The Potential Influence of Obstructive Airways and The Diagnosis of Attention Deficit Hyperactive Disorder in Children

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Abstract: Objective: The aim of this review is to address the potential influence and relationship between Obstructive airway disease and Attention Deficit Hyperactivity Disorder (ADHD) in children. **Method:** A review of the literature was conducted using PubMed from 1980 to 2014 for articles that discuss the relationship between Obstructive airway disease and ADHD in children and the management of each disorder. **Results and Conclusion:** Although the relationship between obstructive airway diseases, behavioral disease and sleep disorders are yet to be fully understood, it is observed that addressing the airway disease improves both sleep and behavioral disorders. While further studies are anticipated to prove or refute the relationship, nonetheless, screening for airway disorders in ADHD children may well be advisable.
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1.Introduction:

Attention-deficit/hyperactivity disorder (ADHD) is a behavioral abnormality seen in children and adolescents.[1,2] It becomes apparent in some children in the preschool years or early at school. It has a wide range of symptoms but most common ones are inattention, hyperactivity, and impulsivity.[2] The prevalence of ADHD in the United States is estimated at 3-7% by the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV).[2]

Hoffman[3] first described ADHD in 1845. A physician who happened to be a poet used to write mini-reading material for his 3 years old son. His book, "The story of Fidgety Philip" was an accurate description of a little boy who had ADHD. But it was not until 1902 that Sir George Still[4] reviewed a series of patients to the Royal College of Physicians of England that described impulsive children who had behavioral problems caused by genetic dysfunction.[4]

The clinical manifestations of ADHD usually are obvious to teachers.[1,2] Inattentiveness is demonstrated by failure to complete tasks once begun, failure to grasp directions, and making errors through inattention rather than lack of understanding of the material presented.[1] Impulsivity refers to the child's difficulty in controlling reactions and responses when he or she faces uncertainty or the need to attend carefully. Impulsive children commonly act without thinking, shifting quickly from one activity to another, and often exhibit the right behavior at the wrong time. They often get into trouble with their peers because they seem socially inept. Distractibility presents as a reaction to environmental noises or visual stimuli that others can ignore. Their own bodies or other objects also may distract distractible children. [1,2,5]

Over activity, although the most noticeable feature of ADHD is not always present.[5] Children with ADHD commonly can be observed swinging their legs, rocking their bodies, tapping fingers, or making odd noises. In more obvious cases they may be in near-constant motion, darting around the room and often ignoring their own or others' safety. The male to female ratio in over activity is 4:1. Girls more typically demonstrate inattention but without hyperactivity.[1,2,5,6]

The physical examination findings typically are normal although there maybe suggestions of neural immaturity. Cranial imaging is not useful unless there are other indications, e.g. seizures.[7,8]

Current classifications include the predominantly impulsive-over active type (more common in boys), the predominantly inattentive type and the mixed combination forms.[1,2,8]

As the ADHD children grow, neurologic maturation may improve their symptoms. However, adolescents who have had ADHD in their early school years often continue to demonstrate school dysfunction, low self-esteem, and social inappropriateness.

Not everyone who is overly hyperactive, inattentive, or impulsive has ADHD. Because everyone shows some of these behaviors at times, the

diagnosis requires that such behavior be demonstrated to a degree that is inappropriate for the person's age. The diagnostic guidelines also contain specific requirements for determining when the symptoms indicate ADHD. The behaviors must appear early in life, before age 7, and continue for at least 6 months. Above all, the behaviors must create a real handicap in at least two areas of a person's life such as in the schoolroom, on the playground, at home, in the community, or in social settings.

A range of risk factors has been established to help prevent ADHD in children. Smoking during pregnancy (hypoxia to fetus *in vitro*), food additives (artificial food coloring), high sugar diet, and social factors (e.g. complex post traumatic stress disorder) are some of factors that have been well noted in the literature.

Primary treatment of the child with ADHD combines pharmacologic and environmental interventions.[9] However, such management is often complicated by the presence of associated learning disabilities that require specific educational interventions. Moreover, many such children have developed emotional reactions to what may be years of social inappropriateness and school dysfunction, and both family behavior patterns and the child's psychologic reaction must be assessed to avoid continuation of undesirable stereotyping. The beneficial effects of medication decrease significantly in the presence of unaddressed emotional or educational needs.

