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Cutting-edge technologies for diagnosis and monitoring of snoring in children

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Abstract

Snoring is a very common problem in children and may be an indication of obstructive sleep apnea (OSA). Appropriate diagnosis is of importance due to detrimental effects of OSA. Polysomnography is considered the gold standard for the diagnosis of OSA. However, it is impractical for several reasons and this is why other tests have been developed as alternatives to formal polysomnography (PSG) for the assessment of children with snoring. In this mini-review basic features of PSG as well as alternative tests are presented and future perspectives are provided in addition to current guideline for the diagnosis and monitoring of childhood snoring. The aim of this review is to highlight briefly currently developed technologies that seem promising for the evaluation of snoring.

Key words: Snoring; Sleep apnea; Polysomnography; Molecular markers; Microelectronics

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Core tip: There are several methods allowing for the screening of obstructive sleep apnea (OSA) patients in a large scale, either in the field of molecular diagnosis or in the field of microelectronics Miniaturization technology as well as advances in wireless devices connectivity and data processing allows for more affordable, convenient and reliable recording of parameters such as oxygen saturation, actigraphy and others. In addition, advances in molecular biology allows for the detection of genetic and non-genetic biomarkers of sleep apnea. However the aforementioned markers and their combinations remain to be validated. Until then polysomnography is considered the gold standard for the diagnosis of OSA.

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INTRODUCTION

Snoring is the most commonly presented symptom

of obstructive sleep apnea (OSA) in children. The estimated prevalence for snoring is 10% to 12%, whereas the estimated prevalence of OSA is only 1% to 3%[1-3]. However, due to the detrimental effects of OSA, children who snore need medical advice and possibly polysomnography (PSG), the sleep test that is considered the gold standard for the diagnosis of OSA[4].

The American Academy of Pediatrics (AAP) clinical practice guideline on diagnosis and management of childhood obstructive sleep apnea syndrome recommends overnight PSG for the confirmation of OSA[5]. In addition to identifying the presence of OSA, PSG also helps define its severity, which can aid in perioperative planning. However, despite the AAP recommendations and documented utility of PSG, only about 10% of pediatric otolaryngologists in United States[6] and probably much less in the rest of the world, obtain a preoperative PSG before tonsillectomy for sleep disordered breathing.

There are several reasons that can explain the variability in obtaining PSG prior to tonsillectomy or for the evaluation of snoring in general. Lack of access, cost, time expended, and concern over the child's emotional distress are the main reasons that explain why other tests have been developed as alternatives to formal PSG for the assessment of children with snoring. However, their role is still controversial.

In this mini-review basic features of PSG as well as alternative tests are presented and future perspectives are provided in addition to current guideline for the diagnosis and monitoring of childhood snoring. The aim of this review is to highlight briefly currently developed technologies that seem promising for the evaluation of snoring even though they have not been proven and qualified in real field.

Polysomnography

Formal PSG requires hospitalization or one night stay in a sleep laboratory. Several parameters are recorded simultaneously (Table 1) that allow for the estimation of specific indexes, with apnea-plus-hypopnea index (AHI) being the most utilized for diagnosis and staging of obstructive sleep apnea. Nevertheless, even the use of AHI is problematic in children since the clinically valid cut-off for normal AHI is unclear in this age group and no consensus has been achieved as to whether children with AHI values between the normal cut-off [< 1/h of total sleep time (TST)] and 5/h TST should undergo adenotonsillectomy[7,8].

Portable monitoring devices

Portable monitoring devices, also referred to as out-of-center sleep testing (OCST), have evolved as an alternative to overnight, attended, in-laboratory PSG in selected patients. Advantages of portable monitoring devices (PM) include its convenience (it can be performed in the patient's home) and its lower costs. However, the major disadvantage is that for most of these devices, fewer physiologic variables are measured than with PSG, which can lead to misinterpretation of the results.

The United States Centers for Medicare and Medicaid Services have released guidelines that state that results from OCST can be used to support a prescription for positive airway pressure therapy in adults[9]. The American Academy of Sleep Medicine has also released clinical practice guidelines to guide clinicians in the use of OCST[10,11]. There are three types of PM: Type Ⅱ device, which has a minimum of 7 channels (*e.g.,* EEG, EOG, EMG, ECG-heart rate, airflow, respiratory effort, oxygen saturation). This type of device monitors sleep staging so the AHI can be calculated; Type Ⅲ device which has a minimum of 4 channels and Type Ⅳ device which usually measure only 1-2 parameters (*e.g.,* oxygen saturation); Type Ⅰ refers to polysomnography which is not actually a portable monitoring device.

At minimum, PM must record airflow, respiratory effort, and blood oxygenation[10,12], thus type IV devices are not supported officially. For example, oximetry has a high positive predictive value (97%) for diagnosis of obstructive sleep apnea, but because not all apneas result in a drop in saturations the negative predictive value is low (53%)[13]. This is because simple oximetry cannot detect: (1) events that result in arousal without desaturation; (2) how long the patient slept; (3) carbon dioxide elevation; (4) prolonged flow limitation without discrete desaturation; or (5) whether they achieved rapid eye movement sleep (the period when respiratory events are most common)[4,14].

