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Evaluation of the effects of adenotonsillar hypertrophy and adenotonsillectomy on growth in children

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Summary

Aim: Several factors including genetic factors, nutrition and environment play a critical role in the growth of children. Adenotonsillar hypertrophy (ATH) can cause growth retardation by obstructing the upper airway. Surgical treatment of ATH has been considered to have a positive effect on growth. The aim of this study was to evaluate the role of chronic ATH on growth by measuring weight, height, body mass index (BMI), bone age, serum insulin-like growth factor 1 (IGF-1) and insulin-like growth factor binding protein 3 (IGFBP-3) values before and after adenotonsillectomy.

Material and Method: The study was approved by the Ethics Committee (4.5.2004; 04/170) and written informed consents were obtained from parents of the participants. A total of 40 prepubertal children who were diagnosed as chronic ATH were enrolled. Obstructive symptoms were questioned in the medical history before surgery. Weight, height, BMI and bone age values were measured and compared with reference values. Preoperative serum IGF-1 and IGFBP-3 values were compared with the control group which consisted of healthy children. Rates of obstructive symptoms, weight, height, BMI, bone age, serum IGF-1 and IGFBP-3 values of the patients were determined seven months after adenotonsillectomy and were compared with preoperative values.

Results: Obstructive symptoms in children with ATH decreased remarkably after surgery. Preoperative mean value of bone age of the patients was statistically lower than reference values ($p<0.05$) and mean value of serum IGF-1 was lower than than the control group ($p<0.05$). IGF-1 and IGFBP-3 values did not increase significantly after surgery ($p>0.05$). However, growth retardation was detected in three out of 40 patients based on the anthropometric measurements.

Conclusions: In this study, antropometric findings showed that chronic ATH did not cause significant growth retardation in prepubertal children. In addition, we could not prove that surgical treatment of ATH improved the growth in the postoperative follow-up period of seven months. This result may be related with our study population with a limited number of patients who had baseline growth retardation and short postoperative follow up period. Further studies with large number of patients and longer postoperative follow-up periods are required to determine the exact role of chronic ATH in growth retardation. *(Turk Arch Ped 2012; 47: 257-262)*

Key words: Adenoid hypertrophy, adenoidectomy, anthropometry, bone age measurement, growth, IGF-1, IGFBP-3, tonsillar hypertrophy, tonsillectomy

Introduction

In children, growth is a multifactorial process in which genetic, nutritional and environmental factors are involved. Adenotonsillar hypertrophy (ATH) leading to upper airway obstruction is one of the factors which may cause growth retardation. Understanding the importance of upper airway obstruction and its complications has started to bring obstructive hypertrophy to the front to a greater extent among adenotonsillectomy indications compared to recurrent infections (1). Sleep disturbances which occur in children with adenotonsillar hypertrophy decrease the efficiency of growth hormone by disrupting the quality and time of REM (rapid eye movement) sleep during which growth hormone is secreted with a higher rate (2,3,4,5,6,7). The serum levels of IGF-1 and IGFBP-3 which mediate the effects of growth hormone vary in proportion to growth hormone levels. Since the secretion of IGF-1 and IGFBP-3 in not pulsatile in contrast to growth hormone, their measurements are widely used clinically (8,9,10,11,12,13).

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In this study, the effect of chronic ATH on growth was examined by comparing weight, height, Standard deviation score (SDS), body mass index (BMI), bone age, IGF-1 and IGFBP-3 values before and after adenotonsillectomy in 40 children with ATH between the ages of 4 and 10 years in whom no other cause for growth failure could be found.

Material and Method

Ethics committe approval was obtained for this study which would examine the effect of adenotonsillar hypertrophy on growth in children (4.5.2004; 04/170). Informed consent was obtained from the parents of the patients.

Patients between the ages of 4 and 10 years who presented to otolaryngology outpatient clinic with complaints including nasal congestion, snoring, sleeping with the mouth open and loss of appetite and whose complaints were found to be related to adenotonsillary hypertrophy were randomly included in the study. Tonsillar hypertrophy was defined according to Brodsky's scale: "0":tonsils do not lead to airway obstruction, "1+": tonsils lead to obstruction in the airway by less than 25%, "2+": tonsils lead to obstruction in the airway by 25-50%, "3+": tonsils lead to obstruction in the airway by 50-75%, "4+": tonsils lead to obstruction in the airway by more than 75%. Only patients with 3+ and 4+ hypertrophy were included in the study. The size of the adenoid was determined with flexible fiberoptic endoscope. Adenoid obstructing the nasopharyngeal cavity by <50% was classified as small, adenoid obstructing the nasopharyngeal cavity by 50-75% was classified as moderate and adenoid obstructing the nasopharyngeal cavity by >75% was classified as large (14). >50% obstruction in the nasopharyngeal airway was considered as adenoid hypertrophy.