The drugs most commonly used in treating ADHD are Methylphenidate (MPH) and Dextroamphetamine (DEX).[9] They are presumed to have their neuropharmacologic effects on dopaminergic neurons in the brainstem reticular activating system. Major side effects of these drugs are appetite and sleep impairment, elevation in the heart rate and blood pressure, irritability on withdrawal and attention over focusing. Patients with motor tics may suffer from exacerbation of their condition by these drugs.[9]

The fact remains; ADHD is a heterogeneous multi factorial disorder that is caused by a combination of factors, namely biological, psychological and/or social conditions. However, the existing research does not clarify the real etiology or the mechanism of ADHD.

Several recent articles have noted that ADHD children often suffer from nocturnal disturbance. Kaplan et al, found that parents of hyperactive children noted that their children have many sleep problems.[6] Up to 50% of the children and adolescents with ADHD suffered from sleep disturbance in Corkum's review.[10] Simonds and Parraga also reported that ADHD children displayed significantly more snoring, head banging, restlessness and problems with nighttime awakening.[9]

There are various types of sleep disorders [e.g. Obstructive Sleep Apnea Syndrome (OSAS), periodic limb movement disorder (PLMD), enuresis, delayed sleep phase syndrome] have been associated with ADHD in children.[6,10,11] Naseem *et al.*'s case report suggested that sleep disorders, especially OSAS maybe one of the underlining causes of ADHD.[11]

Obstructive Sleep Apnea is a sleep disorder characterized by pauses in breathing during sleep.[12,13] By definition each episode should last for 10 seconds.[12] Clinically significant levels of sleep apnea are defined as five or more episodes per hour. Another definition is a drop of 4% in oxygen saturation. Apnea/Hypopnea Index (AHI) classifies the severity of OSAS. AHI of 5-14 is mild, 15-30 is moderate while >30 sever.[12,13] The prevalence of OSAS in the United States is just over 4%.[12,14]

Apnea, in general, has three patterns: (a) Obstructive, (b) Central, and (c) Mixed.[14] An obstructive apneic event is defined by lack of airflow despite ventilatory effort. A central apneic event is defined as the lack of airflow resulting from an absence of ventilatory effort.[13,14] Finally, a mixed event is a partial central and obstructive in nature. A mixed apnea usually begins as a central apneic event and ends as an obstructive event.[13]

OSA patient usually suffers from snoring, restless disturbed sleep and observed gasping or apnea.[13] While during the daytime, the patient usually complains from excessive daytime sleepiness, cognitive impairment and morning headaches. Further evaluation often notes enlarged tonsils and adenoids, deviated nasal septum macroglossia and/or reflux laryngitis. Diagnosis of OSAS is made by Polysomnography [12-14] (also known as Sleep Study), where the documentation of the drop of oxygen saturation is made in a sleep lab.

There are many etiological factors for obstructive sleep apnea. The common factors in children are, deviation of the nasal septum, adenoid hypertrophy, tonsillar hypertrophy, macroglossia, retrognathia, omega shaped epiglottis, and laryngeal-tracheal stenosis.[12-14]

Obstructive sleep apnea children and Attention Deficit Hyperactive Disorder children have many symptoms in common. OSA children suffer from daytime sleepiness and lack of concentration and attention.[2] The earlier the patient is affected by OSA accompanied by delayed management will eventually result in a more dramatic disease. The reason behind this effect is the disturbed sleep at night.[8,15] Obstructive sleep apnea patient cannot maintain a deep sleep.[10,15,16] The abnormal respiratory events that are the hallmark of OSA are generally accompanied

by heart rate variability and arousals from sleep,[16] with frequent arousals being the most important factor resulting in excessive daytime sleepiness. With regards to sleep architecture, it has been noted that a significant increase in light sleep stage (mainly stage 1) at the expense of deep slow wave sleep (stages 3 and 4) and rapid eye movement (REM) sleep. Slow wave sleep is sometimes even completely abolished. However clinically, patients are often not aware of this repetitive sleep interruption (with sometimes hundreds of arousals during one night), but simply do not feel restored in the morning. Other nocturnal symptoms can include restlessness, nocturia, excessive salivation and sweating, gastroesophageal reflux, as well as headache and dry mouth or throat in the morning on awakening.[16]

The extent to which daytime functioning is affected generally depends on the severity of OSA. Symptoms other than excessive daytime sleepiness, which greatly impact daytime functioning, are neuropsychological symptoms such as irritability, difficulty concentrating, cognitive impairment, depressive symptoms, and other psychological disturbances.[16]

