Effect of adenotonsillectomy on nocturnal enuresis in children with OSA

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Abstract Background: Pediatric obstructive sleep apnea (OSA) is the most severe form of SDB. The most important risk factors for the development of pediatric SDB include adenotonsillar hypertrophy. On the other hand, nocturnal enuresis is a common symptom that is associated with (OSA), through influencing the nocturnal secretion of antidiuretic hormone (ADH).

Objective: We aimed to study the relation between polysomnography data of children with OSA due to adenotonsillar hypertrophy and levels of ADH, total and night urine volume.

Subject and method: The study included 23 consecutive non-obese children with age above 5 years old, complaining of nocturnal enuresis, hypertrophied adenoids and tonsils. A polysomnographic evaluation was done together with serum level of ADH, total and nocturnal urine volume were measured pre and 3 months post adenotonsillectomy.

Results: There was a significant negative correlation between ADH and different polysomnographic data including respiratory events (apnea index, total hypopneas, hypopnea index and RDI), oxygen saturation data and the snoring index. There was also a significant negative correlation between night urine volume and desaturation index. Comparison between the data means before and after adenoidectomy were done using the paired t-test; showed a significant improvement of all the polysomnographic data values, and a significant improvement in serum level of ADH, besides the significant decrease in both the 24 h urine volume and the night urine volume being.

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Introduction

OSA has been defined by the American Thoracic Society [1] as a common but underestimated disease that has been related to increased different morbidity. Pediatric obstructive sleep apnea (OSA) is the most severe form of SDB [2] and has a prevalence of 1–3% in otherwise healthy children [3]. The most important risk factors for the development of pediatric OSA include adenotonsillar hypertrophy, obesity, craniofacial anomalies and neuromuscular disorders [4–8]. There is evidence of an interaction between nasal obstruction and pharyngeal narrowing in the pathophysiology of OSA. OSA leads to sleep fragmentation, which develops as a consequence of repeated arousals, together with intermittent blood gas abnormalities (hypoxia and hypercarbia) that characterize OSA and the unreserved integrity of both rapid eye movement (REM) sleep and non-REM sleep [9–12].

All these pathological changes may jointly lead to a wide array of morbid consequences, include reduced intelligence and memory, behavioral, deficits, hyperactivity like, aggressiveness, as well as failure to thrive, enuresis and cardiovascular dysfunction [9,12].

As regards nocturnal enuresis, is a bothersome and common symptom in children with OSA [13] through different proposed factors including: decreased arousal response, impaired urodynamics, increased intra-abdominal pressure during obstructive respiratory events increases bladder pressure and altered secretion of hormones that regulate fluid balance as anti-diuretic hormone whose inappropriate levels are 2.7 times more likely to occur in children complain of bedwetting issues [14].

Previous studies discussed the improvement or reversibility of these morbidities by the adequate treatment of OSA based on etiological factors and the further associated improvement of the overall quality of life [15] and reduced healthcare costs [16].

Based on aforementioned considerations, we hypothesized that children who are referred for symptoms of OSA and sleep fragmentation with nocturnal desaturation are more likely to develop nocturnal enuresis due to inappropriate anti-diuretic hormone (ADH) secretion and would be reversible after adenotonsillectomy.

Subjects and Methods

The study included 23 consecutive non obese children with age above 5 years old, all participants complain of nocturnal enuresis which was considered to be present when responses were in the frequent grade (3–6 times per month) or almost always grade (> 3 times per week) [17].

Conclusion: Children with OSA and nocturnal enuresis, should be considered for early adenotonsillectomy or other treatments to approve normal release of ADH, and subsequent improvement of nocturnal enuresis.

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Clinical evaluation

(a) Detailed medical history taking included duration of illness and current therapy.

(b) Thorough clinical and neurological examination to rule out an organic etiology, exclusion criteria were the presence of familial craniofacial or genetic disorders, cerebral palsy, neuromuscular diseases, or any underlying systemic diseases or acute infectious processes.

(c) Anthropommetrical parameters were assessed; weight, height, BMI (defined as weight in kilograms divided by height in meters squared) [18], and circumference of the neck measured at the level of the cricothyroid membrane (with the patient in the orthostatic position).

(d) Standardized sleep questionnaire [19].

(e) Ear, nose, and throat (E.N.T) assessment were done by ENT surgeon to demonstrate obvious hypertrophied adenoids and tonsils clinically and confirmed by nasopharyngeal CT scan.

