome; BMI: body mass index; WAZ: weight for age Z-sores; HAZ: height for age Z-sores; WHZ: weight for height Z-sores; BMI-Z-score: body mass index Z-score. *: comparisons between the preoperative control and OSA groups, $P<0.05$; †: comparisons between the preoperative and postoperative control groups, $P<0.05$; ‡: comparisons between the preoperative and postoperative OSA group, $P<0.05$.

Table 3. Comparisons of PSG between the control group and the OSA group preoperatively and postoperatively (mean±SD).

PSG	Control group	OSA (preoperative)	OSA (postoperative 6th months)
AHI (time/h)	1.71±1.12	21.72±7.18*	2.07±1.55†
OAI (time/h)	0.69±0.11	1.36±0.67*	0.73±0.16†
AI (time/h)	0.57±0.50	1.80±0.62*	0.60±0.54†
$LSaO_2$ (%)	96.65±0.94	81.15±2.16*	96.09±2.53†

OSA: obstructive sleep apnea syndrome; PSG: polysomnography; AHI: apnea hyponea index; OAI: obstructive apnea index; AI: arousal index; $LSaO_2$: lowest oxygen saturation. *: comparisons between control group and preoperative OSA group, $P<0.01$; †: comparisons between the preoperative and postoperative OSA group, $P<0.01$.

Table 4. Comparisons of BA and OC between the control and OSA groups (mean±SD)

Index		Preoperative	Follow-up 6th month	Follow-up 12nd month	Follow-up 24th month
Chronological age, y	Control group	7.75±1.98	8.25±1.98	8.72±1.95	9.77±1.97
	OSA group	7.59±2.30	8.09±2.32	8.60±2.36	9.53±2.38
	P	0.62	0.62	0.72	0.49
BA, y	Control group	7.67±1.99	8.25±1.99	8.65±1.96	9.70±1.99
	OSA group	7.37±2.18	7.95±2.18	8.51±2.19	9.44±2.14
	P	0.34	0.48	0.66	0.43
BA–chronological age, y	Control group	-0.08±0.05	-0.07±0.05	-0.07±0.05	-0.07±0.05
	OSA group	-0.21±0.17	-0.14±0.10	-0.09±0.06	-0.08±0.05
	P	<0.01	<0.01	0.02	0.21
OC (μg/L)	Control group	8.42±1.20	8.82±1.15	9.08±1.01	9.24±0.99
	OSA group	6.86±1.18	8.47±1.23	8.84±1.15	9.12±0.97
	P	<0.01	0.05	0.15	0.44

OSA: obstructive sleep apnea syndrome; BA: bone age; OC: osteocalcin.

(P<0.01). After being followed up for 6 months, OC serum level of the OSA group was not significantly different from that of the control group (P>0.05).

Correlation between serum OC level and BMI, AHI, OAI, AI, $LSaO_2$ in OSA children

Our analysis showed that serum OC level was negatively correlated with AHI, OAI, AI and $LSaO_2$ in the OSA children (all P<0.01, AHI: r=-0.78; OAI: r=-0.74; AI: r=-0.61; $LSaO_2$: r=-0.85), while no significant correlation between the serum OC level and BMI was identified (P>0.05, r=-0.03).

Discussion

This study provided evidence that the quality of life and PSG indexes were much improved in the OSA children after AT. Moreover, our study also demonstrated that the OSA children had retarded BA and a lower level of OC compared with the healthy controls. The correlation analysis showed that serum OC level was negatively correlated with AHI, OAI, AI and $LSaO_2$ in the OSA children.

Quality of life and the PSG indexes being improved after AT in the OSA children supported that AT contributed to the postoperative outcomes in the treatment of OSA. Childhood OSA is associated with numerous adverse health outcomes, including cognitive and behavioral deficiencies, which is a major concern of parents of OSA children.[24] Our results demonstrated that different degrees of improvements were achieved in sleep disturbance, physical suffering, caregiver concerns, daytime problems and emotional distress after AT in the OSA children. Consistent with the results of the OSA 18-item survey, quality of sleep was significantly improved according to the PSG indexes, including AHI, AI and $LSaO_2$. Our results are consistent with the previous studies showing that the surgical treatment for OSA in children resulted in great relief from the symptoms as well as significant improvements in quality of postoperative life and PSG indexes.[25,26]

Our study also found that the OSA children had smaller BA and lower serum level of OC compared with the healthy children both preoperatively and postoperatively, and the serum OC level in the OSA children returned to the normal level after the 24-month follow-up, suggesting that OSA was involved in the bone development in children. During OSA, recurrent hypoxemia and anoxia may cause disturbance in hemodynamics, endocrine dysfunction and neurological dysfunction system, resulting in damage to multiple systems including the cardiovascular system, the urinary system, the central nervous system, the hematological system, and the endocrine system.[17] Cumulative evidence showed that hypoxia might have unfavorable effects on patients with OSA in bone metabolism, and that nocturnal hypoxia might increase the number and volume of osteoclasts in two experimental models,[27] which might have resulted from the disturbance of the balance between osteoclast and osteoblast in favor of osteoclast in the presence of hypoxia.[28,29] However, the detailed mechanism of OSA causing bone mass loss through hypoxia, inflammatory and oxidative stress in the bone metabolism remains unclear.[30] Experimental models at the bone level suggested that chronic exposure to anoxia could lead to down-regulation of osteogenic differentiation and stimulation of osteoclast formation to promote the osteoblastic activity, which might inhibit bone formation in patients with OSA.[14,28] In agreement with our results, previous studies postulated that OSA patients, as well as patients with lung disease, had impaired bone metabolism with increased bone resorption and relatively suppressed bone formation.[31,32]

In this study, we demonstrated that serum OC level was significantly negatively correlated with AHI, OAI, AI and $LSaO_2$. As AHI, OAI, AI and $LSaO_2$ were monitoring indexes derived from the PSG findings and were all associated with the severity of OSA, our results implied that serum OC levels were negatively correlated with the severity of OSA. These findings were supported by our later results that the serum OC level in the OSA children gradually increased to the normal level after the 24-month follow-up. Therefore, the serum OC level may also be considered as a candidate biomarker for OSA severity in addition to AHI.

In summary, our study provided convincing evidence that OSA had an unfavorable influence on quality of life and bone development in children, and the positive treatment with AT would help to improve the postoperative bone development in OSA children and bring the serum OC levels to the normal level. As childhood is a critical period of growth and development, we suggest OSA children should receive positive surgery treatment.

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Competing interest: None.

Contributors: Zhang QB designed and performed the experiments, and wrote the manuscript. Li YF, Li MX and Kong LY performed experiments and contributed to the writing of the manuscript. Zhang QB, Jiang LF, Feng HW and Fan XL analyzed the data and collated the data, designed and developed the database, carried out data analyses. Zhang QB, Li YF and Li MX contributed to revising this manuscript. All the authors read and approved the final manuscript.

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