THE MAIN CAUSES AND CONSEQUENCES OF SLEEP DISORDERS OF BREATHING IN CHILDREN

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Summary
Sleep disorders of breathing (SDB) have an adverse influence on the intellectual or physical development and the emotional state among children. The SDB occurs in the form of obturative sleep apneas (OSA) or obturative sleep apnea syndrome (OSAS) in about 1-3% of children, mostly in the preschool and school age. The main causes of SDBs and sleep disruption among children are adenotonsillar hypertrophy and obesity. The consequences of the OSAs are daytime sleepiness, change in behavior, inattention and cognitive deficits, and poor quality of life. The most serious complications of the OSAS are cardiovascular disturbances: systemic and pulmonary hypertension. Delayed diagnosis and late proper treatment may lead to a permanent reduction of cognitive function and education potential.

The all-night (overnight) complete polysomnography is the gold standard for identification and differentiation of sleep disorders of breathing in children and adults. It advances diagnostic proceedings and initiation of treatment and can reduce costs of care.

Key words: sleep disorders of breathing, apnea, polysomnography

CHARACTERISTICS OF THE SLEEP DISORDERS OF BREATHING IN CHILDREN

Sleep Disorders of Breathing (SDB) have for years been a growing problem of adolescents, usually revealed by snoring. Gradually more attention has been paid to the problem of snoring among children, a symptom that might indicate a potential SDB (1). Polysomnography has become a more commonly used method, which gives a possibility to examine more and more children who are having problems with restless and interrupted sleep, snoring and pauses in breathing. Studying these disorders turned out to be all the more desirable, considering the observed adverse effects on the physical and mental development of children.

There are two types of apnea both in children and adults: an obturative apnea and a central apnea. An obturative apnea is a lack of air flow through the respiratory tract while respiratory movements of the chest continue (for a time equal or longer than the duration of two breaths) (3). A central apnea is characterized by a lack of air flow through the respiratory tract without respiratory movements of the chest for a time equal or longer than 10 seconds (2). Among adults, the obturative apnea is more frequent (and less frequent are mixed apneas), and it is induced by a hypotonia of the upper respiratory tract, usually occurring during sleep among people who snore. Episodes of apnea among children in the first year of their life, especially in the earliest period after birth, tend to have a more central mechanism and in many cases indicate an immaturity of the central nervous system. The main risk groups are premature newborns and children with low birth weight, as well as newborns from pathological pregnancies and/or prematurely exposed to nicotine and psychoactive substances (2). These apneas occur not only during sleep. Among children above the age of 1, breathing disorders often are accompanied by snoring, and often lead to symptoms that are initially observed mainly at night, and then more during the day. These symptoms are the basis for the diagnosis of the obturative sleep apnea syndrome (OSAS). The main factor predisposing children to develop the OSAS is a narrowing of the upper respiratory tract. In most children with this syndrome occurs a narrowing due to a lymphatic tissue hypertrophy in the pharynx (4). The second most common cause of upper airways obturation in children is obesity (5). In this case, the factor primarily responsible for the obstruction is the infiltration of the throat wall with adipose tissue. The participation of obesity in the pathogenesis of the SBD is increasing. According to the WHO report from 2004, obesity is already present in approximately 22 million children under 5, and in 10% children aged 5-17 the BMI exceeds the 94 percentile (6). A co-occurrence of both of these causes is possible, however, the role of the pharyngeal lymphatic tissue hypertrophy in the pathogenesis of the OSAS is typically less significant in obese children (7). Other, less common causes of obturative breathing disorders during sleep among children include: craniofacial abnormalities (mainly hypoplasia of...
the mandible), endocrine disorders (acromegaly, hypothyroidism) and genetic factors.

POLYSOMNOGRAPHY: PHYSICAL BASIS, THE PARAMETERS MEASURED AND THE TECHNICAL ASPECTS

The first study of sleep was conducted by a German physiologist, Ernst Kohlschutter (1837-1905). He also published the results as his doctoral dissertation, entitled *Measuring the depth of sleep*. The electric activity of the brain was first measured and recorded as an encephalogram by Richard Caton (1842-1926). Thanks to his work, Hans Berger (1873-1941), known as “the father of electroencephalography”, discovered and described the alpha and beta waves. Technological improvements in a short time also to detect and record the higher frequency waves. Further studies of sleep architecture and sleep tracts are associated with the names of three scientists: Loomis, Harvey and Hobart, who in 1937 managed to divide the stages of sleep and low frequency delta waves. This way they could describe deep sleep (slow-wave-sleep). The turning point in the research were the studies of Nathaniel Kleitman and his colleagues, who divided sleep into non-REM and REM phase. They managed to begin the era of specialized research on sleep (8).