Polysomnography

Polysomnographic (PSG) overnight study was done for the participants enrolled in the study and was studied twice, initially and 3 months postoperatively after undergoing curative adenotonsillectomy. All PSG studies were recorded at sleep laboratory of the neurology department, Ain Shams University Hospital. All patients arrived to the sleep lab, about 2 h before their usual bedtime, which is sufficient for electrode application. No drugs were used to induce sleep. The recordings included four EEG channels (C4-O1, C3-O2, A1-C3, and A1-C4), applied according to the international 10–20 systems of electrode placement, two electro oculogram channels, one chin and one tibialis anterior electromyogram channels, nasal airflow, ventilatory belts, electrocardiogram, oxygen saturation (through pulse oximetry), body position and snoring assessment. Only PSGs ≥6 h of sleep were considered adequate for testing the sleep pattern. Sleep stage scoring was done visually according to standard criteria of Rechtschaffen & Kales [20], with 30-epochs. Respiratory parameters analysis was done automatically and confirmed manually. An apnea was defined as a cessation of naso-oral airflow lasting ≥10 s. A hypopnea was scored when there was an obvious reduction usually ≥20% in airflow and/or effort, lasting ≥10 s and accompanied by an arousal or a fall in SaO2 of ≥4%. Obstructive apnea and hypopnea were scored when air flow was absent but respiratory efforts were present. Central apnea and hypopnea were scored in absence of respiratory effort and
nasal-oral airflow, while mixed apnea and hypopnea has an initial central component followed by an obstructive component. The number of respiratory events per hour was defined as the apnea hypopnea index (AHI), also called the respiratory disturbance index (RDI). A periodic limb movements (PLM) index was calculated as number of PLMs per hour of sleep but can be extended to wake state. A PLM index of greater than 5 per hour is considered significant [21]. The polygraph machine used was the Nicolet VEEG system (Viasys Healthcare Inc).

Sample collection and determination

All recruited subjects had water intake controlled at 20–25 ml/kg in one day. Twenty four hour urine and night urine volume samples were collected and measured, venous blood samples were taken with informed consent both on the morning next to the Polysomnography study night on the first diagnostic session and 3 months later after adenotonsillectomy. Samples were examined to detect the levels of ADH in serum using Bio-Rad protein kit for ADH by radioimmunoassay.

Adenotonsillectomy

Children with OSA underwent an adenotonsillectomy under general anesthesia. The adenotonsillectomy was performed with a combination of sharp and blunt dissection using primarily blade electrocautery. Then 3 month postoperative recovery was left before second session polysomnography, when tissue and physiologic function could have repaired.

Data analysis

Analysis was performed using statistical software (SPSS version 17; SPSS, Inc., Chicago, IL). Comparisons between means before and after adenotonsillectomy were performed by using the paired t-test. Simple correlations between variables were examined by calculating Pearson’s product correlation coefficient. Data are presented as mean ± SD, p < 0.05 was considered significant.

Results

Twenty-three patients, 13 males and 10 females, their age ranged from 7 to 14 years and their mean age was (9.67 ± 2.00) year, all were diagnosed as adenoid enlargement, obstructive sleep apnea and nocturnal enuresis, and they were recruited from the sleep laboratory unit of Ain Shams University Specialized hospital. Their descriptive data of age, polysomnography data, 24 h and night urine volume and ADH levels are summarized in Table 1.

Table 1 Patient characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Min.</th>
<th>Max.</th>
<th>Mean</th>
<th>SD</th>
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<td>14</td>
<td>9.67</td>
<td>2.00</td>
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<tr>
<td>Basal_O2, %</td>
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<td>96.50</td>
<td>94.44</td>
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<td>Desaturation index</td>
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<td>23.04</td>
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<tr>
<td>Minimum O2, %</td>
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<td>91.90</td>
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<tr>
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<td>10.77</td>
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<tr>
<td>RDI</td>
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<td>Total arousal</td>
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<td>364.00</td>
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<tr>
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<td>Night_urine, ml</td>
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<td>355</td>
<td>290</td>
<td>43.14</td>
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<tr>
<td>24 h urine, ml</td>
<td>1350</td>
<td>2100</td>
<td>1840.87</td>
<td>218.9</td>
</tr>
</tbody>
</table>

Patient descriptive data regarding age, polysomnography data, ADH, night and 24 h urine volume. RDI, respiratory disturbance index; arousal res, respiratory arousal; arousals NR, non-respiratory arousals; ADH, antidiuretic hormone. Data presented as minimum, maximum, mean ± SD.

Correlation between ADH level and desaturation index ($r = -0.634, p = 0.001$) (Fig. 2), average low oxygen level ($r = 0.554, p = 0.006$), and minimum oxygen saturation ($r = 0.716, p = 0.000$). Regarding snoring events there was a significant negative correlation between the ADH level and the snoring index ($r = -0.641, p = 0.001$) which is illustrated in (Fig. 3).

The correlation between different polysomnographic data and both 24 h urine volume and night urine volume was studied and we found only a significant negative correlation between night urine volume and desaturation index ($r = -0.505, p = 0.014$) which is presented in (Fig. 4) while there were no significant correlation with other data.

