The Ophthalmologist’s Role in Identifying Obstructive Sleep Apnea (OSA) Short Communication/New Technologies

Solveig Magnusdottir*
MyCardio-LLC, SleepImage®, USA

ABSTRACT

Obstructive Sleep Apnea (OSA) has a multisystem effect and is associated with a host of systemic side effects and the eyes are particularly susceptible to both mechanical and vascular consequences of the disease. This emphasizes the importance to increased awareness of both OSA and of ocular complications of this common disorder to prevent vision-threatening complications. The purpose of this short review is to provide ophthalmologist and primary care physicians with knowledge of how recent advances in sensor technology and computing now offer simple and cost-effective ambulatory methods to accurately screen for sleep disorders, including OSA and to encourage more attention to symptoms of sleep apnea in patients with ocular diseases.

Abbreviations:
American Academy of Sleep Medicine; AHl: Apnea Hypopnea Index; CAP: Cyclic Alternating Pattern; CPC: Cardiopulmonary Coupling; CSA: Central Sleep Apnea; CPAP: Continuous Positive Airway Pressure; CVHR: Cyclic Variation of Heart Rate; ECG: Electrocardiogram; EDR: Electrocardiogram Derived Respiration; EEG: Electroencephalogram; eLFCBB: Elevated Low Frequency Broad-band; eLFCNB: Elevated Low Frequency Narrow-band; FES: Floppy Eyelid Syndrome; HRV: Heart Rate Variability; HFC: High Frequency Coupling; LFC: Low Frequency Coupling; NREM: Non-Rapid Eye Movement Sleep; NAION: Nonarteritic Anterior Ischemic Optic Neuropathy; OSA: Obstructive Sleep Apnea; PSG: Polysomnography; REM: Rapid Eye Movement; SA: Sleep Apnea; SAI: Sleep Apnea Indicator; SQI: Sleep Quality Index; vLFC: Very Low Frequency Coupling

Introduction

The importance of sleep is increasingly being recognized as critical to overall health and wellbeing. The Nobel Prize in Physiology and Medicine for 2017 places the focus on what the circadian rhythm fundamentally means for our internal body clocks that helps explain the implications ranging well beyond sleep disorders [1]. Recent advances in sensor technology now offer ambulatory methods to easily collect medically relevant physiological signals that can be analyzed to estimate sleep quantity, sleep quality and sleep...
pathology providing a unique insight into sleep regulation in health and disease [2,3].

Medical providers are increasingly managing an ever-growing number of medical conditions, encompassing all organ systems, many of which are associated with untreated Obstructive Sleep Apnea (OSA). In order to effectively manage these disorders physicians must be educated about disease association, diligent in screening efforts to identify co-morbid conditions and thoughtful in therapeutic management.

Sleep Apnea (SA) is characterized by paused breathing during sleep, disrupting a healthy sleep pattern that has been shown to adversely affect the overall health of SA patients. The most common form of sleep apnea, OSA is characterized by repeated partial, or complete obstruction of the upper airway during sleep, resulting in intermittent hypoxia and transient repetitive sympathetic arousals from sleep. Central Sleep Apnea (CSA) is a less common form of sleep apnea associated with disordered respiratory control [4].

OSA produces a host of systemic side effects and the eyes are particularly susceptible to both mechanical and vascular consequences of the disease. Hypoxia induced by repeated cessation of breathing during sleep has multisystem effects and is associated with an increased risk and progression of diseases like hypertension and cardiovascular disease, [4-6] obesity, [7,8] type 2 diabetes [9] and various ophthalmic diseases [10]. Activation of the sympathetic nervous system during sleep and the intermittent hypoxia may be the primary mechanisms behind the development and persistence of these co-morbid diseases. Today it is estimated that 12% of adults suffer from OSA in the United States and that 80% of the patient population is undiagnosed [11,12].

Obstructive Sleep Apnea (OSA) and Ophthalmic Complications

The various ophthalmic diseases associated with OSA may cause patient discomfort or vision loss over time. Just as it is important for ophthalmologists to be alert to hypertension or mild diabetic retinopathy, it is also critical to recognize visual conditions that might be associated with OSA in patients with predisposing factors presenting with opthalmic diseases. Medical research is continuously demonstrating the importance of multi-disciplinary approach to care management, based on knowledge of the inter-connectedness of disease progression. To provide higher level of care and improve patients’ quality of life, physicians need to be aware of these associations and should screen patients if they have a risk profile for OSA [10].