Children with conditions which lead to growth failure including chronic lung disease, hypothyroidism, chronic renal disease, craniofacial disorders, cerebral palsy, malnutrition, neuromuscular disease, chronic allergic rhinitis and Down syndrome were not included in the study.

Height and weight values of all the patients included in the study were measured. Body weight was measured by a weighing scale with a sensitivity of 100 g. Height measurement was done at a sensitivity of 0.5 cm. Percentile values were determined for each patient. Body mass index (kg/m^2) was obtained. These values were compared with the values of Neyzi et al. (15).

Bone age measurement which is one of the variables of growth was evaluated by a specialist of radiodiagnostics with left hand graphy using Greulich-Pyle tables and the bone age values found were compared with healthy reference values obtained from the same reference (16).

Serum IGF-1 and IGFBP-3 values were measured before the operation. For analyses DSL-5600 Active™ IGF-1 IRMA kit and DSL-6600 Active™ IGFBP-3 IRMA kit in the gamma counter device with 12 detectors (Berthold LB 2111) (Diagnostic System Laboratories Inc., Webster, Texas, USA) were used .

For serum IGF-1 and IGFBP-3 levels a control group consisting of 27 healthy children with matched age and gender distribution was constituted. IGF-1 and IGFBP-3 results were compared with the control group.

Tonsillectomy using dissection technique and adenoidectomy by curettage were performed in the patients under general anesthesia.

The patients were called for a follow-up visit after seven months to evaluate growth. The histories of the patients were taken. Height, weight, bone age, IGF-1 and IGFBP-3 values were measured again. The results obtained were compared with the preoperative values and the reference values in the literature.

The compatibility of the values which could be measured was analysed with Kolmogorov-Smirmov test. Values with a normal distribution were expressed as x±sd. The difference between two groups (patient hormone values and hormone values of the healthy control group) was examined with Student t test. The difference between preoperative and postoperative values was examined with significance test of the difference between the two matches. Values which did not have normal distribution were expressed as median. The difference before and after the operation was analysed with Wilcoxon Signed Ranks test. A p value of <0.05 was considered as significant.

Results

16 of 40 patients included in the study were female and 24 were male. Their ages ranged between 48 months and 114 months (mean: 68.0±17.8). 10 of the 27 healthy children in the control group were female and 17 were male. The mean age was 67.6±16.7 months. The follow-up time of the patients was seven months.

When the complaints of the patients before the operation were evaluated, it was found that the most common complaint was snoring. A considerably important reduction was found in the complaints seven months after the operation (Table 1).

In the preoperative period, height percentile values were below the third percentile in three patients (two girls and one boy). Weight percentile values were below the third percentile in two patients (one girl and one boy). Target heights were calculated and it was found that one patient was behind the calculated target height and the heights of the other two patients were compatible with the target heights. SDS values of the height and weights of the patients were evaluated; height SDS was found to be low in five patients (12.5%) and weight SDS was found to be low in two patients (5%). The percentile and SDS values of the remaining patients were the same with the healthy reference values.

While improvement was observed in one of two patients whose weight percentile values were below the third percentile before the operation, no difference was observed in any of the three patients whose height percentile values were below the third percentile.

After the operation a statistically significant (p<0.05) increase was found in weight SDS values measured before the operation, whereas increase in height SDS values was not statistically significant (p>0.05) (Table 2). One of five patients who had poor height SDS values before the operation and one of two patients who had poor weight SDS values before the operation were found to have reached normal values after the operation.

BMI values recorded before the operation were compared with the values of the children in our country. BMI values were below the fifth percentile in five (13.5%) patients and it was observed that BMI values were increased to above the fifth percentile in all of them after the operation. When the mean BMI values before and after the operation were compared, a statistically significant increase was observed (p<0.05) (Table 2).