Polysomnography plays a key role in the diagnosis of the respiratory disorders during sleep. American Academy of Sleep Medicine (AASM) has identified the parameters that should be recorded and assessed in polysomnography (9). These are:
- electroencephalography (eeg),
- electrooculogram (eog),
- electromiography of the chin muscles,
- electromiography of the leg muscles,
- airflow through the airways,
- the parameters of the respiratory effort,
- saturation,
- body positions.

The analysis of parameters based on a clinical interview and examination determines a correct diagnosis. These parameters include:
- number of times waking up,
- ai- apnea index,
- number of obturative apnea,
- number of central apnea,
- number of mixed apnea,
- AHI index (*apnea + hypopnea index*), i.e. the index of periods of apnea and hypopnea per hour of sleep,
- the average saturation,
- the minimal saturation.

Polysomnography (PSG) is an all-night study, and it ends when the patient awakens in the morning. In centers performing pediatric PSG, children should undergo a psychological examination, aiming to assess the child's development, including the possible consequences of breathing disorders during sleep.

COMPLICATIONS OF BREATHING DISORDERS DURING SLEEP AMONG CHILDREN

Abnormalities of the architecture and track of sleep and the lack of sleep adversely affect the emotional state and the intellectual and physical development of children. Frequent awakenings, preceded by episodes of apnea, may cause changes in one’s functioning during the day, including excessive sleepiness and behavioral disorders (10, 11). Even snoring without perceptible disturbances in sleep architecture and ventilation increases the risk of neurodevelopmental disorders and diseases of the cardiovascular system (12, 13).

EXCESSIVE DAYTIME SLEEPINESS

It is difficult to assess the severity of daytime sleepiness in children. The duration of sleep depends on the age of the child. Neonates and infants can sleep even up to 2/3 of the day. Parents subjectively evaluate the child’s sleep duration. They manage to observe excessive daytime sleepiness among 7% of children with a suspected obstructive sleep apnea (14). According to an objective assessment of sleepiness test – called the multiple latency test – sleepiness occurs in 13-20% of OSA cases, especially in children with obesity (12, 15). It has been reported that excessive daytime sleepiness may occur in up to 40-50% of children with OSA (16). For the assessment of older children, the Epworth Sleepiness Scale (ESS) can also be used. It is a self-assessment scale in which you should mark the points (0-3) and identify the probability of falling asleep in eight everyday situations. Although the questionnaire is mainly used in the evaluation of sleep disorders among adults, Malenders et al. (12) used the ESS in studies of children and confirmed that in obese children excessive sleepiness and hyperactivity more often than non-obese children.

BEHAVIORAL DISORDERS

Many published studies have demonstrated the existence of threats of cognitive and behavioral disorders in children with OSA, resulting from sleep fragmentation and hypoxia (17, 18). Among children the most commonly observed ones are behavioral disturbances, dominated by hyperactivity and lack of concentration. Both sleep fragmentation and episodes of hypoxia lead to the dysfunction of neurotransmitters in the prefrontal cortex, as well as to the damage and loss of neurons in this region (20, 21). O’Brien LM et al. (17) observed that chronically snoring children without OSA (AHI < 5/hour; AI < 1/hour) had higher depressive symptoms, cognitive deterioration and impaired concentration, as well as an impairment of visuospatial functions than children in the control group. Similar results were published by Aronen ET et al. (22). These authors found that children who snored loudly and frequently in early childhood had a greater risk of impaired learning abilities in later years (23). It was observed that the improvement of the quality of sleep has a positive effect on reducing hyperactivity concentration problems (24-27). It was also found
that even 25% of Attention Deficit Hyperactivity Disorder (ADHD) cases may be caused by breathing disorders during sleep. Snoring among children with ADHD occurs three times more often than among healthy children. It should, however, be stressed that not all researchers confirm the existence of a causal relationship between ADHD and respiratory disorders (28).

A delayed diagnosis and delayed proper treatment may also lead to permanent cognitive constraints (23, 27), and in consequence to worse chances for further education. However, not all children with OSA show behavioral problems and lower intellectual ability, which may indicate that genetic and environmental factors also play a role here (20).

EMOTIONAL AND MENTAL DISORDERS

Disorders of the sleep track and the co-occurring respiratory function abnormalities cause fatigue during the day, irritability and a depressed mood. Among children with tonsillar hypertrophy Kurnatowski P et al. (29) found a significant increase in emotional instability, depression and anxiety. Obesity may aggravate both sleep disorders and their consequences, leading to a significant deterioration in the quality of life (30). This mostly applies to children with OSAS (31).

