Assessment of the severity of obstructive sleep apnea syndrome through analysis of desaturations and apnea and hypopnea index: A review article

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Abstract

Purpose: The Obstructive Sleep Apnea Syndrome (OSAS) has been receiving great attention due to the systemic repercussions that can cause, especially to the cardiovascular system. Cycles of hypoxia caused by the obstruction of the upper airways during sleep, generate a change in the O2 oxidative chain increasing the production of free radicals, oxygen species highly reactive with other molecules. The severity of OSAS is assessed only by the quantification of these respiratory events (apnea and hypopnea index - AHI). In order to find new criteria for the definition of OSAS severity, a systematic review was made in the literature in search of other parameters for a better clinical evaluation of OSAS.

Methods: The literature search was conducted in 3 different databases (PubMed, LILACS and Scielo) using as descriptors the terms “obstructive sleep apnea”, “apnea and hypopnea index” and “desaturations”. We found 79 articles from which the titles and abstracts were read, but only 6 were included to read the texts and analyzes.

Results: The main pathophysiological consequences of OSAS occur due to insufficient supply of O2 caused by apnea and hypopnea. However, these events may have a short or long duration provided they have a minimum duration of 10 seconds. Events with prolonged duration and consequently with greater chances of deep desaturation may paradoxically lead to a decrease in AHI.

Conclusion: Quantification of desaturations as well as the depth level of O2 drops should be valued and may help to assess the real severity of OSAS in association with AHI.

To our knowledge, this is the first described case of spontaneous regression of squamous cell carcinoma of sinonasal origin.

Introduction

Among sleep disorders, the Obstructive Sleep Apnea Syndrome (OSAS) has been gaining prominence due to the systemic repercussions that it can cause, especially to the cardiovascular system, being an important cause of morbidity and mortality [1]. Cycles of hypoxia, caused by episodes of total obstruction (apnea) or partial obstruction (hypopnea) of the upper airways during sleep followed by reoxygenation, cause a change in the oxidative balance due to the insufficient supply of oxygen. This oxidative stress increases the number of free radicals, which are highly reactive species of oxygen molecules capable of reacting with other molecules, including proteins, altering their functions, being the main mechanism responsible for vascular endothelial injury and consequent cardiovascular complications [2].

All-night polysomnography is the necessary examination for the diagnosis and definition of OSAS severity, as it determines the rate of apnea and hypopnea (AHI), that is the number of these respiratory events per hour of sleep [3]. Thus, recurrence of respiratory events associated with frequent desaturations, and sleep surface and fragmentation are common findings in the polysomnography of patients with OSAS [4]. However, this is an examination of high cost and limited availability, mainly for the public health. Other alternatives have been proposed, especially as a screening for OSAS, such as pulse oximetry, since it is a low cost and easily performed technique, which is based mainly on periods of falls in O2 concentrations [3].

A task force was instituted by the American Academy of Sleep Medicine (AASM) in 1999 to establish the diagnostic criteria for OSAS, based on clinical and complementary aspects. Patients with OSAS should present diurnal or nocturnal symptoms, and at least 5 respiratory events (apnea/hypopnea) per hour of sleep (AHI ≥5/h) demonstrated through polysomnography [5]. These criteria were revised and modified in 2005, requiring the presence of A + B + D or C + D criteria (Table 1) [6]. The severity of OSAS is determined by three types of AHI ranges. Individuals with AHI ≥ 5/h and <15/h are considered mild. Those with AHI ≥ 15 and ≤ 30/h have moderate disease severity; and those with AHI>30/h are considered severe. Therefore, the severity of OSAS is evaluated only by AHI (Table 2) [5]. The American Academy of Sleep Medicine Scoring Manual recommended definition requires that changes in flow be associated with a 3% oxygen desaturation or a cortical arousal, but allows an alternative definition that requires association with a 4% oxygen desaturation without consideration of

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Table 1. Diagnostic criteria for OSAS in adults according to the American Academy of Sleep Medicine, 2005. Source: The international classification of sleep disorders: Diagnostic and coding manual. Westchester American Academy of Sleep Medicine, 2005.

| CRITERIA | AHI |
|----------|-----|
| A. At least one complaint: | |
| • Unintended sleep episodes during wakefulness, excessive daytime sleepiness, unrepairable sleep, fatigue, or insomnia; | |
| • Waking up with breathing pauses, gagging or choking; | |
| • Companion report loud snoring and / or breathing pauses during sleep. | |
| B. Polysomnography: ≥ 5 respiratory events / hour of sleep (apnea, hypopnea, arousal related to respiratory effort). Evidence of respiratory effort throughout or part of each event. | |
| C. Polysomnography: ≥ 15 respiratory events / hour of sleep (apnea, hypopnea, arousal related to respiratory effort). Evidence of respiratory effort throughout or part of each event. | |
| D. The disorder can not be better accounted for by other sleep disorders, medical or neurological diseases, use of medications, or use substances. | |

Table 2. Determination of OSAS severity by the quantification of AHI, according to the American Academy of Sleep Medicine, 1999. Source: Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. Sleep: American Academy of Sleep Medicine, 1999.

| OSAS Severity | AHI |
|---------------|-----|
| MILD          | ≥ 5 and <15/hour |
| MODERATE      | ≥15 and ≤30/hour |
| SEVERE        | >30/hour |

cortical arousals. Depending on which definition is used, the AHI may be considerably different in a given individual [7].

