# *Obstructive Sleep Apnea Syndrome*

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This syndrome may impact a child in various aspects. The severity of obstructive sleep apnea is frequently related to a higher frequency of symptoms like enuresis, growth retardation, problems of performance in school, attention deficit hyper-activity, and disturbances in conduct. It is surprising that many children have these symptoms for a long time, and their parents and pediatricians don't know about the relation between the symptoms and obstructive sleep apnea syndrome.
The association between enuresis and sleep apnea has been recognized for years. Apparently it is related to a high number of partially awakened episodes that occur during the apneic episodes. It is thought that this could also be related to decreased production of vasopressine and an increase in production of natriuretic peptide.
A paper published in 2001 in the International Journal of Pediatric Otorhinolaryngology analyzes reports of 321 children whose tonsils and adenoids were operated upon; 111 (35%) of them had enuresis. Three months after the surgery, 74 of them were re-evaluated, and 63% of them were free of enuretic symptoms, and 4% had a decrease in them. This and other studies allow us to support the concept that obstruction of the upper airway is probably an etiologic factor in enuresis.
Retardation in children's growth associated with obstruction of the upper airway is probably related to an abnormal secretion of growth hormone. Adenoid and tonsillar hypertrophy could cause a decrease in the amount of IGF-1, affecting the hypothalamic hypophyseal axes. It has also been demonstrated that surgery on the tonsils and adenoids leads to an important decrease in the number of apneic episodes, related to resolution of the obstruction of the airway. This resolution leads to normalization in the amount of hormonal levels and the child's growth.
The effect of obstructive sleep apnea on performance and conduct in school has been demonstrated through many published reports in recent years. These parameters have been analyzed pre- and post-adenotonsillectomy. Gozal in 1998 published a study of school children in the lowest 10% of their class in performance. He found that 18.1% (54) of them had sleep-related respiratory symptoms. Twenty-four of these children were operated upon, and after surgery all of them were found to have a significant increase in their performance and conduct at school in comparison with children with sleep-related symptoms who did not receive surgery, and compared to remaining classmates who did not have sleep-related symptoms.

Li and colleagues published in 2006 a study of 40 children with tonsillar and adenoid hypertrophy who had obstructive sleep-related symptoms and on whom adenotonsillectomy was performed;they were evaluated six months after surgery. A decrease in the apnea-hypopnea index was found, as well as an increase in performance on tests of attention ($p < 0.001$), behavior, and hyperactivity ($p < 0.05$). Stewart and coworkers also demonstrated the impact of surgery on polysomnographic results and on quality-of-life, compared to these factors in a control group.

Mitchel and Kelly, in 2007, published a study in which they analyzed behavioral changes in children with mild respiratory sleep disturbances and children with obstructive sleep apnea, after adenotonsillectomy. Their conclusion was that behavioral disturbances are often seen in both groups, and significant changes were seen in both groups after surgery. David Gozal published, in 2007, a paper on children with sleep-disorders who had behavioral disturbances and neurocognitive disorders. Reference was made to the association of intermittent hypoxia and sleep-fragmentation, with disturbances in memory, attention, and intelligence. There have also been associations between sleep-disorders, behavioral problems, hyperactivity, and alterations in temperament. Individual variability has been seen in the presence and severity of neurobehavioral disturbances. Genetic and environmental factors can affect morbidity. The same author describes that in children with obstructive sleep apnea, especially those who develop neurocognitive deficits, the presence of 4 APOE (varepsilon) is more frequently found.

**Medical Treatment of Obstructive Sleep Apnea**

Treatment of this condition is surgical. There have been some papers published regarding a medical treatment for this condition, based on treatment of the inflammatory process with anti-leukotrienes and topical steroids. Goldbar published a study of 24 children who snored and had respiratory sleep disorders, with an apnea-hypopnea index of $>1<5$ per hour, who were treated for 16 weeks with Montelukast (4-5 mg per night). Nasopharyngeal x-rays and polysomnography were taken of all of them before and after 16 weeks of treatment.

In a parallel study, tonsils and adenoids obtained from children with obstructive sleep apnea syndrome and from children with recurrent tonsillitis were analyzed in search of genetic expression of protein receptors for leukotrienes and their concentrations in tissue. They found that Montelukast produced a significant decrease in the size of tonsils and adenoids and in sleep disturbances shown on the polysomnogram. They found that children with obstructive sleep apnea had an increase of leukotrienes B4/C4/D4/E4 and an increase in the expression of leukotriene protein receptors LT1-R and LT2-R in adenoids. This was not found in children with recurrent tonsillitis. Because of this, the authors' conclusion is that anti-leukotriene treatment may be useful in the treatment of children with mild respiratory sleep disorders.

