Assessment of Sleep Pattern in patients with Alzheimer's disease (AD)

An Egyptian study on elderly population

Thesis

Submitted for partial fulfillment of M.Sc. Degree in Geriatrics and Gerontology

By

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2016

Acknowledgement

First of all, thanks to **GOD** whose magnificent help was the main factor in completing this work.

Great words are really needed to express my gratitude, sincere appreciation and respect to **Prof. Dr. Hala Samir Sweed,** Professor of Geriatrics and Gerontology, Ain Shams University, who continued to provide me her guidance ever since. Without her great help, teaching and supervision, this work would not have been completed.

I would like to express my deepest appreciation, respect and thanks to **Prof. Dr. Tarek Assad Abdu Ahmed,** Professor of Psychiatry, Ain Shams University, for her continuous guide in all aspects of life beside his great science, knowledge and information.

No words can express my deep sincere feelings Towards **Dr. Ahmed Fouad Shaheen,** Lecturer of Geriatrics and Gerontology, Ain Shams University for his continuous encouragement, guidance and support he gave me throughout the whole work.

Last but not least, sincere gratitude to **My Family** for their continuous encouragement and spiritual support.

Abstract

Objective: The current study was conducted to assess disturbance in sleep pattern in patients with AD, and compare it to cognitively healthy elderly individuals. The study included 20 patients with AD with mean age 66.05 ± 2.04 and 20 healthy elderly subjects with mean age 65.25 ± 2.22.

Method: All participants undergone, a full medical, neurological, psychiatric history and clinical examinations, Lab tests (complete blood picture, liver function tests and thyroid profile) and CT scan or MRI brain. For each subject the MMSE was used to provide a simple global measure of cognitive functioning and CDR was used to stage the degree of global severity, the Geriatric Depression Scale (GDS), The Cornell Scale for Depression in Dementia and Taylor Anxiety Scale for excluding patients with depression and anxiety. All patients were subjected to Overnight PSG recordings and psychometric sleep assessment (an Arabic version for sleep evaluation of the Epworth Sleepiness Scale (ESS) and Pittsburgh Sleep Quality Index (PSQI)).

Results: This study showed abnormal subjective sleep quality in all patients and poorer sleep efficiency, prolonged sleep latency and a tendency for more wake after sleep onset high (AI) with highly significant statistical difference of both groups. Moreover, patients spent more time in stage I & II sleep, and had less time in SWS and REM sleep compared to control populations, and delayed REML and more REMD. The results of this study showed no statistical significant difference of as regards sleep parameters (PMLs index and respiratory events) for both control and patient groups. Also, we found no statistical difference as regards sleep parameters (SE, SL, SWS and AI) and grade of dementia assessed by cognitive scoring tests; MMSE and CDR in patient group. This current results showed no statistical significant difference as regards sleep parameters (SE, SL, SWS and AI) and subjective sleep assessment (PSQI) and degree of cerebral atrophy (CT/MRI brain) in patient group.

Conclusion: The current study confirms that sleep is significantly impaired in patients with AD at both the objective by PSG recordings and subjective level. Also this study suggests a role of PSG in diagnosis of AD.
Keywords; sleep pattern, Alzheimer disease, polysomnography, REM and NREM sleep.

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List of Abbreviations

Aβ	Amyloid-β
AD	Alzheimer's disease
AHI	Apnoea-hypopnoea index
AI	Arousal index
APOE	Apolipoprotein epsilon (ApoE)
ARAS	Ascending reticular activating system
CDR	Clinical Dementia Rating
CPAP	Continuous positive airway pressure
CSF	Cerebrospinal fluid
CT	Computerized axial tomography
DR	Dorsal raphe
DSM-V	Diagnostic and Statistical Manual for Mental Disorder.
EDS	Excessive daytime sleepiness
EEG	Electroencephalographic
EMG	Electromyogram
EOG	Electrooculogram
ESS	Epworth Sleepiness scale
GDS	Geriatric Depression Scale
ICSD-3	The International Classification of Sleep Disorders-3
LBD	Lewy body dementia
LC	locus coeruleus
MCI	Mild cognitive impairment
MMSE	Mini Mental State Examination
MRI	Magnetic resonance imaging
MSLT	Multiple Sleep Latency Test
MWT	Maintenance of Wakefulness Test
NDDs	Neurodegenerative disorders
NE	Norepinephrine
NREM	Non-rapid eye-movement
NTs	Neurotransmitters