Considering that in addition to lowering airflow, it is also an absolute criterion for defining any respiratory event the duration of airflow, which should be at least 10 seconds (Table 3) [8]. Thus, there are short and long respiratory events. Longer-lasting events are more likely to result in more significant declines in O2 concentrations and consequent more significant desaturations of oxyhemoglobin, resulting in more deleterious effects on health. So, it is possible that individuals with low AHI, but with long-term respiratory events and, therefore, with more severe oxyhemoglobin desaturations, may suffer more hemodynamic damage than individuals with AHI, but with short respiratory events and milder desaturations of oxyhemoglobin. Kulkas et al. [9] researched new parameters to evaluate the OSAS severity, relating duration and morphology of obstructive events during sleep. They found that subjects with similar AHI had different degrees of upper airway obstruction with different levels of oxyhemoglobin desaturation. Most intriguingly, short respiratory events could raise AHI, but they did not necessarily lead to significant falls in O2 levels. Thus, when using only AHI as a criterion of OSAS severity, one may be underestimating cases with greater severity, but with low AHI, or otherwise, overestimating less severe cases, but with high AHI.

In order to find new criteria for the definition of OSAS severity that support AHI, and therefore together, can more accurately determine the true severity of the disease, a systematic review was performed in the literature in search of other parameters that could contribute to a better clinical evaluation of OSAS.

Methods

Extraction of data

Data search in the literature was performed by 3 researchers independently and in 3 different databases (PubMed, LILACS and Scielo), since January to October 2017. The terms “obstructive sleep apnea “, “apnea and hypopnea index “and “desaturations “were used as descriptors, according to the following search strategies: (“Obstructive sleep apnea "or” sleep apnea, obstructive " All Fields] AND” apnea “[All Fields] AND hypopnea ” [All Fields]) OR “obstructive sleep apnea”) AND “apnea" [All Fields] OR "apnea" [MeSH Terms] OR “apnea” [All Fields] AND “topic” [All Fields] OR "abstracting” [All Fields] AND “indexing” [All Fields] AND “topic” [Fields] AND desaturations [All Fields]. In this way, 79 articles were found from which the titles and abstracts were read. Those who were considered of interest to the research were selected to read the texts in full.

Eligible studies

The articles that were selected for this research should follow the following inclusion criteria: (1) prospective or retrospective studies in adult humans diagnosed with OSAS; (2) analyzes of desaturations in the evaluation of OSAS beyond AHI. Unpublished studies or those that did not meet the above criteria were excluded. Thus, 79 articles were found, but only 10 were included for complete reading of the texts. Each researcher independently carried out the readings of the 10 articles in their entirety, of which 6 were unanimously considered among the researchers of interest to the research and therefore, under which the analyzes should be made [3,9-14]. The main results of each article were extracted and these were compared by the authors, with agreement among them. However, it was not possible to carry out statistical analysis due to the heterogeneity of the variables.

Results and discussion

The treatment of OSAS depends fundamentally on the severity of the disease. All efforts should be made to try to minimize the harmful effects of the disease primarily related to the cardiovascular system. O2 deficiency caused by obstruction of the upper airways during sleep generates intermittent periods of hypoxia that alter oxidative metabolism. This oxidative stress produces an imbalance between pro-oxidant and anti-oxidant factors, increasing the reactive O2 species which have one or more unpaired electrons in their outer orbit, and because of that they are chemically reactive. These free radicals are products normally obtained from O2 metabolism during the cellular respiration process, through enzymatic and non-enzymatic antioxidant systems act to eliminate their excess [10]. However, there is an imbalance of this antioxidant capacity in OSAS, generating a greater quantity of these reactive species of the O2 that are able to interact with other molecules and to change their functions. In addition, they may

Table 3. Criteria for identifying apneas and hypopneas according to the American Academy of Sleep Medicine, 2007. Source: Iber C, Ancoli-Israel S, Cherson JRA et al (2007). The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications. Westchester: IL: American Academy of Sleep Medicine, 1 Ed.

| Respiratory Events | Definition | Duration |
|-------------------|------------|---------|
| APNEA             | Airflow excursion drop by temperature signal ≥ 90%. | ≥10 seconds |
| HYPOPNEA          | Reduction of airflow excursion by nasal pressure signal ≥ 30% of baseline associated with fall ≥ 4% of oxygen saturation (recommended criteria – rule A); OR \ Fall ≥ 50% of the nasal pressure signal associated with fall ≥ 3% of oxygen saturation or an awakening (alternative criterion – rule B). | ≥10 seconds |
also activate proinflammatory factors with cytokine production, such as interleukins 6 and 8 and tumor necrosis factor, which are involved in the genesis of systemic arterial hypertension and atherosclerosis in OSAS [2].

