

Obstructive Sleep Apnea, Nocturnal Enuresis and Obesity: A Vicious Circle entrapping Children¹Mohamed F. Shindy MD and ²Hesham A. El-Ghaiaty MD¹Department of Otorhinolaryngology, Faculty of Medicine, Benha University, Egypt²Department of Pediatrics, Faculty of Medicine, Al-Azhar University, Egypt

Abstract: Objectives: To evaluate the relationship between obstructive sleep apnea syndrome (OSAS) and nocturnal enuresis (NE) in children and if there is a positive therapeutic effect of adenotonsillectomy (AT) on the frequency of bed-wetting. **Patients & Methods:** The study aimed to collect 150 snorer children with present history of bed wetting. Parents were asked to answer a questionnaire to determine the frequency and severity of snoring and enuresis. Only children scored 3 or 4 were considered to be enuretic. All children underwent over-night pulse oximetry and data were scored according the McGill Oximetry Scoring. Patients with McGill scores of 2-4 (n=123) underwent AT and patients with McGill score of one (n=27) were subjected to further evaluation. All enrolled patients were subjected to weight reduction dieting regimen and aerobic exercise for three months. Pulse oximetry and questionnaire were conducted after 6 months of enrolment and scores were compared to preoperative data. **Results:** AT induced significantly lower postoperative (PO) desaturation index and significantly higher PO lowest SaO₂% with significantly lower total PO McGill scores compared to preoperative data. PO enuresis scoring showed significantly higher frequency of low scores with significantly lower PO score compared to pre-treatment score for a total PO success rate of 79.3%. Medical intervention provided a success rate of 59.3%. Mean post-treatment enuresis scoring was significantly lower compared to pre-treatment scores, irrespective of line of treatment with significantly higher post-treatment scores for those had AT. Dietary intervention and exercise induced significant decrease of body weight and BMI of studied patients at the end of 6-months. **Conclusion:** OSAS, NE and obesity constitute a vicious circle endangering quality of life of children. NE is not always a urological problem and consultation of pediatrician and otorhinolaryngologist is mandatory. Adenotonsillectomy provided complete recovery of both OSAS and NE in 55% and improvement in 29% of patients had adenotonsillitis. Weight reduction programs alone or after surgery induced significant body mass index reduction and improved outcome of patients free of adenotonsillitis by rate 59.3%.

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1. Introduction

Childhood nocturnal enuresis (NE), or bedwetting, is a common childhood condition that causes children and their families stress and embarrassment and which can radically affect the lives of these children. Enuresis is defined as repeated, spontaneous voiding of urine during sleep in a child five years or older (**Bayne & Skoog, 2014**).

Primary NE is caused by a disparity between bladder capacity and nocturnal urine production and failure of the child to awaken in response to a full bladder. Less commonly, enuresis is secondary to a medical, psychological, or behavioral problem. A diagnosis usually can be made with a history focusing on enuresis and a physical examination followed by urinalysis. Imaging and urodynamic studies generally are not needed unless specifically indicated to exclude suspected neurologic or urologic disease (**Ramakrishnan, 2008**).

Primary nocturnal enuresis almost always resolves spontaneously over time. However, persistence of enuresis with increasing age, children

may experience psychological problems. Active treatment is therefore required not only to achieve dryness but also to prevent and treat such an experience. At present, treatment can be divided into behavioral modification and pharmacological therapy, despite which many enuretic children remain untreated or are treated ineffectively. Treatment of long-standing chronic enuresis by orthodontic appliances could be used more frequently to give relief to those not responding to conventional treatment (**Bottomley, 2011; Deshpande & Caldwell, 2012**).

Obesity is a worldwide epidemic with increasing importance in both industrialized and developing countries. Obesity is not adulthood and adults conditions, the incidence of childhood obesity ranges today from approximately 8% to 17%, and is an increasing issue in developed and developing countries. Obesity is always associated with co-morbidities, such as obstructive sleep apnoea syndrome (**Mama et al., 2014; Mathew & Narang, 2014**).