Table 1. Comparison of the rates of complaints of the patients before and after operation

Complaints	Before operation	After operation	p
Snoring	80%	10%	<0.05
Sleeping with the mouth open	62%	15%	<0.05
Frequent awakening in the night	75%	5%	<0.05
Loss of appetite	72%	25%	<0.05
Leaving the table early	57%	17%	<0.05
Malaise	60	7%	<0.05
Daytime somnolence	30%	0%	<0.05

Table 2. Comparison of the values of height SSD, weight SDS and BMI before and after operation

	Before operation (X±SD)	After operation (X±SD)	p
Height SDS	-0.47±1.4	-0.003±3.05	0.23
Weight SDS	-0.27±0.98	0.04±1.02	0.00
BMI	15.4±1.9	16.1±1.8	0.00

SD: Standart deviation, SDS: Standart deviation skor, BMI: Body mass index

Table 3. Comparison of the mean and difference values of bone age in the patients and the healthy controls

	Patient	Healthy value	p
Before operation	52.8±20.5	66.4±18.7	0.003
After operation	60.1±20.9	75.7±20.6	0.001
Growth difference (X±SD) (range of distribution)	7.3±7.2 (0-24)	9.3±3.5 (0-13.1)	0.13

SD: Standart deviation

Bone age was found to be retarded compared to the chronological age in 22 (64%) of 34 patients whose bone ages were evaluated. The mean bone age of the patients before the operation was lower compared to the healthy reference values and the difference was statistically significant (p<0.05) (Table 3). After the operation the increase in bone age values in the patients was found to be similar to the increase in the healthy reference values. The difference was not statistically significant (p>0.05) (Table 3). However, it was observed that the bone age of five of the 22 patients who had retarded bone age before the operation reached the chronological age after the operation.

Before the operation serum IGF-1 levels of the patients were statistically significantly lower compared to the control group (p<0.05) (Table 4). There was no statistically significant difference between the patients and the control group in terms of serum IGFBP-3 levels before the operation (p>0.05) (Table 4).

In the patient group, serum IGF-1 levels were increased after the operation compared to the preoperative values, but this increase was not statistically significant (p>0.05) (Table 5). The increase in postoperative serum IGFBP-3 levels compared to the preoperative values was not statistically significant (p>0.05) (Table 5).

Discussion

Adenotonsillar hypertrophy is responsible in 80% of the cases with obstructive sleep apnea and sleep disturbances related to the respiratory system in children (17). The American Pediatrics Academy considered growth failure as a severe complication of untreated obstructive sleep apnea (18). In addition, adenotonsillar hypertrophy may lead to sequelae including pulmonary hypertension, cor pulmonale, facial developmental disorders and behavioral disorders disturbing the quality of life (19,20,21).

In sleep disturbances including simple snoring or obstructive sleep apnea syndrome (OSAS) observed in children with adenotonsillar hypertrophy, the REM period during which hormone secretion is regulated is shortened. As a result of this especially secretion of growth hormone is affected. In children with OSAS, secretion of growth hormone during the night time is frequently decreased and secretion of growth hormone may be improved with surgical treatment of OSAS (22). In addition, increased work load during respiration at nigthtime in upper airway resistance syndrome in which respitaroy effort is increased and hypoxia interrupts sleep at night decreases the quality and time of REM sleep by causing excessive energy loss and respiratory acidosis and decreased activity of growth hormone may result in growth failure in children (23).

In children with adenotonsillar hypertrophy, daytime complaints including loss of appetite and leaving the table early are observed in addition to nighttime findings. As a result of difficulty in feeding casued by obstruction calorie intake decreases, the rate of increase in weight decreases in the short

Table 4. Comparison of IGF values of the patients and the controls before operation

	Patient group (n=40)	Control group (n=27)	t	p
IGF-1 (ng/mL)	114.5±89.5	202,3±106.1	3.6	0.001
IGFBP-3 (ng/mL)	3338.1±1047.5	3394.7±1084.7	0.2	0.83

IGF-1 : Insulin like growth factor 1
IGFBP-3: Insulin like growth factor binding protein 3

Table 5. Comparison of IGF values of the patients before and after operation

	Before operation	After operation	p
IGF-1 (ng/mL) (median/Range of distribution)	80.2 (3.30-347)	126.5 (11.3-802)	0.12
IGFBP-3 (ng/mL) (X±SD)	3338.1±1047.5	3496±886.6	0.38

IGF-1 : Insulin like growth factor 1
IGFBP-3: Insulin like growth factor binding protein 3
SD: Standart deviation

term, the rate of increase in height decreases in the long term and growth failure may develop (24).