Yu-Shu Huang *et al.,*[2] in 2006, studied the effect of addressing OSA as an important cause of ADHD. The study included 86 patients of which 20 were a control group. The other 66 patients are patients with ADHD. All patients were thoroughly examined by an Otolaryngologist and had a Polysomnography done with an AHI of >1. Parents of all 66 patients were given 3 choices, surgery (adenotonsillectomy), MPH or observation. The three study groups were formed accordingly. The study demonstrated an improvement in cognitive function and daytime alertness and social behaviors in patients who had undergone surgery in comparison to the other group. Additionally, the patients treated with surgery also were documented to have a reduction in the AHI.[2]

Yu-Shu Huang stated, *"ADHD is a syndrome defined clinically, and there is a good evidence that several sleep disorders may lead to a clinical presentation similar to ADHD, but sleep disorders may be very much ignored by caretakers".*[2]

All the patients who were involved in the study were AHI 5 or less which is by definition not OSA.[13] But the fact that these patients improved with treatment of their hypopnea, or borderline OSA, and that their improvement was greater than the group managed by MPH or by observation validates the conclusion.

In Sangal's study[7,17] Polysomnography was used as a recruitment effort for a trial of atomaxetine and MPH for the treatment of ADHD. The authors based their standards exclusively on AHI. Their cut of point was 5 events/hour. The conclusion was that OSA was not an etiological factor in ADHD. However, some researches believe that AHI of 1-5 is considered abnormal and may cause sleep disturbance leading to symptoms similar to OSA, hence may have an influence on ADHD.

Furthermore, when corresponding obstructive sleep apnea with other behavioral disorders, e.g. depression, many studies have found relationship between them especially in adults. Among the first studies investigating the relation between OSA and depression, Guilleminault *et al.*[15] reported that 24% of 25 male patients with OSA had previously seen a psychiatrist for anxiety or depression, and Reynolds et al. showed that around 40% of 25 male OSA patients met the research diagnostic criteria for an affective disorder, with a higher risk of depression in those patients who were sleepier during the day.

Similarly, Millmann *et al.*[18] observed that 45% of his 55 OSA patients had depressive symptoms on the Zung Self-Rating Depression Scale, with the group scoring higher for depression also having a significantly higher AHI.[18] Whereas only 26% of OSA patients described themselves as currently depressed, 58% fulfilled DSM-III criteria for major depression of four or more depressive symptoms.[18]

The main challenge in managing obstructive sleep apnea is the understanding of the pathology. OSA is a multilevel disease.[19] It is quite often to encounter a patient with two, or sometimes three level disease. A combination of hypertrophied tonsils and large base of tongue is not uncommon. If an area is neglected, OSA may not improve resulting in a wrong impression of ineffective treatment or failed surgery.[19]

The other important controversy is whether to operate or not. There have been many articles that support the use of CPAP over surgical intervention.[20] These studies base their evidence on the degree of improvement on the polysomnography test, with CPAP having better results. And although most of these studies are based on an adult population, children with OSA are not expected to be very different.

Never the less, treating OSA whether by surgery or conservative management will result in improvement in the AHI level.[15,21] Although many studies have indicated that there is no significant lineal correlation between the severity of AHI and ADHD symptoms, a reduction in AHI level improves symptoms associated with sleep disturbance and subsequently results in a better quality of life.[15] The improvement is quite apparent in patients with sever and OSA (AHI >30) once they are tracheostomized.[15] The reason behind that is the immediate resolution of the OSA since the tracheostomy bypasses all levels of

higher airway obstruction. It is well documented in the literature that patients who have sever OSA, in which some were caused by subglottic stenosis, that required tracheostomy tube insertion noticed a great improvement in the quality of life. This improvement was supported by resolution of OSA in the polysomnography.

In summary, attention deficit hyperactive disorder is a behavioral disorder, which includes symptoms of daytime sleepiness and inattention. Such manifestations are similar to what patients with obstructive airway disease and sleep disorders suffer from. Recent studies and publications have included polysomnography as an investigation pillar in evaluating a child with ADHD. These studies have hinted on a possible relationship between these two diseases. The dilemma in the management makes obstructive sleep apnea a difficult disease to relate to. For that fact, the true relationship between OSA and ADHD is still unclear. There is no study to prove whether it is a correlation or co morbidity.

While a series of studies are awaited to prove or dismiss the relationship, recent studies have strongly put these two diseases close to each other. Although the relationship between obstructive airway diseases, behavioral disease and sleep disorders are yet to be fully understood, it is observed that addressing the airway disease improves both sleep and behavioral disorders, such as depression in adults. Evidence of improved daytime cognitive function, and decreases in daytime sleepiness by management of obstructive airway disease and sleep disorder, strongly suggests a relationship between OSA and ADHD.

For that matter, screening a child suspected to have ADHD for airway obstruction and addressing the problem with a proper management may well be advisable.

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