Chula Med J Vol. 64 No. 1 January - March 2020; 3-11 DOI : 10.14456/clmj.2020.1

Original article

Sleep quality and associated factors of patients with mild cognitive impairment at King Chulalongkorn Memorial Hospital

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Background: Thailand has shifted to an aging society. Sleep disturbance is a common problem in the elderly which affects emotion and cognitive levels. Awareness of sleep problems can help implementing elderly care and preventing dementia in the future.

Objective: To study sleep quality and determine factors associated with sleep quality among patients with mild cognitive impairment (MCI).

Methods: The cross-sectional descriptive study was conducted in MCI patients, aged 50 years and above, from a psychiatric outpatient clinic and cognitive fitness center. The data were collected by questionnaires including demographic data and sleep environment questionnaires; Pittsburgh Sleep Quality Index (PSQI); Sleep Hygiene Index (SHI); STOP-Bang questionnaire; Thai Mental State Examination (TMSE); Montreal Cognitive Assessment (MoCA); Thai Geriatric Depression Scale (TGDS), and Neuropsychiatric Inventory Questionnaire (NPI-Q). The sleep quality was presented as frequency and percentage. The associated factors were analyzed by Chi-square test, Fisher's exact test, and Pearson's correlation coefficient. The predictors of poor sleep quality were analyzed by multiple logistic regression analysis.

Results: Of the 100 subjects, 65 were female with a mean age of 71.3 ± 7.5 years old: 64% of them had poor sleep quality. The associated factors of sleep quality were having a history of psychiatric disorders, use of sedating psychotropic drugs, low to moderate sleep hygiene, and anxiety domain of neuropsychiatric symptoms. TGDS and STOP-Bang scores were correlated with PSQI scores (r = 0.215 and 0.230, respectively). The predictors of poor sleep quality were the use of sedating psychotropic drugs ($P < 0.01$), low to moderate sleep hygiene ($P < 0.05$), and anxiety domain of neuropsychiatric symptoms ($P < 0.05$).

Conclusion: The prevalence of poor sleep quality in MCI patients was 64%. The associated factors and predicted factors of poor sleep quality were the use of sedating psychotropic drugs, low to moderate sleep hygiene, and anxiety domain of neuropsychiatric symptoms. Therefore, sleep quality should be screened in patients with MCI due to the high prevalence.

Keywords: Sleep quality, neuropsychiatric symptoms, mild cognitive impairment.

Thailand has shifted to an aging society and tends to have more aging populations.[1] The longer life expectancy also increases the old age dependency ratio[2] and 3% to 19% of people older than 65 have mild cognitive impairment (MCI), more than half of them later develop dementia within 5 years.[3] A previous study found that amnestic MCI is related to the progression to Alzheimer's disease with a progression rate of up to 10 – 15 % per year, compared to 1 - 2% for normal people.[4]

Neuropsychiatric symptoms (NPS) are commonly found in dementia and MCI patients causing burden and suffering to the patients and caregivers. Studies show that prevalence of NPS in MCI may be as high as 35 – 85% and the most frequently found symptoms are depression, anxiety, irritability, and sleep disturbance is one of the NPS domains.[5, 6]

In adulthood, sleep duration, sleep efficiency and slow wave sleep are significantly decreased with increasing age. A recent study has shown that the prevalence of sleep disturbances in normal elderly

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Received: February 15, 2019
Revised: March 18, 2019
Accepted: March 26, 2019

people is 21% - 54%[7], which is more than the prevalence in other ages. As for the elderly with MCI, the prevalence of sleep disturbances is 14% - 63%.[8 - 10] The elderly have less rapid eye movement (REM) sleep, the period of overnight memory consolidation[11], causing rapidly reduced levels of cognition. Middle insomnia also relates to neuropsychological dysfunction.[12] A previous study has found that depression in patients with MCI is associated with more substantial changes in sleep quality, sleep latency, sleep efficiency, sleep disturbance, and daytime dysfunction. Additionally, depression is related to the use of medications and substances, medical illnesses, reduced levels of cognition, and increased risks of vascular diseases which may affect the sleep quality.[8, 13]

Sleep disturbances affect various body systems, quality of life, emotions, cognitive levels, and excessive use of hypnotic drugs. [14, 15] 20% of people between 55 – 84 years old use hypnotic drugs or alcoholic drinks at least 2 – 3 nights per week. Using hypnotic drugs together with other medication for medical illness in the elderly increases drug interactions. Moreover, hypnotic drugs also have side effects such as impaired cognition, recurrent falls, and functional decline.[15] Therefore, the awareness and prevention of factors associated with poor sleep quality will reduce the excessive use of hypnotic drugs and the risk of drug interactions.