NOCTURNAL ENURESIS

Brooks and Topol (33) showed that the increased incidence of nocturnal enuresis among children with OSAS may be associated with frequent awakenings, uncontrolled contractions of the bladder detrusor muscle and hormonal imbalances. In the study of Su MS et al. (34) where 6147 children were checked, an association between enuresis and SDB was observed only among girls. The overall incidence of nocturnal enuresis was 4.5% more often in boys (6.7% boys and 2.5% girls).

It was shown that bedwetting is linked with obesity and its accompanying obstructive sleep apnea (35). Therefore, OSAS should be suspected among children with obesity and bedwetting, especially if this syndrome is severe. An indirect evidence of the relationship between OSAS and nocturnal enuresis is the reduction or complete disappearance of enuresis after eliminating OSAS (36).

DISORDERS OF THE CARDIOVASCULAR SYSTEM

The most severe complications of obstructive sleep apnea include abnormalities of the cardiovascular system: hypertension and pulmonary hypertension. The relationship between obstructive sleep apnea and cardiovascular diseases is not fully explored. Several mechanisms are taken into consideration, including: increased sympathetic activity, the impact of rapid changes in intrathoracic pressure and the effect of oxidative stress (44). Damage to the vascular endothelium, platelet activation and increased secretion of inflammatory mediators may also play a major role (45).

Repeated episodes of hypoxia and hypercapnia, as well as severe respiratory movements, leading to a negative intrathoracic pressure, cause increased sympathetic activity (44) observed both when one is asleep and when one is awake. This leads to the narrowing of blood vessels, an increased blood pressure and heart rate acceleration (46). It was found that in children with SDB, blood pressure is higher than in children without respiratory distress (47). Additionally, a considerable variability in blood pressure and an increased variability in pressure between the night and day, with a predominance at night, was described (48).

Among children with OSAS (AHI index > 5), hypertension is accompanied by an increased thickness of the left ventricle.

Repeated episodes of hypoxia and reoxygenation cause damaging oxidative stress which damages the endothelium (49). Inflammation occurs as a result of T-cell activation and a release of proinflammatory cytokines (50). Endothelial dysfunction reduces nitric oxide production, resulting in increased vascular wall tension and starts the process of their remodeling (51). The result of these phenomena is a reinforcement of high blood pressure, and, in certain patients, a development of pulmonary hypertension (52, 50). The frequency of pulmonary hypertension occurring as a result of OSAS has not yet been established. However, it was observed that once the respiratory complications are controlled, the cardiovascular system complications disappear and the concentration of inflammation markers decreases (50). The effects of treatment are worse among children with severe OSAS and obese children, in whom weight loss plays a significant role in the treatment.

The occurrence of complications of the cardiovascular system among children with sleep breathing disorders may be co-decided by genetic and environmental factors.

DISORDERS OF PHYSICAL DEVELOPMENT

Consequences of untreated disorders of breathing among children may also include growth disorders. This complication is rare (< 5% of children with OSAS) (52). The factors responsible for the distortions in growth are: decreased appetite, dysphagia associated with enlarged tonsils, and low levels of the insulin growth factor (IGF-1) and the IGF binding protein (IGFBP-3) and probably also reduced secretion of the growth hormone (51). It was found that the rate of growth improves significantly after adenotonsillectomy, even in obese children (52). It is possible that the reduced breathing effort is one of the most significant factors in improving weight gain after the surgery.

OBESITY AND METABOLIC SYNDROME

X. Liu et al. (42) observed that children with obesity sleep less. Obesity also plays a significant role in the development of obstructive sleep apnea. The severity of obstruction symptoms among children with obesity is proportional to the degree of obesity (40). It was calculated that with an increase in BMI by 1 kg/m², the risk of OSAS increases by 12%. Obstructive sleep apnea –
a risk factor for the metabolic syndrome in adults (37) – carries a similar risk in children, especially among obese children (38). The presence of OSAS in children with obesity increases the risk of the metabolic syndrome up to six times (39). However, insulin resistance, as well as lipid disorders, such as increased concentrations of triglycerides and lower levels of HDL, primarily depend on the degree of obesity. The role of obstructive sleep apnea in the development of these disorders is minor (41). It has, however, been reported that among obese children with OSAS the risk of hepatic non-alcoholic steatosis increases (43).

**Summary**

Full polysomnography is the gold standard for the diagnosis and differentiation of respiratory disorders among children and adults. This test also plays a significant role in qualifying children for appropriate treatment. An early PSG examination may significantly shorten the time until the diagnosis of SBD and reduce the cost of treatment. The effects of hypoxia during sleep are not different from the child’s development and have a great impact, especially on the brain tissue and the cardiovascular system. An increased awareness of parents and physicians concerning problems related to sleep disorders and hypoxia should improve the results of short and long-term treatment.

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Received: 22.08.2012
Accepted: 10.09.2012

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