The Effect of Obstructive Sleep Apnea Syndrome on Growth and Development in Nonobese Children: A Parallel Study of Twins

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Objective To explore the effects of obstructive sleep apnea syndrome (OSAS) on children's growth by the study of identical twins.

Study design Seventeen cases of nonobese children with OSAS were included in this study. The control group was their identical twin sibling, who had no signs of OSAS. Data including height, weight, and serum insulin–like growth factor 1 levels were analyzed before tonsillectomy and adenoidectomy (T&A) and at 3, 6, and 12 months after surgery.

Results The mean apnea hyponea index was 3.9 times/hour in patients with OSAS and became normal after surgery. Minimum oxygen saturation gradually increased after T&A. The height and weight of the OSAS group before T&A was lower than the control group. During the follow-up period, height and weight increased but were lower than the control group. Serum insulin–like growth factor 1 levels in the OSAS group before T&A were lower than the control group. The level was significantly increased 3 months after T&A.

Conclusion OSAS impairs growth and development. Significant growth recovery occurs after T&A, and early surgical intervention is an important factor for improvement in growth. *(J Pediatr 2015;166:646-50)*.

Obstructive sleep apnea syndrome (OSAS) is a public health problem that affects approximately 1%-6% of all children.[1,2] Clinically, OSAS is characterized by snoring, difficulty in breathing during sleep, and repeated obstructive apnea.[3] The effects of OSAS include poor growth and development, worsened mental health, and poor quality of life.[4] Polysomnographic criteria for the diagnosis of OSAS include an obstructive apnea index >1 event per hour of sleep and nadir arterial oxygen saturation <92%.[5] Because the sequelae of OSAS are thought to be a function of recurrent hypoxia and chronic sleep deprivation, prompt treatment of the disorder seems imperative. The first-line treatment of pediatric OSAS is tonsillectomy and adenoidectomy (T&A). The efficacy of T&A may be better than 80%, especially in otherwise-healthy nonobese children.[6] Currently no report, however, can confirm the relationship between OSAS and growth impairments because of individual variables. The goal of the study is to examine the effect of OSAS on growth and development by comparing key indicators between twin siblings with and without OSAS, such as apnea hyponea index (AHI), lowest oxygen saturation, weight, height, and serum insulin–like growth factor 1 (IGF-1) levels. We further compared these variables before and after T&A to determine the long-term impact of surgical intervention.

Methods

Data were collected from the Department of Otolaryngology Head and Neck Surgery, Xinhua Hospital Affiliated to Shanghai Jiaotong University, School of Medicine between January 2010 and January 2013. During this period, 3735 children with OSAS were treated in our department, including 113 cases of identical twin patients. In the majority of our twin cases (96 cases, 48 couples), both siblings were diagnosed with OSAS. We identified 17 cases with OSAS in which their identical twin brother or sister did not have OSAS.

These cases were enrolled in our study. None of the patients were obese (body mass index <95th percentile), and 10 twin pairs were boys. The twins ranged in age from 3 to 12 years (6.76 ± 2.59 SD), had similar birth weight and length, were brought up in the same environment, and were all in good nutritional status. The patients were diagnosed with OSAS by clinical signs and multichannel sleep apnea monitoring (polygraphy) and were referred to the Sleep-Wake Disorders Unit of the Ear-Nose-Throat department. Other primary diseases were excluded by extensive evaluations. All twins received polygraphy

AHI	Apnea hyponea index
IGF-1	Insulin–like growth factor 1
OSA	Obstructive sleep apnea
OSAS	Obstructive sleep apnea syndrome
T&A	Tonsillectomy and adenoidectomy

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monitoring to confirm the presence of OSAS. This study was approved by the hospital ethics committee and with the guardians' consent. Tonsil and adenoid hypertrophy was diagnosed in 15 cases who received T&A; 2 subjects diagnosed with adenoidal hypertrophy were treated with adenoidectomy.

Plus multichannel sleep devices (Compumedics Company, Melbourne, Australia) were applied to monitor sleep apnea overnight. The equipment records signals from external and built-in sensors. The built-in sensors include an airflow pressure transducer, a body position sensor, and an ActiGraph sensor (Pensacola, Florida). The external sensors that can be used are electrodes to assess abdominal and thoracic respiratory effort and oximetry. Cessation of chest and abdomen movement and nose and mouth airflow over 2 respiratory cycles is defined as obstructive sleep apnea (OSA). Nose and mouth flow peak reduced by 50% accompanied by more than 3% decreased arterial oxygen saturation for at least 2 respiratory cycles is defined as hypopnea. The recording data comprised electrocardiography, nose and mouth breathing, chest and abdomen movement, heart rate, pulse, and oxygen saturation. The follow-up studies were performed at 3, 6, and 12 months after T&A. All the results are presented as mean ± SD.