Obstructive sleep apnea syndrome (OSAS) in children has an estimated prevalence of up to 3%.

Snoring is the most characteristic symptom of OSAS which can be associated with neurocognitive and behavioral abnormalities, and also cardiovascular complications. Enlarged tonsils and adenoid or obesity predispose to OSAS which are accompanied by arousals, restless sleep, and frequently daytime sleepiness, inattention, hyperactivity, and academic difficulties (**Malakasioti et al., 2011**).

The therapy of choice in the treatment of OSAS consists of tonsillectomy alone or combined with adenoidectomy and multiple studies indicated its beneficial effects on various manifestations associated with OSAS. **Friedman et al. (2003)** reported that impaired neurocognitive functions are mostly reversible, at least 3 to 10 months following adenotonsillectomy. **Elverland et al. (2004)** reported a beneficial effect of tonsillectomy and adenoidectomy on hemoglobin and iron metabolism in OSAS patients. **Zhang et al. (2008)** detected that adenotonsillectomy is helpful to reduce the force caused by increasing narrowness of upper airway obstruction and the long-existing obstructive sleep and helpful to the normal facial growth.

The current study aimed at evaluation of the relationship between OSAS, NE and obesity and to evaluate the impact of adenotonsillectomy alone or in association with weight reduction program on NE as snoring associated co-morbidity.

2. Patients & Methods

The present prospective study was conducted at Departments of Pediatrics & Otorhinolaryngology, Hospital, since Jan 2012 till Sep 2013 to allow at least 6 months follow-up period for the last case enrolled in the study.

After approval of the study protocol by Local Ethical Committee and obtaining written fully informed parents' consent, a survey questionnaire about their child's sleeping habits as regards snoring and/or enuresis was applied for all parents attending with their children aged 5-10 years to Pediatrics or Otorhinolaryngology outpatient clinics. The survey continued until enrollment of 150 children with both

snoring and enuresis. Children who were excluded of the study. Collected data included gender, age, weight, height for calculation of body mass index (BMI) according to table for BMI adjusted for age and gender.

The questionnaire included questions on whether the child had difficulty in breathing during sleep, mouth breathing, witnessed apnea, daytime sleepiness, and enuresis and its frequency. Snoring and its severity were graded as "never" (score=0), "rarely" (once/week, score=1), "occasionally" (twice/week, score=2), "frequently" (3-4 times/week, score=3), and "almost always" (4 times/week, score=4), (**Muzumdar & Arens, 2008**). The responses on the frequency of enuresis, were graded as "never" (score=0), "rarely" (once/ month, score=1), "occasionally" (twice/month, score=3), "frequently" (2-6 times/month, score=3), and "almost always" (3 times/week, score=4). Only children scored 3 or 4 were considered to be enuretic (**Hjalmas et al., 2004**).

Routine urinalysis and culture was done to exclude secondary nocturnal enuresis. Children were excluded if they had any known genetic or craniofacial syndromes. All children completed the questionnaire were admitted at Pediatrics wards for one night for determination of sleep SaO₂ saturation by pulse oximetry using Nellcor (Pleasanton, CA) N-200 (mode 2, fast averaging) oximeter. The following data obtained by pulse oximetry were interpreted according to **Brouillette et al. (2000)** where 1: Normal or inconclusive oximetry recordings; 2: mildly abnormal recordings, predictive of OSA, 3: markedly abnormal recordings, with a pattern consistent with OSA and 4: severely abnormal recordings, with a pattern consistent with OSA. Then data were scored according the McGill Oximetry Scoring System (**Nixon et al., 2004**) which recommended additional evaluation of breathing during sleep to rule out OSA in patients scored 1 and adenotonsillectomy for the other scoring categories, (Table 1). Desaturation index (number of episodes of desaturation per hour) and lowest SaO₂% were also determined.