The same author studied 50 snorers and 12 controls with polysomnography and analysis of exhaled air, in search of levels of leukotrienes and prostaglandins, and found a statistically significant elevation of leukotriene B4 in the group with a index of apnea/hypoapnea $>5$ compared with $<5$ for controls. Leukotrienes

C4, D4 and E4 were also elevated compared with those in controls ($p$ <0.01). Concentration of G2 prostaglandins were similar in both groups. He concluded that his results provide supporting evidence for inflammation of the upper airway in obstructive sleep apnea, and that it is related to the severity of the apnea.

Kheirandish and coworkers, in a study of 22 children with adenotonsillectomy who persisted with an apnea/hypopnea index of >1 - <5 and who received Montelukast and intranasal budesonide for 12 weeks, demonstrated that the children had a significant improvement of their index (3.9 to 0.3) compared with results for a control group. They also improved in oxygen-saturation and decreased the number of arousals from sleep. In a study done by Brouillet and colleagues, fluticasone was shown to decrease the index of apnea/hypopnea in children with adenotonsillar hypertrophy (10.7-5.2), without suppressing it nor decreasing the size of the tonsils and adenoids.

It is also well known that some children with obstructive sleep apnea can persist with a high index of apnea/hypopnea after surgery. Guilleminault in 2007 studied 199 children who were adenotonsillectomized because of obstructive sleep apnea. He found that 45% of them had an abnormality in the post-operative polysomnogram, mainly associated with retroposition of the mandible, and the like. These facts show the need for re-evaluating children after surgery, in search of persistence of obstructive symptoms of the airway.

**Recommended readings**

1. Effectiveness of Adenotonsillectomy in the Resolution of Nocturnal Enuresis Secondary to Obstructive Sleep Apnea. Basha et al., Laryngoscope 115:1101-3, 2005.
2. Nocturnal Enuresis and Upper Airway Obstruction. Ugur Çinar et al., Int.J Pediatr Otorhinolaryngology 59(2):115-8, 2001.
3. The Effects of Tonsillectomy and Adenoidectomy on Serum IGF-I and IGFBP3 Levels in Children. Ylmaz, Mustafa Deniz MD; Laryngoscope 112(5): 922-25, 2002.
4. Impact of Adenotonsillectomy on Behavior in Children with Sleep-Disordered Breathing. Li Hsueh et al., Laryngoscope 116; 1142-1147, 2006
5. C-Reactive Protein, Obstructive Sleep Apnea, and Cognitive Dysfunction in Achool-Aged Children. Gozal D. Am J Respiratory Crit Care Med 176(2);188-93, 2007.
6. Leukotriene Modifier Therapy for Mild Sleep-Disordered Breathing in Children. Goldbart A et al. Am J Respiratory Crit Care Med 172;364-70, 2005
7. Inflammatory Mediators in Exhaled Breath Condensate of Children with Obstructive Sleep Apnea Syndrome. Goldbart et al.. Chest 130; 143- 148, 2006.
8. Intranasal Steroids and Oral Leukotriene Modifier Therapy in Residual Sleep-Disordered Breathing After Tonsillectomy and Adenoidectomy in Children. Kheirandish et al.. Pediatrics 117; 61-66, 2006.

9. Adenotonsillectomy and Obstructive Sleep Apnea in Children: A Prospective Survey. Guilleminault et al., Otolaryngol Head Neck Surg 136(2);169-175), 2007.
10. Adenotonsillectomy for Obstructive Sleep Apnea in Children: Outcome Evaluated by Pre and Postoperative Polysomnography. Mitchel Ron . Laryngoscope 117;1844-1854 oct 2007.
11. Pediatric Obstructive Sleep Apnea: the Year in Review.R. Mark and Charles M Bower. Current Opinion in Otolaryngology & Head and Neck Surgery"005, 13: 360-365.
12. Sleep-Disordered Breathing and School Performance in Children. David Gozal. Pediatrics 1998;102;616-620.
13. Increased Upper Airway Collapsibility in Children with Obstructive Sleep Apnea During Wakefulness. Am Respir Crit Care 169;163-167, 2004.
14. Increased Morning Brain Natriuretic Peptide Levels in Children with Nocturnal Enuresis and Sleep-Disordered Breathing: a Community–Based Study. Capdevilla, 121(5): 1208-14, 2007.