OSA	Obstructive sleep apnea
OSAH	Obstructive sleep apnea and hypopnea
PD	Parkinson's disease
PET	Positron emission tomography
PLM	Periodic limb movements
PSG	Polysomnography
PSQI	Pittsburgh Sleep Quality Index
RBD	REM behavior disorder
REM	Rapid eye-movement
REMD	Duration of REM time in total sleep time
1st **REMD**	First REM period duration
REML	REM latency
RLS	Restless leg syndrome
SCN	Suprachiasmatic nucleus
SE	Sleep efficiency
SL	Sleep latency
SPO2	Oxygen Saturation
SRBD	Sleep related breathing disordered
SWS	Slow-wave sleep
TLREMD	Total REM density
TMN	Tuberomammillary nucleus
TST	Total sleep time
VLPO	Ventrolateral preoptic area
WASO	Wake after sleep onset

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Introduction

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The percentage of sleep disturbances increases with age suggesting that sleep is affected by aging itself and/or by aging-related conditions **(Stepnowsky and Ancoli-Israel, 2008).** Approximately 42% of older adults report difficulty initiating and maintaining sleep. Older adults have an increased prevalence of many primary sleep disorders including insomnia (40-50%), circadian rhythm disturbances, sleep-disordered breathing (24%), periodic limb movements in sleep, restless legs syndrome and rapid eye movement (REM) sleep behavior disorder (RBD) (40%) **(Ancoli-Israel and Ayalon, 2006 and Roepke ; Ancoli-Israel, 2010).**

Sleep disorders affect quality of life of the elderly in many aspects. Poor sleep may lead to daytime sleepiness include unintentional napping and falling asleep at inappropriate times during the day **(Deschenes and McCurry, 2009).** Such excessive sleepiness can cause social and occupational difficulties as well as reduced vigilance. Also could lead to cognitive deficits, which may be particularly relevant in those patients with baseline cognitive impairment. Inadequate sleep is also associated with significant morbidity and mortality in older adults. As patients report decreased quality of life with more symptoms of depression and anxiety. All of these factors may lead to difficulties in balance, ambulation and vision, with an increased risk of falling **(Ancoli-Israel and Ayalon, 2006).**

Sleep disorders related to neurodegenerative diseases (NDDs) include sleep related breathing disorders (SRBD);

obstructive sleep apnoea seen in about 15% to 37% of multiple system atrophy patients, REM parasomnias and REM behavior disorder (RBD) in about 46% to 58% of idiopathic PD patients, restless legs syndrome (RLS) and periodic limb movements (PLM) in about 88% of patients with multiple system atrophy **(Raggi and Ferri, 2010).**

Sleep disorders have been reported in 25-56% of Alzheimer's disease (AD) patients **(García-Alberca et al., 2013)**. These include nighttime sleep fragmentation, increased sleep latency, decreased slow-wave sleep, severe nocturnal restlessness, and increased daytime napping and sleep–wake cycle reversal **(Anderson et al., 2008)**.

Sleep disorders in AD are multifactorial. The pathophysiologic changes caused by the disease may interrupt normal sleep progression. Damage to neuronal pathways like cholinergic pathways that are effective in initiation and maintenance of sleep may contribute to the sleep alterations in AD **(Vitiello and Borson, 2001).** Polysomnographic (PSG) studies of AD patients show REM sleep abnormalities, which is indicative for the deterioration of cholinergic pathways and may be closely linked to declarative memory impairment **(Kundermann et al., 2011).**

In addition, the circadian pacemaker in the SCN is destroyed in AD patients and this may have a role in developing sleep disorders **(Tractenberg et al., 2006).** Moreover, the severity of dementia was found to be related to circadian rhythm disorders which in turn affect sleep **(International Classification of Sleep Disorders, 2005)**.

Sleep disturbances are associated with increased memory and cognitive impairment. Also, there is increasing evidence of the role of sleep disturbances in the pathophysiology of AD and a bidirectional relationship has been proposed **(Benedict et al., 2015 ; Villa et al., 2015).**

Disturbed sleep is one of the most common reasons why families and caregivers are no longer able to care for a patient and may result in institutionalization **(García-Alberca et al., 2013).** These data highlight the need to give greater consideration to sleep disorders in AD in the form of clinical and PSG features, its potential role for diagnosis of AD and AD patients care.

Aim of the Study

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To assess the disturbance in sleep pattern in patients with AD, and compare it to cognitively healthy elderly individuals