OSA is the most frequent systemic disease associated with Floppy Eyelid Syndrome (FES), a condition where the upper eyelid becomes highly elastic and is easily inverted or folded upward leaving the eye susceptible to discomfort and visual symptoms related to exposure. Frequency of FES in patients with OSA has been found to be high, 25 -56% and increase among those with severe OSA [13,14]. Glaucoma is also known to be more prevalent in patients with OSA, though less than FES or 11% particularly in severe cases and although the relationship between OSA and glaucoma is not yet fully understood, it is generally accepted that there is an association between the two diseases. Nonarteritic Anterior Ischemic Optic Neuropathy (NAION), a painless unilateral vision loss, has been found to be twofold more prevalent in patients with OSA than in the general population or 16% [15]. The incidence of second eye involvement varies from 5-25% and given the possible association between OSA and NAION, it is essential for those patients to be screened for OSA and have treatment initiated when appropriate, to prevent the risk of second eye involvement [16,17].

With this increased risk of vision-threatening ocular conditions, suspicion of OSA should be thoroughly assessed by an ophthalmologist during ophthalmic examination, due to the implications in the management of ocular diseases. In management of OSA, it is highly important that patients understand that treatment of sleep apnea leads to improvements, not only in sleep symptoms but also in a variety of co-morbid diseases as well as improved overall health and wellbeing. Continuous Positive Airway Pressure treatment (CPAP) is effective in reducing the morbidity and mortality associated with OSA and given the possible association.
between OSA and ophthalmic diseases, CPAP treatment can thus contribute to preventing further progression of these co morbid diseases [18,19]. Therefore, a crucial part of the disease management is to educate the patient on the association between sleep apnea and these co morbid diseases, on the importance of adherence to treatment to facilitate improved outcomes and to track therapy efficacy to maximize medical benefits. Management of OSA and its associated conditions should involve the primary care physician as well as ophthalmologists and other specialists.

**Methods to Screen and Diagnose Sleep Disorders**

Accepted clinical methods used to screen for sleep disorders have mostly been limited to subjective questionnaires for reasons of convenience and cost. Questionnaires were originally created in a response to a lack of technology available to screen for sleep disruptions and sleep disorders outside of the sleep laboratory. They are relatively effortless to conduct but are based on respondents’ own subjective perception of their sleep. Even though questionnaires have historically been perceived as accurate, when compared to objective physiological data, their results have shown a level of inconsistency to make them unreliable [20,21]. Subjective estimates undoubtedly can be useful to a degree but people with sleep complaints and sleep disorders may not accurately estimate sleep quality or duration as their perception depends heavily on extraneous factors including demographics and co morbidities, and they often tend to underestimate sleep time and quality [22]. OSA patient’s sleepiness and daytime functioning varies widely between patients as some patients subjectively report excessive daytime sleepiness while others do not [23,24]. Generally, if a questionnaire has a high sensitivity, it is at the expense of poor specificity, and vice versa, deeming them inaccurate tools to rely on in isolation, and it is likely that most of the questionnaires will in accurately classify a significant proportion of sleep disorder patients [20,21]. For patients identified to have insomnia based on subjective responses to a questionnaire, a diagnostic test such as a Polysomnography (PSG) is not used for routine evaluation unless the screening test is inconclusive, or behavioral or pharmacologic treatment fails [25]. However, emerging evidence suggests that sleep related breathing disorders like OSA, may be an under-recognized cause of insomnia complaints, even among individuals who deny symptoms of sleep apnea at initial presentation [26,27]. It is recommended that positive results for identifying OSA based on sleep questionnaires is followed up with a diagnostic test for OSA. PSG is the reference standard for diagnosis of OSA before treatment is initiated, and an attended study is recommended [28]. PSG tests can be challenging to obtain, as the procedure is time consuming, labor intensive, costly and not available to all at-risk patients. Home Sleep Testing (HST) is less expensive and can be somewhat less challenging to obtain, but lacks the sensitivity to rule out OSA diagnosis as it does not record sleep onset, sleep duration, sleep efficiency or wakefulness. If a patient suspected of having OSA has a negative HST, there commendation is to follow up with a PSG test [29]. Then, when a therapy is recommended, it is expensive and burdensome to use PSG or HST to determine efficacy of prescribed therapy. This process is costly, time consuming and impractical in the population of at-risk patients suffering from co morbid disorders associated with OSA.

**Cardio Pulmonary Coupling and Cyclic Variation of Heart Rate Analysis**

Recent advances in sensor technology now offer ambulatory methods to easily collect single lead ECG data [2,30]. The Sleep Image® system (My Cardio LLC, Broomfield, CO) is FDA approved for evaluating sleep disorders to inform or drive clinical management based on clinically validated algorithms analyzing single-lead ECG data to provide an objective measure of sleep duration, sleep quality and sleep pathology. The CPC analysis was performed and described in detail [30,31]. The Sleep Image® wearable sleep data recorder collects a continuous ECG signal. One electrode pad is attached to the device that is then connected to a second electrode using a thin ECG cable across the chest. Activity and body position is measured by internal
accelerometers and gyroscopes and snoring is detected by tissue vibration (Figure 1).

Figure 1: SleepImage® Sleep Data Recorder.

