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
Sleep apnea is a condition characterized by repeated episodes of breathing cessation during sleep. The severity of obstructive sleep apnea syndrome (OSAS) can be assessed through the analysis of desaturations and apnea and hypopnea index (AHI).

### Methods

#### Extraction of data

Data search was performed by 3 researchers independently and in 3 different databases (PubMed, LILACS and Scielo), from 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" obstructive "[All Fields]" OR" obstructive sleep apnea") AND "apnea" [All Fields]) AND ("apneas" [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].

#### Eligible studies

The articles were selected for this research based on 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. 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. 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...
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 O₂. 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 such as George et al. [11]. In that study, the authors used a computerized algorithm to detect falls in O₂ 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 of O₂ saturation. A file with all events was created and correlated to the stages of non-REM and REM sleep, indirectly determining an AHI. Each patient underwent a conventional polysomnography to determine the traditional AHI through the visual reading of the technician to mark the respiratory events, and then they were also submitted to analysis through the computerized algorithm proposed for the determination of indirect AHI based on desaturations. There was a strong correlation between the 2 methods, suggesting that AHI can be easily estimated by the number of desaturations, as well as being a more easily analyzed method and not subject to human error (Table 4).

Gyulay et al. [12] made a comparison between polysomnography and home oximetry for the diagnosis of OSAS. Analyzes of pulse oximetry-based desaturations were highly specific for the disease, when desaturations were greater than 4% and generated an index of desaturations ≥ 15/h as they were equated to an AHI ≥ 15/h. The authors concluded that home oximetry is applicable as a screening for OSAS (Table 4).

Guilleminault et al. [13] evaluated lean OSAS patients through baseline polysomnography, analyzing all respiratory events according to the criteria established by the AASM 1999 (rule C), and by the variation of the criteria revalidated by the AASM in 2007, in which there are 2 options for defining hypopnea (rules A and B), according to the level of O₂ desaturation or the presence of cortical arousal. According to rule A, hypopnea is considered when there is an airflow drop of at least 30%, but only if it is associated with a desaturation ≥ 4%. Rule B, however, considers hypopnea when there is at least 50% drop in airflow accompanied by desaturation of 3% or an awakening. As can be observed, according to rule B there may or may not be O₂ desaturation. Rule C of 1999 used only 1 criterion for hypopnea, and may or may not be associated with desaturations (drop ≥ 50% of airflow associated with desaturations of ≥ 3% or wakefulness). All 35 patients in the study had an AHI <15/h according to rule A. Rule B resulted in 11 subjects with AHI below 15/h, while by rule C no patient had AHI below 15/h. These results are intriguing because they show that depending on the rule used to label hypopneas, the value of AHI may be underestimated or overestimated. The authors concluded that desaturations are clearly important especially for the recognition of OSAS (Table 4).

Another very interesting research was carried out in 2013 by Kulkas et al. [9]. The authors highlighted the analysis of desaturations correlating them with the severity of OSAS through the determination of AHI. 160 patients with suspected OSAS were evaluated for the number, duration and morphology of respiratory events and desaturations, and not only by counting these events per hour of sleep as determined by AHI. They found that the prolonged duration of apnea and hypopnoea may paradoxically lead to a fall in AHI, although this has more serious health consequences than shorter events. The variety aspect of the duration of these events is not included in the traditional AHI. Another aspect to be considered is the morphology of O₂ desaturation events that is also not considered in AHI. Deep and long respiratory events of O₂ desaturation presumably contribute more to pathophysiological stress than mild and short events. In addition to AHI, the authors used a new evaluation parameter because of the suspicion of differences in severity of events in patients with similar AHI: severity of obstruction and desaturation, duration of obstruction and desaturation. There was a moderate correlation between AHI and the new severity parameters (r²=0.581-0.689, p<0.001). Since patients with similar AHI showed significant differences in values of obstruction severity parameters, this could provide different diagnoses of severity for OSAS patients. Thus, the severity of OSAS could be better estimated based on these new criteria (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 Schlotthauer 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 O₂ 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

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Source: the authors

| Table 4. Human studies on OSAS assessment criteria beyond AHI. |
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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