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SLEEP DISORDERS IN ALZHEIMER DISEASE

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Abstract

Sleep disorders have a variable spectrum and are present in all forms of dementia, especially in Alzheimer's disease (AD). Elderly patients generally present with sleep disturbances, but this association is more frequent in patients with AD. The aim of this work was to perform a narrative review on the alterations in sleep that occur in patients with AD. A literature review was conducted using MEDLINE, LILACS, Web of Science, Scopus, Science Direct as databases and Alzheimer disease, sleep wake disorders, dyssonias as descriptors. It has been observed that sleep disorders are framed as one of the symptoms of AD, in addition to being related to physiological and genetic patterns. The main symptoms are getting up at night and waking up at night thinking it is day. The incidence of these symptoms was detected in patients with worse cognitive and functional status, lower socioeconomic status and depression. The relationship between insomnia, aggression, paranoid delusions and anxiety was observed. Recent studies have seek to clarify the etiology of sleep disorders, considering associations between absence of healthy sleep with greater deposition of amyloid load in brain regions such as angular gyration, frontal medial orbital cortex, cingulate gyrus and precuneus. Disorders of orexin levels in the cerebrospinal fluid in patients with AD were observed, promoting a change in the activation of the Wake-active monoaminergic system and the deactivation of the REM-on cholinergic groups, reducing sleep homeostasis. Lower body temperature at the end of the day causes disorders of the circadian rhythms in AD and a deficiency in the negative regulation of the proximal blood flow of the daytime skin has been found which may also affect the process. These researches initiate the development of new treatments, which will impact the patient's cognition and, consequently, their quality of life. We conclude, therefore, that the sleep disorders are one of the fundamental clinical aspects that must be evaluated in AD patients, specially due to its role as a prognostic changer for the disease.

Introduction

Sleep disorders are common health issue found in general population and occur mainly in the elderly population(1). However, its spectrum is more varied, specially when it comes to the context of Alzheimer's Disease (AD)(2). The circadian alteration in these patients do not evolve in isolation, but in an association of cognitive and functional impairment on the central nervous system(3). There are indications of the correlation between the frequency of daytime naps and the severity of dementia, which become more present in the pathology's evolution(4).

There is a direct association of sleep alteration variations, such as longer wakefulness, with decreased scores in Mini-Mental Exam(5), confirming the importance of characterizing the pattern of these alterations to observe the evolution of the disease. In this perspective, the objective of this work was to perform a narrative review of these disorders in patients with AD.

Methods and Materials

This study consists in a literature review of the narrative type. For the research, it was used the MEDLINE, LILACS, Web of Science, Scopus and Science Direct databases with the following descriptors: Alzheimer disease, sleep wake disorders and dyssomnias. After crossing the descriptors, a total of 866 published articles were found. First, articles published from 2000 to 2018 were selected in English, Portuguese and/or Spanish. After the complete reading and critical analysis of pre-selected articles, 11 articles were chosen fitting the objective of the review.

Results and Discussion

Sleep disorders have been observed as a relevant symptom of AD, establishing a relationship with physiological and genetic patters(6). Of these symptoms, the main are getting up at night and waking up at night thinking it is day. In addition, the most frequent daytime behaviours in the elderly group with AD, when compared with non-demented elderly, were diurnal drowsiness and daytime naps. The association with sleep-respiratory disorders was also found in this group(5).

The incidence of these symptoms was associated with patients with worse cognitive and functional status, lower socioeconomic status, and the occurrence of psychiatric symptoms, such as depression (5, 7, 8). It was found a relation between maintenance insomnia, aggression, paranoid delusions and anxiety, and a direct association of diurnal napping frequency and the severity of dementia (4).

Patients with AD showed increased total wake time, as well as more time sent in bed (9), representing a more fragmented and less efficient sleep, which was directly proportional to the worst demential status (5). Sleep fragmentation had a tendency to present an earlier onset in the context of AD (1), in which the disease worsens previous sleep disorders, or anticipate them (6).

There is, in the literature, a search for the clarification of sleep disorders' etiology, in which there is a correlation between the absence of healthy sleep with greater deposition of amyloid load in brain region regions, such as angular gyrus, orbitofrontomedial cortex, cingulate gyrus and pre-cuneus, due to an increased clearance of this substance during sleep (10).

In addition, one study had shown that disturbances in orexin-A levels in the cerebrospinal fluid are related to changes in REM-sleep and sleep fragmentation in this patients, reducing sleep homeostasis, and may result in insomnia, prolonged sleep latency and nocturnal waking. Elevated orexin-A levels were found in patients with AD with complaints of sleep disorders (11).

On the other hand, dysfunction of the suprachiasmatic nucleus in AD leads to the rupture of several circadian activities, besides the sleep-wake rhythm, such as changes in body temperature control, in which there are greater deviations of temperature in relation to outpatients of the same age, and the occurrence of Sunset Syndrome, in which there is an increase in motor activity and agitation during the afternoon and early evening. Observing this symptoms confirms the progression of circadian alterations associated with the evolution of the disease (3). There is an association between central body temperature (CBT) and sleep-wake rhythms, in which sleep has higher quality at low levels of CBT, as well as skin temperature levels, which seem to modulate quality and may be associated with this processes in AD(9).

Conclusions

We conclude that the sleep disorders are one of the fundamental clinical aspects that must be evaluated in AD patients, specially due to its role as a prognostic changer for the disease. New discoveries based on its etiology can bring new treatment and develop several changes in the health care of these patients, bringing them more life quality associated with improvement of their sleep conditions, affecting also their cognition and aging process.

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