A previous study in Thailand has shown that factors related with sleep quality in the elderly with Alzheimer's disease are as follows: internal factors are age, gender, cognitive deficits, medical conditions (cardiovascular diseases, respiratory diseases, diabetes, musculoskeletal disorders, gastrointestinal diseases, neurological diseases), and behavioral and psychological symptoms of dementia (BPSD). External factors are: types of medication received, psychosocial activities, and environmental factors (light, sound, temperature, and strange environment).[16] However, there has not been any study regarding MCI patients in Thailand.

Evidently, poor sleep quality in the elderly is prevalent and should be emphasized, because poor sleep quality affects emotion and cognitive levels, leading to dementia in the future. This research was conducted to study sleep quality and to find factors associated with sleep quality in MCI patients, in order to be implemented in elderly care and to prevent dementia in the future.

Materials and methods

Sample collections

This is a cross-sectional descriptive study, conducted in the psychiatric outpatient clinic and cognitive fitness center at King Chulalongkorn Memorial Hospital. The sample size was calculated using "$n = z^2_{1-\alpha/2}\, pq / d^2$" with the *P* - value based on the study of McKinnon A, *et al*. ($P = 0.63$)[8], resulting in a calculated sample size (n) of 100.

Inclusion criteria were 1) mild cognitive impairment patients, aged ≥ 50 years, diagnosed by a psychiatrist, using the criteria of the International Working Group criteria for general MCI [17], by reviewing medical records, and evaluation with cognitive tests, Thai Mental State Examination score > 23 and Thai version of Montreal Cognitive Assessment score < 25; 2) able to understand and communicate in Thai; 3) having a caregiver who is ≥ 18 years of age, can understand and communicate in Thai, regularly in contact with the subjects, and capable of assessing the subjects' ability to do daily activities and psychiatric symptoms. The subjects were excluded if they met the diagnostic criteria for dementia.

Data collection was conducted from November 2017 to April 2018. This study was approved by the Institutional Review Board (IRB), the Faculty of Medicine, Chulalongkorn University (COA No. 703/2017). All subjects and caregivers were informed of the objectives and methods of the present study.

Measurements

All subjects completed seven questionnaires including 1) demographic data and sleep environment questionnaires 2) Thai version of the Pittsburgh Sleep Quality Index (PSQI) 3) Sleep Hygiene Index (SHI) 4) STOP-Bang questionnaire 5) the Thai Mental State Examination (TMSE) 6) Thai version of the Montreal Cognitive Assessment (MoCA) and 7) Thai Geriatric Depression Scale (TGDS). Neuropsychiatric symptoms were assessed by caregivers using the Thai version of the Neuropsychiatric Inventory - Questionnaire (*NPI-Q*).

Demographic data and sleep environment questionnaires consisted of sex, age, marital status, current occupation, income, education level, current alcohol and caffeine drinking, history of medical illnesses and psychiatric disorders, obstructive sleep apnea, use of Continuous Positive Airway

Pressure (CPAP), drugs for medical illness, sedating psychotropic drugs, exercise, and sleep environmental problems such as light, noise, temperature, odors and bed discomfort.

