REM behavior disorder associated with sleep disordered breathing

Transtorno comportamental do sono REM associado com distúrbio respiratório do sono

Maria Isabel Montes 1,3, Rosa Hasan2, Stella Tavares3, Geraldo Lorenzi Filho3

ABSTRACT

REM behavior disorder (RBD) is a parasomnia characterized by muscle tonus during REM sleep and presence of vigorous movements which can be potentially harmful. RDB is mostly prevalent in men between 40 and 70 years and it is usually associated with neurodegenerative disease. Obstructive Sleep Apnea (OSA) is a common disorder in the general population and may present multiple clinical manifestations that include disrupted sleep. Arousals with vigorous movements may be present in patients with OSA and may express a clinical manifestation known as pseudo RBD. Using the keywords “Obstructive sleep apnea” and “REM behavior disorder” in the main data bases we found a total of 99 articles, but 94 articles were excluded because they did not specifically approached the relationship between the 2 diseases. Therefore, 5 articles were initially evaluated and we included 2 more relevant studies that were quoted by the initially selected articles. The articles reviewed consisted mainly of case reports or small case series. Pseudo RBD is usually associated with severe OSA and severe oxyhemoglobin desaturations. The small number of reports may indicate a low awareness of this condition.

Keywords: electromiography, obstructive sleep apnea, polysomnography, REM behavior disorder.

INTRODUCTION

REM behavior disorder (RBD) is a parasomnia characterized by behavioral release during rapid eye movement sleep (REM) caused by the loss of normal muscle atonia during REM. The behavior manifestation is variable, ranging from talking, singing, to complex episodes of vigorous movements that are related to unpleasant and combative dreams that can be potentially harmful to patient and bedfellow1,2. The overall prevalence of RBD in the general population ranges from 0.38% in Hong Kong3 to 0.5% in the United States4. RBD may be associated with extrapyramidal disorders and often precede the clinical onset of Parkinson disease, Lewy body dementia or multiple system atrophy. Any evidence for RBD should be as it may have major clinical implications. Neuroimaging studies have revealed that RBD may affect several levels of cerebral organization, from neurotransmission (presynaptic striatal dopaminergic) to neuroanatomical integrity (lesions in mesopontinetegmentum) and brain function (frontal, temporoparietal and cingulate cortex dysfunctions)5.

Obstructive sleep apnea (OSA) is distinguished by recurrent obstruction of the upper airway leading to repeated episodes of either complete (apnea) or partial (hypopnea) reductions of airway flow. OSA is characterized by intermittent hypoxia and increased negative intrathoracic pressure during breathing effort against an occluded upper airway. The obstructive episodes are typically terminated by an arousal or awakening from sleep that restores the upper airway muscle tone to the awake level and allows the patient to breathe6. The typical clinical
manifestation of OSA are loud and irregular snoring, disrupted and non-restorative sleep and excessive daytime sleepiness. In contrast to RDB, OSA is extremely common in the general population. For instance, a recent large epidemiological study at the city of São Paulo, Brazil estimated that 33% of the adult population present OSA syndrome, as characterized by more than 5 events per hour of sleep plus symptoms or more than 15 events/hour of sleep, independent of symptoms\(^7\).

OSA and RBD have different pathophysiologic substrates. While OSA is caused by repetitive obstruction of the upper airway during sleep, RBD is thought to reflect dysfunction of the brainstem structures that modulate REM sleep\(^8\). The clinical manifestations of OSA and RBD are also considered fundamentally different. However, it must be stressed that patients with OSA present a fragmented sleep and may show movements during sleep. Dream-enacting behaviors can also occur among patients with OSA during arousals from NREM sleep and REM sleep, a clinical situation termed pseudo RBD\(^9\).

Given the fact that OSA is extremely common in the general population, it is therefore possible that several patients with clinical manifestations of RDB may in reality present OSA and therefore should be classified as pseudo-RBD. It is also possible that some patients will present both RDB and OSA. The aim of the present study was to review all articles that reported on pseudo RDB.

METHODS
We used the following data base Pubmed, Scielo, Cochrane, Bireme, Lilacs, and we searched for articles with the relationship between RBD and OSA or with the term Pseudo RBD. We used the following keywords: “Obstructive sleep apnea” and “REM behavior disorder”. We also included older relevant articles that were quoted by the selected articles.

