ORIGINAL RESEARCH

Insomnia in patients on hemodialysis for a short versus long duration

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Background: Many studies have investigated insomnia and the factors associated with this condition in hemodialysis (HD) patients, although the influence of HD duration has not been thoroughly investigated. In the present study, we investigated the factors, especially the duration of HD, associated with insomnia in HD patients.

Patients and methods: A total of 138 patients undergoing HD were recruited, and the Japanese version of the Pittsburgh Sleep Quality Index (PSQI) was used to assess the quality of sleep. Subjects with a total PSQI score up to 4 and those with a score of at least 5 were identified as normal subjects and subjects with insomnia, respectively. Additionally, we assessed restless legs syndrome, depression using the Center for Epidemiologic Studies Depression Scale, and health-related quality of life (QOL) using the Short Form 8 Health Survey. We divided the subjects into two groups according to the median HD duration.

Results: The prevalence rate of insomnia was 54.3% among all the subjects. Twenty-one subjects (15.2%) had depression, 26 (18.8%) had restless legs syndrome, and 75 (54.3%) had insomnia. The median HD duration was 4 years. The scores of components 1 and 4 of the PSQI, subjective sleep quality and habitual sleep efficiency, did not show a significant difference between the normal and insomnia groups. The score of component 7, daytime dysfunction, showed a significant difference between the short and long HD duration groups. In multiple regression analysis, the score of the Short Form 8 Health Survey showed a significant association with the PSQI score in the long HD duration group, but no variable showed a significant association in the short HD duration group.

Conclusion: Patients with a longer duration of HD indicated that insomnia has an influence on their daily activities, with a significant association between insomnia and QOL. Greater attention should be paid to poor QOL and troubles in daily activities caused by insomnia in patients with a longer HD duration.

Keywords: sleep disorders, kidney, quality of life, duration of hemodialysis

Introduction

Patients with chronic disease frequently have comorbid psychiatric disease or psychological distress. Many studies have investigated the association between end-stage renal disease or hemodialysis (HD) and depression.[1–7] A review of the literature shows that 25%–50% of HD patients exhibit depressive symptoms.[1,2,8] Although some single-center studies reported rates of depression or major depressive disorder in HD patients of 25%–30%,[9–11] a multicenter international study showed large differences in rates between the countries where the investigations were conducted; for instance, the rate was 2% in Japan but 21.7% in the US.[12]

Insomnia is one of the symptoms of depression, and many recent studies have reported an association between insomnia and HD.[13–17] Almost all of these reports

showed a higher prevalence of insomnia or restless legs syndrome (RLS) in HD patients, although the precise association between insomnia and HD remains unclear. One study identified uremia, iron deficiency, and diabetes mellitus (DM) type 2 as potential causes of RLS,[18] and these conditions are also associated with HD or the state of patients needing HD.

Regarding the associations between insomnia or RLS and characteristics of HD patients, Yildiz et al and Einollahi et al reported that DM was significantly associated with insomnia and RLS and that HD patients with DM were significantly more likely to have poor quality of sleep and RLS.[13,15] Ezzat and Mohab investigated the association between insomnia and laboratory data and reported that treatment of anemia, hyperphosphatemia, and hypoalbuminemia could improve the insomnia of HD patients.[16] In addition to these internal medical factors, some studies have investigated the contribution of depression and quality of life (QOL) to insomnia.[19–21] Trbojevic-Stankovic et al reported that insomnia or poor sleep quality and depression, as evaluated using the Beck Depression Inventory (BDI), were related to each other.[19] Using the Kidney Disease Quality of Life questionnaire, Parvan et al studied QOL in HD patients and showed that lower QOL was associated with poor sleep quality.[20] Afsar and Elsurer studied both depression and QOL in HD patients using the BDI and the 36-item Short Form Health Survey (SF-36) and showed that the BDI score and SF-36 score were significantly positively and negatively associated with insomnia evaluated using the Pittsburgh Sleep Quality Index (PSQI) and the Epworth Sleepiness Scale questionnaire, respectively.[21]

Thus, many studies have investigated insomnia in HD patients and the factors responsible for this association, although the influence of the duration of HD has not been thoroughly investigated. As the result of daily bed rest or other influences from long-term HD, a longer HD duration might influence insomnia in HD patients. In the present study, we investigated the factors, especially the duration of HD, associated with insomnia in HD patients.