Table (1): McGill Oximetry Scoring System (Nixon et al., 2004)

Oximetry score	Comment	Criteria			Others	Recommendations
		No. of drops in SaO ₂ to				
		<90%	<85%	<80%		
1	Normal/inconclusive for OSA	<3	0	0	Stable (<3 clusters of desaturation) and SaO ₂ >95%.	Additional evaluation to rule out OSA
2	Mild OSA	≥3	≤3	0	≥3 clusters of desaturation	Adenotonsillectomy
3	Moderate OSA	≥3	>3	≤3		
4	Sever OSA	≥3	>3	>3		

Management plane

All patients irrespective of undergoing surgery or not were subjected to weight reduction dieting regimen and scheduled for aerobic exercise for three months for weight reduction. Patients with McGill Oximetry scores of 2-4 were subjected to adenotonsillectomy under general inhalational anesthesia supplemented by intravenous non-depolarizing muscle blockers, short-acting narcotics, dexamethasone, and ondansetron at doses appropriate for patient weight. Prophylactic antibiotic were administered. Tonsillar tissue was removed using monopolar electrocautery and conventional technique, and hemostasis was obtained with suction electrocautery. Adenoid tissue was removed by suction electrocautery and conventional technique.

Follow-up plane

Pulse oximetry and questionnaire of the same items were conducted 6 months after surgery and scores were compared to preoperative data. Patients

with McGill score of one were subjected to further evaluation.

Statistical analysis

Obtained data were presented as mean±SD, ranges, numbers and ratios. Results were analyzed using Wilcoxon ranked test for unrelated data (Z-test), paired t-test for related data and Chi-square test (X^2 test) comparison of numerical data. Statistical analysis was conducted using the SPSS (Version 15, 2006) for Windows statistical package. P value <0.05 was considered statistically significant.

3. Results

The study included 150 children; 85 males (56.7%) and 65 females (43.3%) with a M:F ratio of 1.3:1. Mean age of enrolled children was 7.6 ± 1.6 ; range: 4-10 years. Mean BMI of enrolled children was 22.9 ± 4.4 ; range: 15.6-35.5 kg/m^2 . Details of patients' enrollment data are shown in table 2.

Table (2): Patients' distribution according to constitutional data

		Data			
Age (years)	Strata	≤6	41 (27.3%)	5.5±1.1	
		>6-8	62 (41.4%)	7.7±2.1	
		>8-10	47 (31.3%)	9.4±2	
	Total		150	7.6±1.6	
Gender	Males	85 (56.7%)			
	Females	65 (43.3%)			
	M:F	1.3:1			
Body mass data	Weight (kg)	32.2±3.9 (23-43)			
	Height (cm)	120.3±9.3 (105-138)			
	BMI (kg/m^2)	Strata	<20	42 (28%)	18.2±1.1 (15.6-19.8)
			20-25	57 (38%)	21.7±1.3 (20.1-24.8)
			>25-30	47 (31.3%)	28±1.7 (25.2-32.7)
>30			4 (2.7%)	32.8±2.2 (30.8-35.5)	
Total		22.9±4.4 (15.6-35.5)			

Data are presented as mean±SD & numbers; ranges & percentages are in parenthesis; BMI: Body mass index

At time of enrollment, McGill Oximetry Scoring System defined 27 children (18%) had score of one and were ruled out as surgical cases, 80 patients (65%) had score of 2 indicating mild OSA, 29 patients (23.6%) had score of 3 indicating moderate OSA and 14 patients (11.4%) had score of 4 indicating severe OSA with mean score of total studied patients of 2.5 ± 0.7 ; range: 2-4. These 123 patients with oximetry scores ranged between 2 (mild OSA) and 4 (severe OSA) were assigned for adenotonsillectomy. Mean desaturation index and lowest $\text{SaO}_2\%$ estimated at time of enrollment were 5.86 ± 1.2 ; range: 4-8 episode/hr and 82.8 ± 2.1 ; range: 78-86%, respectively.

