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CLINICAL REVIEW

Wrist actigraphy for measuring sleep in intervention studies with Alzheimer's disease patients: Application, usefulness, and challenges

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SUMMARY

Sleep disorders are common in patients with Alzheimer's disease (AD). An important aspect of intervention studies in patients with sleep disorders is the choice of assessment strategy. This paper presents a literature review concerning assessment strategies for measuring sleep in intervention studies with AD patients, with a focus on actigraphy.

Thirty-seven articles were selected for this review, having analysis of sleep/nocturnal rhythm disturbances by actigraphy as the primary or secondary outcome. The advantages and limitations of actigraphy were discussed *vis-à-vis* polysomnography and subjective interventions. The following methodological aspects were addressed: impact of experimental design and patient setting, inclusion and exclusion criteria, placement of the actigraphy device, adherence to the regimen, duration of recordings and the choice of sleep parameters.

Our analyses suggest that the methods used in intervention studies encompassing sleep disorders and dementia could be improved by increasing accuracy of diagnosis, categorization of sleep disturbances, adherence to actigraphy, and by clearly defining the variables and endpoints in each study. Also, controlling variables that could interfere with sleep and describing the data processing and analysis might improve interpretation of results.

Introduction

Sleep disorders, particularly those associated with substantial changes in the sleep/wake rhythm, strongly affect the lives of patients with dementia and their caregivers. Cross-sectional studies have found that up to 44% of patients with Alzheimer's disease (AD) have sleep disorders that reduce quality of life and have a negative effect on cognition and functionality, increasing the burden on caregivers.[1] Among the many types of sleep disorders affecting patients with dementia, sundowning (increased confusion starting at dusk and persisting through the night), nocturnal perambulation, difficulty with sleep onset and maintenance, fragmented sleep, and abnormalities of the circadian rhythm are of the greatest concern.[2,3] A longitudinal study assessing the sleep/wake pattern of patients with AD found that the frequency of waking episodes after sleep onset (WASO) progresses over the course of the disease.[4]

Many factors contribute to abnormalities in the circadian rhythm and hence to sleep disorders in older adults with dementia, including neuronal loss and/or destruction of the suprachiasmatic nucleus of the hypothalamus,[1] deficient exposure to and capture of light (caused by macular degeneration and/or cataracts), use of multiple drugs, behavioral and psychological symptoms, among others. In view of the strong negative effects of such disorders on demented patients, treatment of sleep disturbances is of critical importance. To date, most intervention studies on sleep disorders have used non-pharmacological[5–7] and behavioral/environmental approaches.[8–29]There are only a few reports on the use of drugs,[30–34] perhaps because the definition of criteria to establish an appropriate treatment poses a challenge for clinical care, since aspects such as the efficacy and safety of most of the available drugs remain undetermined. Nevertheless, the limited amount of trials conducted so far prompts caution when it comes to pharmacological treatment of sleep disorders in demented subjects.

Along with the concerns raised above, measuring improvement in the sleep pattern of patients with dementia is a practical

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Abbreviations

AD	Alzheimer's disease
ADAS cog	Alzheimer's disease assessment scale – cognitive subscale
ADCS-ADL	Alzheimer's disease cooperative study activities of daily living
BEHAVE-AD	behavioral pathology in Alzheimer's disease rating scale
CDR	clinical dementia rating
DAD	disability assessment for dementia
IS	interdaily stability
IV	intradaily variability
L5	lowest mean activity during any stretch of five continuous hours
M10	highest mean activity during any stretch of 10 continuous hours
MMSE	mini-mental state examination
NPI	neuropsychiatric inventory
RA	relative amplitude
SDI	sleep disorders inventory
TENS	transcutaneous electrical nerve stimulation
WASO	waking after sleep onset

challenge. The tools employed for this purpose range from parametric methods including polysomnography and wrist actigraphy to more subjective, interview-centered sleep logs and scales such as the sleep disorders inventory (SDI).[35] However, many of these instruments have limitations when used in patients with dementia.