The Thai version of the Pittsburgh Sleep Quality Index (PSQI) is a self-rated questionnaire which assesses sleep quality over a 1-month time interval. 19 individual items generate 7 component scores, at the cut-off value of a global score > 5 indicates poor sleep quality. [18]

The Sleep Hygiene Index (SHI) consists of 14 questions. Result interpretation is by calculating the mean score of all questions, a high mean score indicates good sleep hygiene practice. At the cut-off value 1.00 – 2.33 is low sleep hygiene, 2.34 – 3.66 is moderate sleep hygiene, and 3.67 – 5.00 is high sleep hygiene.[19]

The STOP-Bang questionnaire is a tool for screening risk of OSA. It comprises of 8 self-rated questions. If the answer is 'yes' from 3 or more questions, the risk of OSA is high.[20]

The Thai Mental State Examination (TMSE) was used to screen cognitive impairment. The researchers assessed subjects in 6 domains including orientation, registration, attention, calculation, language, and recall, with the cut-off point of 23 out of 30 points indicating cognitive impairment.[21]

The Thai version of the Montreal Cognitive Assessment (MoCA) was used to assess cognitive function in 8 domains, with a total score of 30. One point was added for those who have ≤ 6 years of education. A total score of less than 25 indicates an abnormal level of cognition.[22]

The Thai Geriatric Depression Scale (TGDS) consists of 30 self-rated items. At the cut-off value of the total score 0 - 12 indicates normal, 13 - 18 indicates mild depression, 19 - 24 indicates moderate depression and 25 - 30 indicates severe depression.[23]

The Thai version of the Neuropsychiatric Inventory Questionnaire (NPI-Q) consists of questions about neuropsychiatric symptoms (NPS) in 12 domains. A previous study found that NPI-Q has acceptable levels of internal consistency. We asked caregivers whether the subjects had these symptoms during the past 4 weeks. There is no cut-off point, but a higher score indicates a higher severity of NPS.[24]

Statistical analysis

The data were analyzed using SPSS for Windows version 22.0. Sleep quality was presented by frequency and percentage. The associated factors of poor sleep quality were analyzed by chi-square test, Fisher's exact test, and Pearson's correlation coefficient. Significant factors from theoretical review and univariate analysis were entered into multiple logistic regression models (Odds ratio: OR and 95% CI) in order to identify the potential predictors of poor sleep quality. A *P* - value of less than 0.05 was considered statistically significant.

Results

There were 100 subjects recruited: 47 from the psychiatric outpatient clinic and 53 from the cognitive fitness center, with a mean age of 71.3 ± 7.5 years. Most of them were female (65%), married (66%), and had an income (63%). The median of personal income was 17,000 baht/month, and 96% of the subjects had at least one medical illness; the two most common medical illnesses were dyslipidemia and hypertension. 10% of the subjects had obstructive sleep apnea (OSA), 6% used CPAP while 4% did not. Most of the subjects were under medication for medical illnesses (83%); 22% had a history of psychiatric disorders and 30% used sedating psychotropic drugs. Only 5% consumed alcohol, whereas 56% consumed caffeine. 60% had a disturbing sleep environment. Most of them took regular exercise (85%). The mean TMSE and MoCA score were 27.8 ± 1.9 and 21.7 ± 3.0, respectively. Most of the subjects had a high risk of OSA (60%). Concerning the sleep hygiene, 60% had high sleep hygiene, and 40% had moderate sleep hygiene. Mild depression from TGDS presented at 12% (Table 1).

The prevalence of poor sleep quality according to PSQI was 64% and the mean total score was 6.8 ± 3.3.

The associated factors of poor sleep quality were a history of psychiatric disorders ($P < 0.05$), use of sedating psychotropic drugs ($P < 0.01$), sleep hygiene ($P < 0.05$), and the anxiety domain of NPS ($P < 0.05$) (Table 2).

TGDS and STOP-Bang scores were positively correlated with PSQI scores ($r = 0.215$ and 0.230, respectively) (Table 3).

Logistic regression analysis found three factors that were statistically significant predictors for poor sleep quality of patients with mild cognitive impairment in King Chulalongkorn Memorial Hospital, namely; use of sedating psychotropic drugs, low to moderate sleep hygiene, and the anxiety domain of NPS ($P < 0.05$) (Table 4).

Table 1. Subjects' characteristics.