Thus, the main pathophysiological consequences of OSAS occur due to the insufficient supply of $O_2$. Quantification of desaturations as well as the depth level of $O_2$ drops should be valued and may help to assess the real severity of OSAS in association with AHI such as George et al. [11]. In that study, the authors used a computerized algorithm to detect falls in $O_2$ saturation greater than 3%, evaluating the saturation in two moments: at the end of inspiration and at the end of expiration. The program scanned through time series between peaks and depressions detect falls in $O_2$ saturation greater than 3%, evaluating the saturation in assess the real severity of OSAS in association with AHI such as George Otorhinolaryngol Head Neck Surg, doi: 10.15761/OHNS.1000152 due to the insufficient supply of $O_2$. Quantification of desaturations as in the genesis of systemic arterial hypertension and atherosclerosis in as interleukins 6 and 8 and tumor necrosis factor, which are involved

Schlotthauer G, et al. [3], in which an algorithm based on the empirical decomposition method for the detection of desaturations associated with OSAS was demonstrated, using signals obtained by pulse oximetry, in order to estimate the AHI as a mode similar to AHI obtained through polysomnography, but using only information on oxygen desaturations measured by oximetry. Only $O_2$ falls of at least 3% and lasting for at least 10 seconds were considered equivalent to the occurrence of some respiratory events. The authors concluded that the algorithm used based on desaturations may contribute to the estimation of AHI (Table 4).

The nocturnal oximetry analyses have been used as screening for potential diagnosis of OSAS, but the interpretation of the signal is highly dependent on the technician. Some studies have shown that when appropriate algorithms are used, nocturnal oximetry can be a really sensitive and specific method for OSAS. This was demonstrated by Schlothauer et al. [3], in which an algorithm based on the empirical decomposition method for the detection of desaturations associated with OSAS was demonstrated, using signals obtained by pulse oximetry, in order to estimate the AHI as a mode similar to AHI obtained through polysomnography, but using only information on oxygen desaturations measured by oximetry. Only $O_2$ falls of at least 3% and lasting for at least 10 seconds were considered equivalent to the occurrence of some respiratory events. The authors concluded that the algorithm used based on desaturations may contribute to the estimation of AHI (Table 4).

A recent study published by Kulkas et al. [14], in which the duration and depth of desaturations were evaluated in the respiratory events (apnea and hypopnea) of 395 patients undergoing an all-night polysomnography, which were divided into groups according to duration of desaturation events. For marking of hypopneas, the authors considered desaturations from 3%. There was a statistically significant correlation between the time and depth of desaturations and the duration of apnea and hypopnea (p<0.001), and also observed that the events of desaturations caused by apneas were more significant than desaturations after hypopnea (p ≤ 0.004). The authors concluded that the longer respiratory events generally induce more severe desaturations and therefore, more detailed analyzes of the severity of desaturations and duration of respiratory events should be performed for an adequate estimate of OSAS severity (Table 4).

The above studies point to the importance of desaturations as an attempt to diagnose OSAS, and only the studies by Kulkas et al. [9,14] make some relation between the severity of OSAS and the number

| Researches about evaluation of OSAS beyond AHI | Main findings refer to desaturations |
|---------------------------------------------|-------------------------------------|
| George CF, et al. [11]                      | Estimation of AHI through desaturations |
| Gyulay S, et al. [12]                       | Estimation of AHI through desaturations |
| Guilleminault C, et al. [13]                | Variation of AHI according to the rule used for marking hypopneas |
| Kulkas A, et al. [14]                       | Assessment of the severity and duration of desaturations as parameters of OSAS severity |
| Schlothauer G, et al. [3]                   | Estimation of AHI through desaturations |
| Kulkas A, et al. [14]                       | Desaturation events differs between hypopnea and obstructive apnea events |

Source: the authors
and degree of desaturation depth. There is evidence that the worst consequences of OSAS have a strong relationship with low levels of O₂ concentration. However, more studies are needed to prove the correlation between falls in O₂ concentrations and the severity of the disease.

Conclusion

The quantification of respiratory events per hour of sleep remains the only criterion recommended for the determination of OSAS severity, and although polysomnography provides information on the number and depth of desaturations, it is not yet a criterion used to determine the severity of the disease. There are some published studies that establish a relationship between desaturations and AHI, but we did not find studies that correlated AHI, desaturations and OSAS severity. Thus, it is necessary to establish new criteria that together with the AHI determine the real severity of OSAS.

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