RESULTS
We found 99 articles in Pubmed, and only one article in Scielo, Cochrane, Bireme and Lilacs, respectively. The articles published in Scielo, Cochrane, Bireme and Lilacs were also present in Pubmed. Ninety four articles were excluded because they did not specifically approached the relationship between the 2 diseases. Therefore, 5 articles were initially evaluated. In addition, we included 2 more articles that were not found in the search\(^9,10\), but were quoted by all the selected articles Figure 1. A summary of articles with RBD and OSA evaluated with year and journal of publication, study design, number and characteristics of the patients and conclusions are described in Table 1. The reports consisted mainly of case reports or case series. The main findings are discussed below.

DISCUSSION
The present review found only 7 relevant articles and highlights the small number of studies that have evaluated the relationship between RDB and OSA. In addition, the reports included in the present review are represented by case reports or small case series. This may reflect the low awareness of the potential importance of pseudo RDB. Despite these limitations, several important conclusions can be drawn from this review. First, pseudo RDB is usually associated with severe OSA and severe oxyhemoglobin desaturations. The apnea-hypopnea index (AHI) of the patients with OSA that were reported to have pseudo RDB ranged from 31 to 124 events/hour of sleep\(^8,10\).

One paper also reported on severe oxygen desaturations in these patients\(^8\). Second, the physiopathology of pseudo RBD is not completely understood. It has been reported that OSA induced arousals detected in NREM and REM sleep or only in the REM sleep, with dream-related complex and violent behaviors occurred just at the end of obstructive sleep apneic events\(^8\).

Some authors speculated that pseudo RBD is a form of a confusional arousal secondary to a combination of severe levels of oxyhemoglobin desaturations during the apneic events\(^8,9\). RBD may be associated incidentally with OSA, one study found OSA in patients with previous diagnostic of RBD presumed that OSA is extremely frequent in older people making the chance association of OSA with RBD possible\(^11\).

In the other hand, RBD has been proposed to be protective against OSA\(^10\). Supporting this theory, Huang et al. reported that patients with RBD and OSA presented shorter duration of apneas and hypopneas during REM than NREM sleep. Therefore, excessive EMG activity associated with RBD probably protected from long apneas resulting in shorter respiratory events, less REM sleep-related exacerbation, and probably a lower frequency of apneas and hypopneas\(^12\).

The diagnosis of RDB must be made with video-polysomnography (VPSG). This is the only test that can simultaneously diagnosis OSA and RDB and also clearly observe if the abnormal motor and vocal behaviors occur at the end of an obstructive events during sleep\(^6\). One study aimed to distinguish patients with the independent association of idiopathic RBD and OSA (that can be present in the same patient) vs. patients with moderate to severe OSA with pseudo RBD\(^13\).
authors used cardiac (123)I-metaiodobenzylguanidine (MIBG) scintigraphic that. MIBG is taken up and accumulates in cardiac sympathetic nerve postganglionic fibers. Marked reduction of cardiac MIBG uptake seems to be a specific marker of Lewy bodies, that in turn have been found in patients idiopathic RBD. However, in this study MIBG was reduced both in patients with RBD and pseudo RBD. Therefore, this study did not provide a mechanism to explain why MIBG was low in all forms of RBD and was not able to distinguish RDB and pseudo RDB.

One study found the association between Chiari, central sleep apnea and RBD(1). The authors speculated that the proximity in the brain stem of neuronal groups responsible for the control of breathing and the control of REM sleep may help to explain this association. REM sleep control centers and some of the respiratory control centers are situated between the caudal region of the facial nucleus and the ambiguous nucleus located in the lateral tegument of the giganto-cellular region of the medulla. The respiratory system during REM sleep when damaged would therefore be responsible for central apneas.

CONCLUSION

We conclude that it is important to distinguish RBD from OSA because they have different clinical connotations and outcomes. Moreover, OSA and RBD require very different treatments. Clonazepam is the treatment of choice for RBD and may worsen coexisting OSA(8) or may induce OSA in some predisposed patients(14).

Diagnosis of RBD in a subject with no evidence of underlying neurodegenerative disease must be accurate since idiopathic RBD frequently precedes the onset of a parkinsonian or cognitive disorder. On the other hand, OSA is a risk factor for cardiovascular disease and the treatment of choice is the use of continuous positive airway pressure. If we consider that OSA is highly prevalent in the general population, pseudoRBD could be more common than currently recognized. Pseudo RBD must become a differential diagnosis of RBD. The reasons why only some patients with severe OSA present pseudo RBD remains not established.

REFERENCES

2. Schenck CH, Mahowald MW. REM sleep behavior disorder: clinical, developmental, and neuroscience perspectives 16 years after its formal identification in SLEEP. Sleep. 2002;25(2):120-38. PMID:11902423