Characteristics	N (%)	Characteristics	N (%)
Sex		**History of medical illness**	96 (96.0)
Male	35 (35.0)	Dyslipidemia	55 (55.0)
Female	65 (65.0)	Hypertension	53 (53.0)
Age (years) 71.3 ± 7.5 (Min 52, Max 89)		Musculoskeletal disorders	27 (27.0)
Marital Status		Diabetes	23 (23.0)
Single	13 (13.0)	Cardiovascular diseases	19 (19.0)
Married	66 (66.0)	Neurological diseases	12 (12.0)
Widowed	17 (17.0)	(old CVA 7, Parkinson 2, brain tumor 1,	
Divorced/Separated	4 (4.0)	focal seizure 1, TBI 1)	
Education		Allergy	10 (10.0)
Lower than primary school	12 (12.0)	Obstructive sleep apnea	10 (10.0)
Primary school	3 (3.0)	Genitourinary diseases	8 (8.0)
Junior high school	9 (9.0)	Respiratory disease	6 (6.0)
Senior high school	14 (14.0)	Gastrointestinal diseases	5 (5.0)
High vocational certificate	9 (9.0)	Thyroid disease	5 (5.0)
Bachelor degrees or higher	53 (53.0)	**Use of cognitive enhancer**	
Current occupation		No	74 (74.0)
No	78 (78.0)	Yes	26 (26.0)
Government official	2 (2.0)	**Use of sedating psychotropic drugs**	
Self-employed/Trading	17 (17.0)	No	70 (70.0)
Employee	3 (3.0)	Yes	30 (30.0)
Income		**Current caffeine drinking**	
No	37 (37.0)	No	44 (44.0)
Yes	63 (63.0)	Yes	56 (56.0)
Income (baht/month)		**Current alcohol drinking**	
median (IQR) = 17,000 (0 - 30,000)		No	95 (95.0)
		Yes	5 (5.0)
History of psychiatric disorders	22 (22.0)	**Sleep environmental disturbance**	
Depressive disorder	11 (11.0)	No	40 (40.0)
Anxiety disorder	8 (8.0)	Yes	60 (60.0)
Insomnia	2 (2.0)		
Bipolar disorder	1 (1.0)		

Table 2. Factors associated with sleep quality.

Variables	Sleep quality				*P* - value
	Good (n = 36)		Poor (n = 64)		
	n	%	n	%	
Sex					
Male	14	40	21	60	0.541
Female	22	33.8	43	66.2	
Age group (years)					
< 65	7	36.8	12	63.2	0.932
≥ 65	29	35.8	52	64.2	
History of medical illness					
No	3	75.0	1	25.0	0.132[a]
Yes	33	34.4	63	65.6	
History of psychiatric disorders					
No	32	41.0	46	59.0	0.049*
Yes	4	18.2	18	81.8	
Depressive disorder					
No	34	38.2	55	61.8	0.319[a]
Yes	2	18.2	9	81.8	
Anxiety disorder					
No	34	37.0	58	63.0	0.707[a]
Yes	2	25.0	6	75.0	
Insomnia					
No	36	36.7	62	63.3	0.535[a]
Yes	0	0.0	2	100.0	
Use of sedating psychotropic drugs					
No	33	47.1	37	52.9	< 0.001**
Yes	3	10.0	27	90.0	
STOP-Bang questionnaire					
Low risk for OSA	18	45.0	22	55.0	0.126
High risk for OSA	18	30.0	42	70.0	
Current caffeine drinking					
No	12	27.3	32	72.7	0.107
Yes	24	42.9	32	57.1	
Current alcohol drinking					
No	33	34.7	62	65.3	0.348[a]
Yes	3	60.0	2	40	
Sleep hygiene					
Low to moderate	9	22.5	31	77.5	0.022*
High	27	45.0	33	55.0	
TGDS					
Normal	35	39.8	53	60.2	0.051[a]
Mild	1	8.3	11	91.7	
Sleep environmental disturbance					
No	18	45.0	22	55.0	0.142
Yes	22	30.0	42	70.0	
Neuropsychiatric symptoms (NPS)					
No	15	42.9	20	57.1	0.295
Yes	21	32.3	44	67.7	
NPS except sleep domain					
No	16	41.0	23	59.0	0.402
Yes	20	32.8	41	67.2	
Anxiety domain of NPS					
No	30	42.3	41	57.7	0.041*
Yes	6	20.7	23	79.3	

*$P < 0.05$, **$P < 0.01$, [a] = Fisher's Exact

Table 3. Correlations with PSQI scores.

Variables	PSQI score	
	Pearson's correlation coefficient	*P* - value
TMSE	0.069	0.497
MoCA	- 0.25	0.807
TGDS	0.215	0.032*
STOP-Bang	0.230	0.022*
SHI	- 0.114	0.258

*$P < 0.05$

Table 4. Stepwise multiple logistic regression.