Adenotonsillectomy induced significant improvement of patients' breathing during sleep

manifested as significantly lower PO desaturation index (1.2 ± 0.4 ; range: 0-3 episode/hr) and significantly higher PO lowest $\text{SaO}_2\%$ (89.1 ± 3.4 ; range: 84-97) estimated in the 123 patients underwent surgery compared to their preoperative estimates, (Fig. 1). Moreover, postoperative McGill Oximetry scoring defined 94 as totally free of OSAS with score=1 and only 29 patients had score of 2 indicating mild OSAS with significantly lower frequency of patients had score of 1 compared to preoperative frequency. Total PO McGill Oximetry score was 1.2 ± 0.4 ; range: 1-2 and was significantly lower compared to preoperative score, (Table 3, Fig. 2).

Table (3): Pre- and PO oxygenation data of patients (n=123) underwent adenotonsillectomy

Data		Findings		
		Preoperative	Postoperative	P value
McGill Oximetry scoring	1	0	94 (76.4%)	<0.001
	2	80 (65%)	29 (23.6%)	
	3	29 (23.6%)	0	
	4	14 (11.4%)	0	
	Mean	2.5±0.7	1.2±0.4	<0.001
Desaturation index (episode/hr)		5.86±1.2 (4-8)	1.2±0.4 (0-3)	<0.001
Lowest SaO ₂ %		82.8±2.1 (78-86)	89.1±3.4 (84-97)	<0.001

Data are presented as mean±SD & numbers; ranges & percentages are in parenthesis

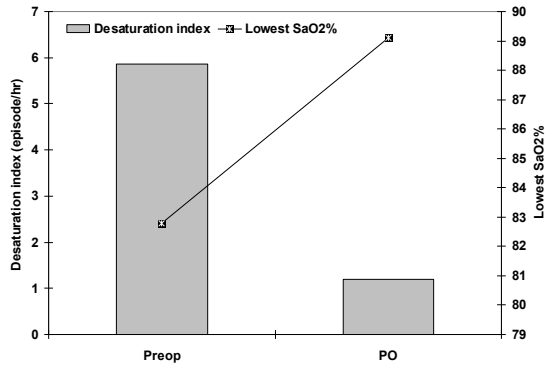


Fig. (1): pre- and postoperative desaturation index & Lowest SaO₂% of patients underwent adenotonsillectomy

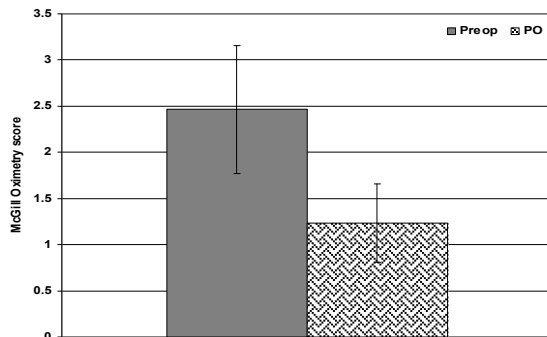


Fig. (2): Mean Pre- and Post-operative McGill Oximetry score of studied patients

Complete otorhinolaryngological and pediatric examinations of the remaining 27 patients defined 6 patients having prognathism and were transferred for dental consultation. Seven patients had history of previous asthmatic attacks and were managed accordingly. Fourteen patients were free of pathology inducing snoring which was attributed to obesity and were maintained on dieting regimen and advised for performing aerobic exercise for weight reduction which on follow-up was found to improve sleep breathing disorders.