Opening of the airway after adenotonsillectomy affects growth in a positive way. Increase in calorie intake by increased appetite, decrease in calorie consumed at night and improvement of the function of growth hormone are involved in this (2,3,24,25,26,27,28,29).

Some studies have shown that adenotonsillar hypertrophy has a negative effect on growth with a rate of up to 40% (30,31,32). Excessive obstruction and presence of additional problems including laryngomalacia and Down syndrome increase this rate (33,34,35).

Presence of specific findings of adenotonsillar hypertrophy and its appropriate anatomic localization for examination make the diagnosis easy. Polysomnographic test is not needed before the operation in patients with a marked adenotonsillar hypertrophy on physical examination and a history of snoring and apnea. Polysomnographic test should be done in children who have a suspicious history, inappropriate examination findings and who are in the high-risk group for surgery.

In this study, 87.5% of the patients had 3+ and 12.5% of the patients had 4+ adenotonsillar hypertrophy. Most of these patients had complaints including snoring (80%), frequent awakening at night (75%), sleeping with the mouth open (62%), loss of appetite (72%), leaving the table early (57%) and malaise (50%). Seven months after adenotonsillectomy somnolence at daytime disappeared in all patients, snoring, frequent awakening at night, sleeping with the mouth open, loss of appetite, leaving the table early and malaise disappeard in a large proportion of the patients.

Generally, measurements including weight, height, BMI, IGF-1 and IGFBP-3 are used in evaluation of growth failure caused by adenotonsillar hypertrophy alone where other factors which may affect growth have been excluded (24,31).

Weigh and height values are the variables used frequently for evaluation of growth and nutrition and SDS values are used to indicate the extent of low weight and short stature and to follow up the efficiency of treatment. These variables are interpreted by comparing them with previously determined values of children which show normal growth appropriate for age and gender. In growth curves which are formed based on normal limits, the lower line is equivalent to the third percentile and the children below this line are considered low-weight. Height values below 2 SD value of the mean value or height values below the third percentile in height percentile curves which we use frequently for evaluation are considered as short stature.

Ersoy et al. (27) evaluated the growth of 28 children with ATH between the ages of 3 and 10 years by comparing the measurements performed on the 6th and 12th days after adenotonsillectomy with the measurements of 20 healthy children. They found that the height and weight values of the patients before operation were lower compared to the healthy group, but the difference was not statistically significant, but the height values of the patients reached the levels of the healthy children predominantly in the first year after operation.

Selimoğlu et al. (3) compared the weight and height SDS values of 29 prepubertal patients with adenoid hypertrophy with the values of 20 healthy children and found that the height and weight values of the patient group with ATH before adenotonsillectomy were lower compared to the values of the healthy control group and there was no significant difference between the weight and height SDS values of patients and the control group after operation.

In the study performed by Aydoğan et al. (23), the weight values of 38 patients between the ages of 4 and 10 years with recurrent tonsillitis were found to be within normal limits before operation. A statistically significant increase was found in weight SDS values 12-18 months after adenotonsillectomy, whereas the increase in height SDS values was not found to be statistically significant.

In the study performed by Vontetsianos (34) in which the follow-up period after adenotonsillectomy was 6-13 months, weight SDS values and height SDS values (especially in children younger than 5 years of age) were found to be significantly increased after operation.

In this study, it was observed that weight and height percentiles and SDS values were found to be normal in most of the patients before operation. Only a total of five patients (12.5%) were found to have values in favour of growth failure (height percentile in three patients (7.5%), weight percentile in two patients (5%), height SDS in five patients (12.5%) and weight

SDS in two patients (5%)). In two of the five patients who were found to have growth failure, normal values were found seven months after operation. Low values of both height and weight may be indicators of genetic factors and structural growth delay. When the target heights of the three patients whose growth did not improved were calculated, it was found that two of them had familial short stature. One patient who had no improvement was started to be followed up. A statistically significant increase in weight SDS value was found in the patients after operation ($p<0.05$), whereas the increase in height SDS value was not found to be statistically significant ($p>0.05$).

BMI which is used to show nutritional status is easily calculated and is a clinically important test showing subcutaneous and total body fat. However, certain BMI percentiles determined for the area where the child lives should be known to evaluate this accurately.