Collected data is uploaded to the Sleep Image® secure, cloud-based system for automatic analysis where the Cardiopulmonary Coupling algorithms generate sleep metrics and other physiological data including spectrographic analysis of the sleep period (Figure 2). The automated data output are presented as the Sleep Quality Index (SQI), providing a summary measure of CPC describing sleep duration, sleep stability, sleep fragmentation, and sleep pathology to generate a number between 0 and 100. Sleep Apnea Indicator (SAI) is an automated measure of CVHR during unstable breathing (tidal volume fluctuations in breathing) detecting oscillations in cardiac intervals often associated with prolonged cycles of sleep apnea. Displaying this physiological reaction occurring in the cardiovascular system as a consequence of arousals and/or drop in oxygen saturation as an indicator that helps to identify patients suffering from sleep disordered breathing [2].

A detailed methodology on the basic algorithms has been published. The technique uses continuous ECG-data collected during sleep that extracts and couples Heart Rate Variability (HRV) and ECG-Derived Respiration (EDR) to generate frequency maps of coupled autonomic-respiratory oscillations, the ECG-derived sleep-spectrogram (Figure 2) [30,31]. The sleep-spectrogram reveals that Non Rapid Eye Movement sleep (NREM) has a bimodal-type structure marked by distinct alternating and abruptly varying periods of high and low frequency Cardio Pulmonary Coupling (CPC). Stable sleep (high frequency coupling, HFC) occurs during part of stage N2 and all of stage N3 NREM sleep and is associated with periods of stable breathing, non-cyclic alternating pattern (non-CAP) electroencephalogram (EEG) morphology, increased absolute and relative delta power, strong sinus arrhythmia, and blood pressure dipping. Conversely, unstable sleep (low frequency coupling, LFC) is characterized by temporal variability of tidal volumes, Cyclic Alternating Pattern (CAP) EEG morphology, non-dipping of blood pressure and lower frequency cyclic variation in heart rate. Fragmented Rapid Eye Movement Sleep (REM) has an LFC signature, while normal REM sleep and wake show very Low Frequency Coupling signature (vLFC). A subset of low-frequency coupling, termed elevated Low-Frequency Coupling Broad-Band (eLFCBB) defines periods of apneas-hypopneas and elevated Low-Frequency Coupling Narrow Band (eLFCNB) distinguishes between apneas caused by upper airway anatomical obstruction and respiratory dyssynchrony [32].

Using the Sleep Apnea Indicator (SAI) together with the Sleep Quality Index (SQI), eLFCBB and eLFCNB it is possible to identify the presence and severity of Sleep Disordered Breathing (SDB). It also categorizes SDB as obstructive, central or complex sleep apnea [2,32].

The CPC technique accurately identifies insomnia [33] and sleep apnea in adults [2,34] and captures treatment effects in sleep apnea in both adults [34-37] and children [38, 39]. In this way, the NREM sleep phenotype extends beyond conventional scoring of AHI and its reliance on absolute delta power and SQI may be expected to increase as CVHR and SAI are expected to decrease, as the disease is successfully treated and healthy sleep patterns dominate [2,31].

This improved ambulatory screening method for sleep apnea will help clinicians to improve diagnostic accuracy for sleep apnea. It can also provide objective evidence and feedback for patients regarding effectiveness of therapy and can therefore assist in improving therapy.
management for both sleep apnea and related co-morbid diseases. Utilizing a medically accurate, practical and cost-effective method to track the dynamics of sleep over prolonged periods of time is likely to provide unique insight into sleep management in health and disease. While the relationship to untreated sleep disorders may not be the most immediately obvious observation to aid clinical diagnosis in ophthalmology, it should not be ignored or overlooked given the implications of how untreated sleep disorders can adversely affect progression of various ophthalmic diseases.

**Conclusion**

Ocular complications are common in patients suffering from OSA. Therefore it is important for physicians to be aware of OSA symptoms and screen for the disease as ocular complications are common in OSA patients and untreated it can adversely affect the progression of their ocular disease. As it is estimated that 80% of patients with OSA are undiagnosed thus creating a need for accurate and efficient screening methods and the involvement of both primary care and other specialty physicians like ophthalmologists in identifying these patients is important. Recent advances in sensor technology now offering ambulatory methods to easily

---

**Figure 2:** Sleep Spectrograms for a Healthy Sleeper (left) and Unhealthy Sleeper (right). Note the difference between the two with respect to the proportion of the recording spent in HFC and LFC, and increase in both eLFCBB and eLFCNB in the case of unhealthy sleep.
collect bio-signals like ECG, which provides opportunities and possibilities to collect objective data to analyze and improve clinical diagnosis and treatment decisions.

References
1. The Nobel Prize in Physiology or Medicine 2017.


adenotonsillectomy in pediatric sleep apnea. Laryngoscope. 122: 2115-2121.