Baseline enuresis scoring according to the data of questionnaires defined 82 patients (54.7%) as frequently enuretics (score=3), while 68 patients (45.3%) were almost always enuretics (score=4). Six months after initiation of management, irrespective of being surgical or conservative, parents of 72 children (48%) denied occurrence of post-treatment bed wetting

totally "Never enuretic" (score=0), 32 patients (21.3%) were scored one for a rate of bed wetting of once/month and 15 patients (10%) were scored two for a rate of bed wetting of twice/month. Post-treatment scoring showed significantly higher ($p<0.001$) frequency of low scores compared to pre-treatment scoring with significantly lower ($p<0.001$) mean total post-treatment score compared to pre-treatment score. Unfortunately, the questionnaire defined 10 patients (6.7%) who were still almost always enuretics (score=4) and 21 patients (14%) were still frequently enuretic (score=3) and these 31 patients were considered as failure of therapy for a rate of 20.7%, (Table 4, Fig. 2).

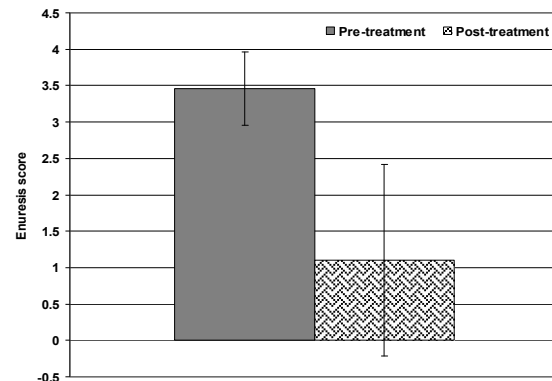


Fig. (3): Mean Pre- and Post-treatment enuresis score of total studied patients

Concerning line of treatment, 103 adenotonsillectomy patients had dry bed at the end of 6 months after surgery for a success rate of 83.7%, while only 16 patients received conservative therapy for other causes than adenotonsillitis had dry bed for a success rate of 59.3% with significant ($p<0.01$) difference in favor of surgical treatment. Moreover, mean post-treatment enuresis scoring was significantly lower compared to pre-treatment scores, irrespective of line of treatment with significantly higher post-treatment scores for those had adenotonsillectomy compared to those had conservative therapy for causes other than adenotonsillectomy, (Table 4, Fig. 3).

Dietary intervention and exercise induced significant decrease of body weight and BMI of studied patients at the end of 6-months. Moreover, patients

showed change into lower BMI strata with significant frequency compared to pre-treatment frequency, (Table 5, Fig. 4).

Table (4): Enuresis scores reported prior to and after treatment of studied patients categorized according to line of therapy

Data	Conservative		Surgical		Total		
	Pre	Post	Pre	PO	Pre	Post	
Scoring grade	0	5 (18.6%)	0	67 (54.5%)	0	72 (48%)	
	1	6 (22.2%)	0	26 (21.1%)	0	32 (21.3%)	
	2	6 (22.2%)	0	9 (7.3%)	0	15 (10%)	
	3	17 (63%)	7 (25.9%)	65 (52.8%)	14 (11.4%)	82 (54.7%)	21 (14%)
	4	10 (37%)	3 (11.1%)	58 (47.2%)	7 (5.7%)	68 (45.3%)	10 (6.7%)
P	p ₁ <0.001		p ₂ >0.05	p ₁ <0.001 p ₃ <0.001	p ₁ <0.001		
Mean score	3.4±0.5	1.9±1.3	3.5±0.5	1±1.3	3.5±0.5	1.1±1.3	
P value	p ₁ <0.001		p ₂ >0.05	p ₁ <0.001 p ₃ <0.05	p ₁ <0.001		
Success rate	59.3%		83.7%		79.3%		
P value	p ₄ <0.01						

Data are presented as mean±SD & numbers; ranges & percentages are in parenthesis, Pre: preoperative, PO: postoperative, p₁: significance versus pre-treatment, p₂: significance versus pre- conservative treatment, p₃: significance versus post- conservative treatment, p₄: significance versus conservative treatment success rate