Variables	Adjusted OR	95% CI of Adjusted OR		*P* - value
		Lower	Upper	
Use of sedating psychotropic drugs	10.456	2.720	40.200	0.001*
Low to moderate sleep hygiene	3.612	1.333	9.788	0.012**
Anxiety domain of NPS	3.191	1.047	9.723	0.041**

*$P < 0.01$, **$P < 0.05$

Discussion

The findings indicated that patients with mild cognitive impairment (MCI) at King Chulalongkorn Memorial Hospital had poor sleep quality (64.0%). This conformed with previous international studies and literature reviews which discovered the prevalence of sleep disturbance among the elderly with MCI (14 - 63%).[8, 9] The factors related to sleep were divided into the intrinsic and extrinsic factors.

Regarding the intrinsic factors, this study found that having a history of psychiatric disorders was related to sleep quality. This was similar to the study of McKinnon A, *et al*.[8] who found that depressive disorder in patients with MCI was related to sleep disturbance. Considering the relationship between the TGDS scores and the PSQI scores, a low positive correlation was found ($r = 0.215$). However, when individually analyzed, each disease, i.e. depression, anxiety, or insomnia, there was no relationship with sleep quality, because there were a few subjects with such psychiatric disorders and the subjects did not have severe depression, based on TGDS scores. Most of their depressive scores were normal to mild depress. Moderate to severe depression was not found at all. Furthermore, we reviewed the previous diagnoses in which patients might have been treated, their sleep problems might get better.

This study also found that the anxiety domain of NPS was related to sleep quality, similar to the previous study of Spira AP, *et al*. in 2009[25] who found anxiety in elderly female was related to poor sleep efficiency and elevated sleep fragmentation. Stress activates the hypothalamic-pituitary-adrenal (HPA) axis and locus ceruleus, leading to excessive secretion of cortisol as well as norepinephrine. As a consequence, the sympathetic nervous system is activated, followed by initial insomnia, elevated sleep fragmentation, and reduced slow wave sleep (SWS).[26]

As mentioned above, patients with psychiatric disorders who have symptoms of insomnia and inadequate doses of medication may suffer from poor sleep quality. On the other hand, getting long-term sedating psychotropic drugs will also affect sleep quality, following the concept of the bidirectional relationship model.[27] Sleep problems may be symptoms of anxiety and depressive disorder. This study did not exclude subject with psychiatric disorders at first, so it could be confounding.

It was found that the risk of obstructive sleep apnea (STOP-Bang scores) had a positive correlation with PSQI scores. This was similar to the study of Sirirattanapan J, *et al*.[28] Patients with obstructive sleep apnea have short sleep duration and sleep architecture changes. That is because low arterial

oxygen levels stimulate the respiratory center in the brain to awaken other parts of the brain for more respiration. As a result, slow wave sleep is reduced, impinging on lower sleep efficiency and sleep hours, including elevated sleep fragmentation.

For the extrinsic factors, it was found that the use of sedating psychotropic drugs was associated with sleep quality. This point was consistent with the study of Assantachai P, *et al*. [15] on the prevalence and the factors associated with insomnia in the elderly with mild to moderate degrees of poor cognitive ability, and the study of Frighetto L.[29] The use of sedating psychotropic drugs, such as benzodiazepine, reduces REM sleep and NREM3 sleep, bringing about poor sleep quality. On the other hand, patients with sleep problem require even more sedating psychotropic drug use. Less REM sleep causes less long-term memory consolidation. Similarly, anticholinergic effects of tricyclic antidepressants (TCA) have a great impact on cognition.[30]

Sleep hygiene was also related to sleep quality. To demonstrate, low to moderate sleep hygiene increased the risk of poor sleep quality (adjusted OR 3.612, $P < 0.05$). Previous studies exhibited that sleep hygiene promotion programs helped increase sleep quality and relieve stress in the elderly.[31]

Medical illness and exercise did not relate to sleep quality. This corresponded with the study of McKinnon A, *et al*. [8] who found that medical burden, exercise, BMI, and vascular risk factors were not related to sleep quality. However, Maneethanue O, *et al*.[16] studied factors related to sleep quality in the elderly with Alzheimer's disease and found that medical illnesses were related to poor sleep quality.