Ersoy et al. (27) found that BMI and BMI SDS values of children with ATH before and 6 and 12 months after adenotonsillectomy were higher compared to the healthy group, but the difference was not statistically significant ($p>0.05$); the results were proposed to be caused by the fact that the weight values of the patients were similar to the healthy group and height values of the patients were lower compared to the healthy group.

Nieminen et al. (36) found that the BMI values of 30 patients with obstructive sleep apnea syndrome, 40 patients with primary snoring and 30 healthy children were very close to each other ($p>0.05$).

In this study, BMI values of the patients before and after operation were compared with the reference values determined by Neyzi et al. (15) in our country. It was observed that the BMI values of five of the patients (12.5%) were below the fifth percentile before operation and increased above the fifth percentile at the seventh month after operation. When BMI values before and after operation were compared, a significant increase was found in BMI in 32 patients (80%). In 8 patients (20%) in whom the increase in height for weight was greater after operation, BMI values were found to be lower after operation compared to the baseline values.

One of the best criteria used to evaluate growth is determining the degree of maturation of the bones. Nieminen (36) reported that the bone age of children with obstructive sleep apnea and primary snoring was delayed compared to the healthy group. It was found that the bone age in 22 (64%) of the 34 patients whose bone age was calculated was delayed compared to the chronological age and five of these (12.5%) were found to have reached the chronological age seven months after operation.

Thyroid hormones, growth hormone stimulation tests, IGF-1 and IGFBP-3 levels are used in evaluation of hormonal factors related to growth (3,23,27,36,37). Anabolic and growth accelerating effects of growth hormone are mediated by IGF-1 during the postnatal development. Insulin like growth factor-1 is mainly secreted by the liver and the peripheral tissues and measurement of serum IGF-1 levels may be used to determine GH deficiency. Serum IGF-1 levels are affected by the chronological age, sexual maturation degree and nutritional status. Therefore, these results should be interpreted after excluding causes including chronic diseases and malnutrition. Serum IGF-1 levels show very little increase in the prepubertal period (38,39). In this study, all of the children were in the prepubertal period and they had no chronic disease.

Selimoğlu et al. (3) found that serum IGF-1 levels were significantly lower in patients with ATH before operation compared to the healthy group and no significant difference was found between the levels measured in the preoperative period and the levels of the healthy group. In the same study, no significant difference was found between serum IGFBP-3 values measured both in the preoperative and postoperative period and the values of the healthy group (3).

Nieminen et al. (36) found a significant increase in IGF-1 and IGFBP-3 levels after adenotonsillectomy compared to the levels measured before operation and they related the increase in IGF-1 level to improvement of GH release during the night after airway obstruction was eliminated (36).

Aydoğan et al. (23) found that the increase in serum IGF-1 values of the patients with recurrent tonsillitis observed after operation was not statistically significant ($p<0.05$), but the increase in IGFBP-3 value was significant. Ersoy et al. (27) found that serum IGF-1 values in patients with ATH were statistically significantly lower in the preoperative period compared to the healthy group ($p<0.05$), no significant difference was found between serum IGFBP-3 values ($p>0.05$), a significant increase was found in serum IGF-1 values of the patients after operation ($p<0.05$) and the increase in serum IGFBP-3 levels was not significant ($p>0.05$).

Gümüşsoy et al. (40) observed that IGF-1 and IGFBP-3 values were increased statistically significantly at the 6^{th} month after adenotonsillectomy in 44 prepubertal children with a diagnosis of ATH.

In this study, hormone values of the patients measured before operation were compared with an age-matched healthy group. Serum IGF-1 values in children with ATH before operation were significantly lower before operation compared to the control group ($p<0.05$), serum IGFBP-3 values were found to be similar to the values of the control group ($p>0.05$), the increase in serum IGF-1 and IGFBP-3 values at the 7^{th} month after adenotonsillectomy was not significant, either ($p>0.05$).

Conclusively, serum IGF-1 and bone age values in children with chronic ATH were found to be lower compared to the healthy reference values, but the antropometric findings showed that chronic ATH did not cause significant growth failure in prepubertal children. In addition, no adequate evidence showing that surgical treatment of ATH accelerated growth in prepubertal children in the postoperative period of seven months could be found. This result may be related with the fact that a small number of patients with growth failure in the preoperative period were included in the patient group and the follow-up time after operation was short.

The effects of adenotonsillar hypertrophy and its surgical treatment may be demonstrated more prominently by large-scale studies with longer follow-up periods.

Conflict of interest: None declared.

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