Table (5): Pre- and Post-treatment BMI data of studied patients

Data		Number		Mean	
		Pre-treatment	Post-treatment	Pre-treatment	Post-treatment
Strata (kg/m ²)	<20	42 (28%)	72 (48%)	18.2±1.1 (15.6-19.8)	17.5±2.9 (14.8-19.9)
	20-25	57 (38%)	43 (28.7%)	21.7±1.3 (20.1-24.8)	22.1±1.4 (20.1-24.4)
	>25-30	47 (31.3%)	33 (22%)	28±1.7 (25.2-32.7)	27.2±1.2 (25.4-29.6)
	>30	4 (2.7%)	2 (1.3%)	32.8±2.2 (30.8-35.5)	32.3±1.9 (31-33.8)
Total		150 (100%)	150 (100%)	22.9±4.4 (15.6-35.5)	21.4±4.1(14.8-33.8)
P value		<0.05		=0.009	

Data are presented as mean±SD & numbers; ranges & percentages are in parenthesis

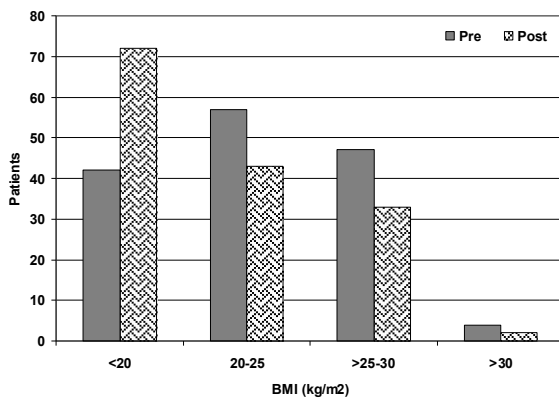


Fig. (4): Pre- & Post-treatment patients' distribution among BMI strata

4. Discussion

The current study aimed to evaluate the relationship between OSAS and nocturnal enuresis (NE) in children and if there is a positive therapeutic effect of adenotonsillectomy (AT) on the frequency of bed-wetting. Thus, the study was based on selective basis so as to collect snorer children with present history of bed wetting. Selection of enrolled children was relied

on a questionnaire designed to fulfill selection basis and allow grading of the present problem and answered by parents. In line with this strategy, multiple studies relied on varied questionnaires for patients' selection and evaluation (Sogut *et al.*, 2009; Brockmann *et al.*, 2012; Wolfe-Christensen).

The ability of the study to enroll 150 children fulfilling that inclusion criterion indicated a possible relationship between both complaints and its high prevalence and supported that previously reported in literature wherein Aydil *et al.* (2008) reported a frequency of obstructive upper airway problems in primary NE patients of 65.6% and concluded that obstructive upper airway problems are very common in primary NE patients and primary NE is a common symptom of obstructive upper airway problems. Barone *et al.* (2009) found that overweight and NE are associated with OSAS but not with each other and OSAS should be considered in overweight children with NE, especially when they display other symptoms of OSAS or fail to respond to standard NE treatment programs. Wolfe-Christensen *et al.* (2013) using Obstructive Sleep Apnea Syndrome-18-Item

Questionnaire, Pediatric Sleep Questionnaire and Pediatric Symptom Checklist found that patients with monosymptomatic NE who snored had significantly more externalizing problems and total psychosocial problems, in addition to significantly more impairment in all areas of health related quality of life compared to children with monosymptomatic NE who did not snore.

Lehmann et al. (2012) and **Wolf et al. (2014)** found that NE occurred in 38.9% of studied children with sickle cell anemia and was significantly associated with an obstructive apnea-hypopnea index of ≥ 2 and enuresis severity was associated with $\geq 3\%$ desaturation occurring ≥ 2 times/hour with and without snoring.