Polysomnography concerns

Despite being the gold standard tool to assess younger individuals, the use of polysomnography is not recommended in advanced stages of dementia because it relies on the patients' understanding of the method.[36,37] Furthermore, polysomnography can induce a 'first-night effect', which is the tendency to experience a worse sleep pattern during the first evaluation because of discomfort produced by electrodes and wires, an unfamiliar sleeping environment or other factors. This may impair the reliability of such assessments and contribute to increase patient burden and research costs.[12] In addition, the accuracy of electroencephalography to score sleep and wake periods is poor, and the wisdom of using the method in patients with dementia is questionable.[36,38] We have experienced a situation in which an elderly patient with dementia damaged most of the equipment in the sleep laboratory during an episode of night-time agitation (unpublished).

Polysomnography has been used by a few intervention studies dealing with sleep disorders in AD patients.[39–41] Moraes and coworkers[39] evaluated the effects of donepezil on sleep in patients with mild to moderate AD. In that study, 35 patients were submitted to a nonconsecutive five-day protocol of polysomnographic recordings. Technical difficulties may be inferred from their report based on a high exclusion rate of 12 (25%) of the initial sample of 47 subjects due to difficulties associated with polysomnography recordings. The same group investigated donepezil for obstructive sleep apnea (OSA) in patients with mild to moderate AD and a similar pattern was observed, with 7 (23%) patients out of 30 excluded for frequent movement artifacts. In another study[41] investigating sleep parameters in 52 AD patients with OSA, a third night of polysomnography recordings to evaluate a three-week post-placebo intervention was not possible, reflecting the method's technical shortcomings.

Subjective self-report concerns

Sleep logs and questionnaires are often completed by caregivers and can be misleading; problems with daily diary recordings have been reported in a number of studies.[19,38] In fact, sleep misperception is common in caregiver-reported evaluations.[42] Given the difficulty in assessing an individual's sleep, logs are inherently unreliable to provide an objective measure of sleep patterns.[43] Notably, in clinical practice we have observed low accuracy of proxy reporting, reduced caregiver adherence, and difficulty in objectively assessing total wake–sleep time at night.

Many factors can affect caregiver observation and consequently sleep assessments. Even though there are no studies evaluating the effect of time on the method's sensitivity, daily sleep logs are arguably hard to keep for prolonged periods. In addition, studies suggest bidirectional associations in the sleep patterns of care recipient/caregiver dyads in the context of a chronic illness (dementia included),[44] with worsened functional status increasing caregiver burden and affecting the accuracy of the caregivers' report.[42,45] Finally, even though the caregivers' own characteristics are usually not taken into account, personal features such as indifference and most notably caregiver criticism as a behavior management strategy might influence the overall quality of the registries.[42]

Furthermore, studies have found over- or underestimated caregiver reports. Hoekert and co-workers showed that caregivers generally overestimate sleep time by more than 90 min.[46] Conversely, McCurry et al. found that the multiple sleep disturbances reported by the caregivers of 46 AD patients were not supported by actigraphic estimates, which showed good nighttime sleep and total nocturnal sleep time.[42]

The use of a single scale such as the SDI to assess the efficacy of interventions on sleep can also present limitations in studies with demented patients. In one study, a significant posttest improvement detected by actigraphic records was not replicated by the SDI.[12] A recent study showed that the value of sleep questionnaires is limited in early and moderate-stage AD.[47] The literature recommends that studies evaluating sleep/wake cycles in patients with AD using subjective measures of sleep disruption be supplemented with objective tools such as actigraphy.[48]

Actigraphy concerns

The use of actigraphy in patients with dementia has increased in the past decade.[49] Wrist actigraphy technology has been improved and refined with new devices and software. Actigraphic analysis employs an accelerometer to measure the degree and intensity of body movement. Current devices have sufficient digital memory to record up to several weeks or months, allowing the efficacy of treatments to be tested in long term studies. Additional advantages of actigraphy include the feasibility of home-based assessments for individuals who do not tolerate sleeping in an unfamiliar environment (e.g., in the laboratory) and the capability of providing objective measurements that are representative of daily variations and sleep quality and tend not to be influenced by patient expectations or recall bias.[43,50]

In patients with dementia, the correlation between actigraphy and polysomnography has been reported to range from 0.81 to 0.91 for total sleep time, and from 0.61 to 0.78 for the percentage of sleep time relative to the total rest period.[36] Furthermore, some authors argue that each device should be validated individually, and that the results from one population might not be generalizable to other populations.[51]

Actigraphy has often been used to assess the effects of cognitive/behavioral therapy and drug interventions in patients with AD associated with sleep disorders. The American Academy of Sleep Medicine