REM Sleep Behavior Disorder of older people-A review

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Running title: Sleep Behavior Disorder

**Abstract**

Approximately 43% of patients with REM sleep behavior disorder (RBD) will develop Parkinson's disease and 25% with Lewy body dementia. The long-term clinical trial of RBD patients showed over 90% risk of developing neurodegenerative diseases. REM sleep behavior disease is characterized by the enactment of dreams, involving complex motor functions. The disease is now considered a prodrome to Parkinson’s disease. In the future, it is recommended for researchers to investigate the potential of REM sleep without tension as a clinical indication of neurodegenerative diseases, for which physicians can rely on to detect diseases for early intervention and treatment.

Keywords: Parasomnia; REM sleep behavior disorder; Neurodegeneration; Parkinson’s disease; Lewy body dementia.

**Introduction**

Rapid eye movement sleep behavior disorder is more likely to occur in middle-aged and elderly men and most cases have no specific cause, even though it is now believed to be related to neurodegeneration[1]. However, there are reports of acute onset of the disease due to withdrawal of alcohol or sleeping pill, as well as the use of specific antidepressants. Patients with this disease, with the sign of abnormal rapid eye movement, tend to develop Parkinson’s disease or other neurodegenerative diseases in the future, when compared with the healthy population[2]. RBD affects about 1% of the general population and 2% of the elder population at age 50 or older[1,3]. The prevalence rate may be underestimated for that the disease is difficult to diagnose, not to mention the half of the world population may not even realize having the condition. People having sleep disorder is as prevalent as the elderly having Parkinson’s disease and they may well experience periodically uncontrolled limb movement or restless leg syndrome[4]. We now know that restless leg syndrome is associated with degeneration of involuntary motor nerves, commonly seen in Parkinson’s disease, despite the lack of empirical evidence to support a relationship between the syndrome and other neurodegenerative disease, such as Alzheimer’s disease[4,5]. Most cases of RBD are caused by alpha-synuclein neurodegeneration and by antidepressants, narcolepsy, and pontine lesions such as those from stroke or multiple sclerosis[6].

**Clinical Features of REM Sleep Behavior Disorder**

Rapid eye movement sleep behavior disorder is parasomnia with behavior of dream-enactment that happens during the sleep-associated muscle atonia. Idiopathic RBD occurs in the absence of any neurological diseases or other possible causes[7]. It is predominantly seen in males. The course of disease is chronic but progressive[8,9]. The enactment behavior, in order of severe to mild, may include gentle hand gesture to violent thrashing, punching and kicking. The sleep pattern changes with age. For example, REM sleep accounts for about 50% of neonatal sleep time and it starts to decrease to about 25-30% by the time of school age and adolescence. Patients of RBD are at 90% risk of developing neurodegenerative diseases in long term[10]. Thus, it is suggested for the future studies to focus on evaluating REM sleep-associated muscle atonia as a clinical marker to indicate the possibility of developing neurodegenerative diseases for patients[11]. Nevertheless, RBD alone can be regarded as a precursor of neurodegenerative diseases and prompts physicians to early intervene and treat the patients. Delusion or hallucination in patients of Parkinson’s disease are often the result of medications. Given our understanding of the cause of Parkinson’s symptoms as the lack of dopamine in the brain, the drug treatment of the disease focuses on supplementing the compound. However, dopamine is not only for controlling movements but also gives people a sense of happiness. If the dosage were not controlled properly, it may cause hallucination or delusion. As a side note, psychological stress is also known to aggravate the symptoms of RBD[12-15].

**Differential Diagnosis of REM Sleep Behavior Disorder**

People with isolated rapid eye movement sleep behavior disorder (iRBD) will always have high risk of developing neurodegenerative disease, such as dementia, in their lifetime, even though the percentage of this risk is still under debate. It is speculated that almost all neurological diseases may be attributed to some type of sleep disorder, including dementia, Parkinson’s disease/syndrome, epilepsy, stroke, neuromuscular disease, etc[16]. For example, in the restless leg syndrome, the symptom may simply be leg cramp during sleep at night and the pain experienced in the morning. It is possibly due to the incorrect nerve signal conduction that results in abnormal contraction of the leg muscles in the night. Although suspecting the following conditions to be related to the disease, such as dehydration, poor blood circulation from sedentary lifestyle, muscle fatigue from excessive exercise or lack of warm-up beforehand, imbalance of electrolytes like calcium, magnesium, and potassium in seen diabetic or kidney dialysis patients, hypoglycemia or hypothyroidism, and medications for treating hypertension, hyperlipidemia, obstructive pulmonary disease, osteoporosis, Alzheimer's disease or Parkinson's disease, researchers still have no idea of what causes RBD. Animal studies suggested that it may have to do with certain neural pathways in the brain, since normal individuals have shown to deploy certain neural pathways to inhibit muscle activities during sleep. It is the disruption of these neural pathways that leads to REM sleep of muscle atonia[17-19].

**The Treatment**

Drug treatment has proven to be effective in controlling these muscle activities. Physicians usually prefer an anti-convulsant drug, Rivotril (Clonazepam), as the first-line medication. If the patient also experiences periodic involuntary limb movement, or the patient simply has Parkinson’s disease, anti-Parkinson’s drug may help. Please note that it is necessary to distinguish Parkinson’s disease from epilepsy, as well as seizures, specifically of the frontal lobe[19,20]. Melatonin is an endogenous hormone normally secreted by the pineal gland in response to darkness and is responsible of the circadian rhythm of the body. Although uncertain of the underlying mechanism, melatonin in high dose (6-18mg) before bedtime will augment the REM sleep and muscle atonia to improve the symptoms, while low dosage has no effect. Furthermore, Benzodiazepines and antidepressants can be used to decrease REM sleep [19-21].

**Conclusion**

Sleep disorders, including RBD, are common in people who've been diagnosed with Parkinson's disease. But studies have suggested the disease as part of symptoms of Parkinson’s disease and may occur years before any motor dysfunctions. Other possible early signs include constipation, depression, etc. Long-term insomnia will subject the patient to cardiovascular diseases if not properly managed. Thus, this disease is worth investigating. RBD is characterized by dystonia during dreaming and is usually manifested as limb movements, which mirror the actions in the dream. RBD is an abnormal sleep state that often occurs in adults over the age of 50. In recent years, studies have found that rapid eye movement sleep behavior disorder may be a precursor to Parkinson's disease. 80% of the patients have insomnia, poor sleep quality, and daytime fatigue, as well as anxiety or depression, but they are unlikely to do harm to self or others. RBD is now considered a precursor to neurodegenerative diseases because research has shown the higher percentage in patients with Parkinson’s disease and the patients usually have the symptoms of RBD years before the onset of Parkinson’s disease. But the association between RBD and Parkinson's disease still needs to be clarified. Benzodiazepines and antidepressants are used to decrease REM sleep. Current data have also suggested the posttraumatic stress disorder and traumatic brain injury to be critical risk factors of RBD. Given the association of RBD with Parkinson’s disease, this provides a crucial indication for physicians when diagnosing sleep disorder in veterans and elderly.

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