A total of 4 mL of fasting blood was collected between 7:00 and 7:30 a.m., centrifuged (4°C, 3000 rpm) for 10 minutes, and stored in a refrigerator set to -70°C. Serum IGF-l levels were measured by an enzyme-linked immunosorbent assay (Senxiong Co, Ltd, Shanghai, China).

All patients were followed in the outpatient clinic of Sleep-Wake Disorders Unit of Ear-Nose-Throat department 3 and 6 months and 1 year after surgery. At each follow-up visit, subjects were asked about symptoms; all were studied by PSG overnight. Heights and weights were recorded, and blood samples were collected.

Statistical Analyses

Height, weight, serum IGF-1 levels, and AHI before surgery, 3 months, 6 months, and 1 year after T&A were collected and statistically analyzed by a generalized estimating equation model and 2-tailed *t* tests for paired data with SAS software package (StataCorp LP, College Station, Texas). In the generalized estimating equation model, 2 by 2 exchangeable structures were used to model the correlation between the twins at each time point, and the AR(1) structure was used to model the correlation within each person overtime. Z-score was calculated based on the Center for Disease Control and Prevention growth charts from the Research Institute Web site of the Children's Hospital of Philadelphia (http://stokes.chop.edu/web/zscore/).

Results

Two weeks after T&A, patients returned for follow-up visits with their surgeons for tonsil surgical field examination. All 17 patients with OSAS showed normal feeding and a significant improvement of snoring and nose-breathing 2 weeks after surgery. During the follow-up period, the patients showed a more rapid increase of height and weight than their twin siblings. All parents were satisfied with growth and development progress after T&A surgery.

The AHI was 3.9 ± 0.9 (mean ± SD) events/hour in patients with OSAS, which was greater than controls (AHI: 0; $P < .001$). AHI was 0.2 ± 0.6 events/hour and 0.2 ± 0.4 events/hour after 6 and 12 months, respectively. There were no significant changes to the control group ($P > .05$; **Table I**).

The preoperative lowest nocturnal median oxygen saturation in the OSAS group was 87% and in their twin sibling was 100%. The minimum oxygen saturation was gradually increased after T&A in patients with OSAS and was not different at 6 months ($P > .05$; **Table I**). The Z-value of height between the groups was −6.38, Z-value for weight was −7.82, and the Z-value for IGF-1 was −6.99 (**Table II**). After surgery, Z-values of growth index improved. The height of OSAS group before T&A (111.20 ± 13.47 cm) was significant lower than the control group (122.20 ± 15.85 cm, $P < .001$; **Table III**). After T&A, height rapidly increased in the OSAS group, although the height of patients with OSAS remained lower than the control group. The gap between 2 groups was reduced from 11.0 to 6.3 cm (**Table III**).

All patients with OSAS showed an obviously lower body weight than their siblings before T&A (17.88 vs 24.06 kg, $P < .001$). After surgery the weight standards improved in OSAS group, but differences between the 2 groups persisted at 1 year of age ($P < .001$) (**Table III**).

Children with OSAS had lower z-scores than their siblings before surgery. Z-scores in the OSAS group increased 3 and 6 months later but still did not catch up with the control group. Z-scores were all below zero, likely reflecting physical differences between Asian and American children (**Table III**).

Increases in height were greater in patients of 6 years of age than in older patients after T&A (**Figure 1**). Weight gain also increased rapidly in the control group during follow-up, and the weight gap was reduced from 3.4 to 1.1 kg (**Figure 2**; available at www.jpeds.com).

Serum IGF-1 levels of the OSAS group (54.47 ± 9.87 ng/mL) before T&A were lower than the control group (238.00 ± 66.01 ng/mL, $P < .001$). The level was significantly

Table I. Polygraphy values

	Lowest oxygen saturation			AHI		
	Mean ± SD	t	*P* value	Mean ± SD	t	*P* value
Control	100%			0		
Before T&A	87% ± 3%	19.84	<.001	3.9 ± 0.9	18.70	<.001
3 months	98% ± 2%	2.73	.018	0.2 ± 0.6	1.73	.104
6 months	99% ± 2%	1.65	.117	0.2 ± 0.4	1.82	.095
1 year	99% ± 2%	1.79	.090	0.2 ± 0.4	1.85	.083

Polygraphy values of patients with OSAS and their twin siblings (17 cases). The polygraphy evaluation was performed for all patients and their control twins before T&A and also performed for patients 3 months, 6 months, and 1 year after surgery. t and *P* values were all calculated between the control and patient group at different time points.