After adenoidectomy was done for all children, post-operative polysomnography, serum ADH level, and both calculated 24 h and night urine volumes were done and comparison between the data means before and after adenoidectomy were done using the paired t-test. Regarding the polysomnographic data there were a significant improvement of all the data values; the difference between the mean RDI ($t = 6.827,$

Figure 1 Correlation between RDI and ADH, significant negative correlation ($r = -0.884, p = 0.000$).
Regarding the ADH levels there was a significant elevation of the abnormally decreased levels of serum ADH \((t = -32.030, p = 0.000)\), this change is illustrated in (Fig. 6).

As regards the urine volumes, there was a significant difference in both the 24 h urine volume and the night urine volume being significantly decreased with improvement of polyuria. The significant difference of the volume of the 24 h urine \((t = 15.403, p = 0.000)\) and the night urine \((t = 12.815, p = 0.000)\) is illustrated in (Fig. 7).

**Discussion**

There is a recognized link between SDB and polyuria/nocturia previously studied [21], thus it would be fair to hypothesize that the nocturnal polyuria frequently seen in children with primary nocturnal enuresis could be associated with OSA [22]. Compelling evidence for an association between OSA and nocturnal enuresis was reported in the current study of the 23 participating children, indeed, significantly negatively correlation between the levels of ADH with the severity of the nocturnal hypoxemia and the frequency of the respiratory events and the snoring index. Moreover, we also observed the another significant negative correlation between DI and urine volume during night-time sleep in children with OSA preoperatively. Our results agree with other studies which reported that children with OSA and habitual snorers diagnosed by polysomnography significantly correlated with nocturnal enuresis [23,24].

Physiologically, during the four stages of sleep, the ADH (antidiuretic hormone) is produced in the fourth stage of sleep [9–12], since children with OSA never reach the fourth stage of sleep due to increased mean arousal index and the unpreserved integrity of both rapid eye movement (REM) sleep and non-REM sleep with constant awakening episodes and therefore

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**Figure 2** Correlation between desaturation index and ADH, significant negative correlation \((r = -0.634, p = 0.001)\).

**Figure 3** Correlation between snoring index and ADH, significant negative correlation \((r = -0.641, p = 0.001)\).

**Figure 4** Correlation between desaturation index and night urine volume, significant negative correlation \((r = -0.505, p = 0.014)\).

**Figure 5** Comparison between both the mean RDI and the mean DI before and after adenoidectomy using paired-T test \((t = 6.827, p = 0.000\) for RDI and \(t = 6.716, p = 0.000\) for DI).

**Figure 6** Comparison between the mean ADH level before and after adenoidectomy using paired-T test \((t = -32.030, p = 0.000)\).
ADH is not appropriately released [15]. Normally the nocturnal secretion of ADH slows nighttime urine production and prevents nocturia, thus inappropriate secretion of ADH results in inability to concentrate the urine leading to excess urine production during the night [18].

Besides, sleep apnea sufferer slips from deep sleep to light sleep again and again, and when this happens, the bladder sphincter relaxes, releasing urine. Adding onto possibility of increased bladder pressure with increased effort of breathing against increased upper airway resistance in the participants with OSA [10].

Previous studies [25,26] have shown similar results with somewhat different inclusion criteria, which suggest the possibility that OSA with desaturation, influences the normal secretion of ADH leading to the change in nocturnal urine volume.

After analysis of the polysomnography data obtained 3 months post adenotonsillectomy proved that data as regards RDI and DI significantly decreased than those recorded preoperatively. Moreover, the serum ADH level and both total 24 h urine and night urine volume were significantly improved than that of those preoperative.

Therefore, adenotonsillectomy for the participants, removing the upper respiratory tract obstruction which was the cause of OSA, results in a dramatic improvement in respiratory parameters as measured by polysomnography 3 months to full recovery. The present study approves others demonstrated that the reduction of the total and night urine volume postoperatively adenotonsillectomy, is associated with absence and improvement in nocturnal oxygen desaturation [27].

Children who are known to be at high risk for persistent postoperative SDB, are those exhibiting obesity, allergies, craniofacial, neuromuscular and genetic problems, thus they were excluded from the current study and all the participating children showed complete resolution and improvement in sleep parameters as demonstrated by polysomnography 3 month postoperatively.

In summary, the results of this study suggest that pediatric SDB influence appropriate ADH secretion that is associated with nocturnal enuresis which is reversible after curative adenotonsillectomy. Therefore, children with OSA, complaining of nocturnal enuresis, should consider early adenotonsillectomy or other treatments based on etiological factors to remove the upper respiratory tract obstruction to prevent nocturnal oxygen desaturation resulting in the normal release of ADH and in turn abolishing nocturnal enuresis, which may be conducive to children’s physiological and psychological health.

References