Environmental disturbances were not related to sleep quality. This was different from previous studies,[16] because the subjects in this study were mostly disturbed by sleep environmental factors at a low level. There were both extrinsic and intrinsic factors that disturbed sleep quality. Thus, poor sleep quality in the subjects possibly arose from other factors besides the environment.

Regarding other factors, for example, alcohol drinking and substance use, the study found that alcohol drinking was not related to sleep quality whereas it was found to be related to poor sleep quality in previous studies.[32] Low to moderate alcohol drinking initially promoted sleep, decreased sleep latency, decreased REM sleep and increased slow wave sleep (deep sleep). However, drinking continually for a period of time leads to decreased slow wave sleep and elevated sleep fragmentation along with REM rebound, resulting in poor sleep quality. [33] The discordant results may be owing to the subjects with small intakes of alcohol and no use of other addictive substances at all. Focusing on caffeine consumption, previous studies described that large amounts of caffeine drinking was related to poor sleep quality and less time in bed. Those with good sleep quality on average consumed less caffeine than those with poor sleep quality (67 mg per day, approximately one cup of instant coffee).[34] In this study, caffeine drinking was not relate to sleep quality. It can be assumed that these contradictory results emerged on account of no data collection in terms of types, amount, and time of the consumption in the subjects.

Limitations and future research: This is a descriptive study, we can only indicate prevalence of poor sleep quality and associated factors, but not causal relationships. Moreover, we recruited the subjects from King Chulalongkorn Memorial Hospital, a tertiary-care hospital, so they might not represent all of the elderly population. The characteristic of the subjects is that most of the patients had moderate to high sleep hygiene. This may be because most of the subjects were female, with high education, and income. Therefore, they had the adequate knowledge in upholding physical and psychological health. There might be some sampling bias in the process as sampling was only performed from the psychiatric outpatient clinic and the cognitive fitness center which have MCI patients with more psychiatric diseases than the samples of other clinics. This may result in difficulty in indicating whether the prevalence of poor sleep quality from this research is the result of psychiatric diseases.

This study did not exclude patients with psychiatric disorders, so we cannot indicate whether poor sleep quality is caused by the existing psychiatric disorders or mild cognitive impairment. Additionally, the tools used in this study are subjective, by which the patients provide the scores themselves, which may be less accurate than the objective measuring tools. The PSQI is a self-rated questionnaire for assessing sleep quality in the past month. The process of recalling questions in MCI patients may easily create recall bias. However, the bias is reduced by utilizing both open ended and selective answers. We also did not use tools for measuring anxiety symptoms nor collect detailed caffeine consumption which may affect the sleep quality as well.

Future research should be in a comparative manner to control other factors which may affect sleep quality. The number of subjects should be increased and extended to other clinics or communal patients. The subjects with a history of psychiatric disorders or using sedating psychotropic drugs should be excluded. Additional associate parameters in other aspects of sleep quality should be accounted for e.g. self-care, health perspective, BMI, tools for anxiety, type and amount of caffeine consumption, etc. Additional objective measurements such as wrist actigraphy may be used. A long term follow-up should be added to study the cognitive level or quality of life reduced by the sleep problems.

Conclusion

The prevalence of poor sleep quality in mild cognitive impairment patients was 64%. The associated and predicted factors of poor sleep quality were the use of sedating psychotropic drugs, low to moderate sleep hygiene, and the anxiety domain of NPS. Therefore, sleep quality should be screened in patients with mild cognitive impairment due to the high prevalence.

Acknowledgements

We would like to express appreciation to Professor Nipon Poungwarin for advocating the use of the TGDS, Associate Professor Tawanchai Jirapramukpitak for advocating the use of the Thai version of the PSQI, Associate Professor Wish Banhiran for advocating the use of the Thai version of the STOP-Bang questionnaire, Associate Professor Solaphat Hemrungrojn for advocating the use of the Thai version of the MoCA and NPI-Q, and Ms. Pattarieya Keawphang for advocating the use of SHI.

Conflict of interest

The authors, hereby, declare no conflict of interest.

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