In general, false negative rates may be as high as 17% in unattended PM studies and the role of PM, as an alternative to formal PSG, in assessing children with sleep disordered breathing is controversial[10]. Unattended PM for the diagnosis of OSA should be performed only in conjunction with a comprehensive sleep evaluation. Moreover, in-laboratory polysomnography should be performed in case the PM test is technically inadequate or does not provide the expected result[10].

Miniaturization technology as well as advances in wireless devices connectivity and data processing allows for more affordable, convenient and reliable recording of parameters such as oxygen saturation, actigraphy and others. Thus the future of portable monitoring, especially in conjugation with other tests, seems promising.

Additional tests

An extended review of PSG and related monitoring is beyond the scope of this article. Furthermore, measures derived from PSG are poor predictors of OSA-associated morbidities[15]. The aforementioned tests can be combined with a validated questionnaire (*e.g.,* health status or quality of life questionnaire). Such questionnaires have been shown recently to be of benefit for childhood obstructive sleep apnea course prognosis[16] and can be utilized in the decision making process, *e.g.,* prior to a tonsillectomy.

Other modalities that are being investigated for the diagnosis and management of sleep apnea are genetic

Table 1 Parameters most commonly recorded in a polysomnography study

Pulse oximetry
Airflow from nasal canula thermistor and/or X-flow (AASM recommends RIP technology)
Snoring
End-tidal CO_2
Esophageal pressure and other methods for monitoring respiratory effort
ECG/heart rate or heart rate variability
Arterial tonometry
Electroencephalography
EOG
Actigraphy
Body position
Chin EMG
Limb EMG
Additional channels, *e.g.*, for CPAP/BiPap levels, pH, *etc.*

AASM: American academy of sleep medicine; RIP: Routing information protocol; ECG: Electrocardiograph; EOG: Electro-oculogram; EMG: Electromyography; CPAP: Continuous positive airway pressure.

Table 2 Potential biomarkers of obstructive sleep apnea and/or its comorbidities in children

Non-genetic	Genetic
8-isoprostane	CRP 1444C/T
Adiponectin	CRP 1919A/T
APOEe4	IL-6-174C/IL-6 597A
Catecholamines	NOS1 and NOS3 16SNPs
Catestatin	EDN2 and EDN3 5 SNPs
CRP	MIF gene SNP rs10433310
IL-6	NADPH oxidase (NOX) rs6520785 and rs4673
HOMA	ApoE rs405509
MRP8/14	
TNF-α	
Urinary neurotransmitters	

CRP: C-reactive protein; NADPH: Nicotinamide adenine dinucleotide phosphate; IL: Interleukin; TNF: Tumor necrosis factor.

and non-genetic biomarkers (Table 2). As mentioned earlier, PSG results are poor predictors of OSA-related morbidities and there is the need of tests that can identify the most "vulnerable" patients, who would more likely benefit for specific therapeutic interventions[8]. Of the potentially promising morbidity biomarkers, plasma IL-6 and high sensitivity C-reactive protein appear to exhibit a favorable profile, and may discriminate OSA patients with and without morbidities in both adults and children. MRP 8/14 have been utilized as a cardiovascular morbidity-associated biomarker in children. In addition, urinary neurotransmitters may also provide a good tool for screening OSA cognitive morbidity in children[8].

The above mentioned biomarkers are non-genetic, their concentrations can be measured with various methods, *e.g.*, ELISA, chromatography and others, and depend on the course of the disease, thus they have the potential to provide information related to prognosis and response to treatment. On the contrary, gene polymorphisms (single nucleotide polymorphisms, insertion/deletion and copy number variants) show the genetic predisposition for OSA and are independent of the course of the disease. Because of the lack of genome-wide studies on the field, especially in children, there are only very few SNPs (Single Nucleotide Polymorphisms) that have been associated with obstructive sleep apnea and its comorbidities[17-19] (Table 2). Since simple SNPs or sequences cannot be patented, what is expected in the near future is that panels (or combination) of them that can be IP protected, to arise and to be validated.

Later developments in the field of chromatography and molecular biology techniques, such as multiplex PCR and sequencing, allow for the detection of various markers not only in serum but also in other samples such as saliva, urine and exhaled breath condensate. This is of special important for children, because nconvenient and painful blood tests can be avoided. Moreover, the cost of these methods has already been reduced and is almost certain that we will witness further costs reductions in the near future. Thus, methods allowing for the screening of OSA patients in a large scale already exist, either in the field of molecular diagnosis or in the field of microelectronics. These methods have the potential to provide us with affluent data. The field of sleep disorders will be revolutionized in case accurate verification of this data, probably in the form of validated and patented algorithms, is accomplished.

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