Medical evaluation of the enrolled snorer/enuretic children detected adenotonsillitis in 123 patients, while 27 patients were free of adenotonsillitis. These 27 patients were found to have other associated medical problems; 6 patients having prognathism and were transferred for dental consultation, 7 patients had history of previous asthmatic attacks and were managed accordingly and 14 patients were free of pathology inducing snoring which was attributed to obesity. Correction of these problems provided success rate manifested as decreased scoring of both snoring and NE by 59.3%. On contrary, adenotonsillectomy provided a success rate of 82.9%, thus confirming the relationship between snoring and NE and indicating the efficiency of the operative decision and goes in hand with **Waleed et al. (2011)** reported an improvement rate of 87.8% in enuretic children with sleep disordered breathing and about 50% of patients were cured completely, and concluded that all enuretic children with sleep disordered breathing who underwent surgery exhibited a significant reduction in daytime enuresis. **Jeyakumar et al. (2012)** conducted systematic analysis of the literature to identify studies included children who had sleep disordered breathing (SDB) and enuresis and found that in a total of 587 children with SDB and enuresis, and underwent AT; the postoperative prevalence of NE was 16% and concluded that SDB in children is associated with NE and AT is associated with a significant improvement in NE in children with SDB.

Ahmadi et al. (2013) investigated the effect of AT on NE in children with adenotonsillar hypertrophy and found that at 3-months after AT, enuresis had resolved completely in 60.7% of children and 26.2% of children had shown relative improvement, but NE had not improved in 13.1% of children and concluded that AT can improve enuresis in the majority of children with adenotonsillar hypertrophy

Thottam et al. (2013), reported that AT is a treatment option for children with OSAS and NE with postoperative resolution of NE in 51.4% of patients who underwent AT and children with both severe OSA and prolonged stage 2 sleep were 3.4 times as likely to

have postoperative resolution of NE. **Kovacevic et al. (2013)** reported that among 417 children underwent AT, 101 (24%) had NE, and of these 24 had associated diurnal incontinence (6%); NE responded to AT in 49 patients and in 30 patients NE resolved within 1 month postoperatively and diurnal incontinence resolved in 4 children (17%).

In support of the beneficial effect of AT, **Wireklint & Ericsson (2012)** reported that six years after tonsillectomy or partial intra capsular tonsillectomy/tonsillotomy, 91% of young adults reported persisting benefits in well-being, reduced obstructive problems and fewer infections. **Mohsen et al. (2014)** documented that surgical therapy with AT is associated with marked improvement in quality of life in both obstructive and infective adenotonsillar disease.

All patients were included in dieting regimen and aerobic exercise, irrespective of therapeutic intervention, and showed significantly lower BMI compared to enrollment BMI and those were free of adenotonsillitis showed improvement on evaluation questionnaire concerning both snoring and NE scoring. These findings indicated the effect of weight reduction on both disease entities. In line with these data, **Khaleghipour et al. (2013)** reported that after breathing exercises performed for 45 minutes in the morning and prior to sleeping for four weeks NE decreased significantly in patients compared to the control group and concluded that breathing exercises may reduce the frequency of NE in the patients with the oral breathing and nocturnal snore. In support of the relation between obesity and NE, **Weintraub et al. (2013)** reported enuresis in 8.8% normal weight, 16% overweight and 30% obese youth with significantly higher frequency in obese compared with normal weight children and concluded that obese children are at increased risk for enuresis.

The obtained results allowed concluding that OSAS, NE and obesity constitute a vicious circle endangering quality of life of children. NE is not always a urological problem and consultation of pediatrician and otorhinolaryngologist is mandatory. Adenotonsillectomy provided complete recovery of both OSAS and NE in 55% and improvement in 29% of patients had adenotonsillitis. Weight reduction programs alone or after surgery induced significant BMI reduction and improved outcome of patients free of adenotonsillitis by rate 59.3%.

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