Methods
Participants
This study was conducted between April and June 2015. A total of 138 patients (96 males and 42 females) undergoing HD were recruited from Oyokyo Kidney Research Institute in Japan. Clinical information was obtained from medical records. Blood sampling was performed no later than 2 weeks prior to assessment. Albumin, total protein, sodium, potassium, uric acid, creatinine, blood urea nitrogen, and the amount of HD were measured with standard analytical techniques.

This study was approved by the Ethics Committee of the Hirosaki University School of Medicine, and all subjects provided written informed consent before participating in this study.

Assessment of insomnia, RLS, depression, and health-related QOL
We used the Japanese version of the PSQI to assess the quality of sleep of the subjects in the present study.[22,23] The PSQI consists of seven components: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleep medication, and daytime dysfunction. Each component (C), C1–C7, is scored from 0 to 3, and the maximum total PSQI score is 21. Subjects with total PSQI score of ≥5 show poor sleep quality,[24] thus, in the present study, we defined those subjects with poor sleep quality as "insomnia subjects".

We recorded the symptoms of RLS according to the criteria put forth by the International Restless Legs Syndrome Study Group.[25] The diagnostic criteria for RLS include the following: an urge to move the legs with or without abnormal sensations, worsening of symptoms at rest, improvement in symptoms with activity, and worsening of symptoms in the evening/night.

The Japanese version of the Center for Epidemiologic Studies Depression Scale (CES-D) was also administered to all participants to measure their depressive status.[26] This questionnaire has been widely used to measure depressive symptoms in community populations, and it is also used as a screening tool for depression.[27] The CES-D is a 20-item self-report scale that focuses on depressive symptoms within the week prior to administration of the questionnaire. The maximum score is set at 60, and higher scores are associated with depression. CES-D scores of ≥16 have generally been thought to indicate clinically relevant depressive symptoms, including both minor or subthreshold depression and major depressive disorder.[28,29] Participants whose CES-D score was ≥16 were defined as having CES-D depression.

Health-related QOL of the subjects was assessed using the Short Form 8 Health Survey (SF-8). This survey includes eight items, and each item corresponds to an item of the SF-36; the SF-8 is shorter and easier to use than the SF-36.[30] In the present study, we used a Japanese version of the SF-36, which was translated and validated by Fukuhara and Suzukamo.[31]

Statistical analysis
We used t-tests and chi-square tests to compare the subjects with and without insomnia with regard to demographic and

clinical data. Additionally, we compared the demographic and clinical data of the subjects by assigning them to two groups according to the median HD duration: a short HD duration group and a long HD duration group.

We performed multiple regression analysis using the total PSQI score as the dependent variable for subjects with a short HD duration and using demographic data, the SF-8 score, depression, and RLS as dependent variables for those with long HD duration.

The data were analyzed using SPSS for Windows 22 (IBM Corporation, Armonk, NY, USA). A P-value ≤0.05 was considered statistically significant.

Results
Demographic and clinical data of the entire group and comparisons between subjects with and without insomnia
Table 1 shows the demographic and clinical data of all the subjects. The mean age, HD time, HD duration, SF-8 score, CES-D score, and total PSQI score of the subjects were 66.8±11.9 years, 3.8±0.4 hours, 6.5±6.2 years, 15.8±6.2, 8.2±7.2, and 4.9±3.0, respectively. The median duration of HD was 4 years.

According to the definitions described in the "Assessment of insomnia, RLS, depression, and health-related QOL"

section, 21 subjects (15.2%) had depression, 26 (18.8%) had RLS, and 75 (54.3%) experienced poor sleep quality or had insomnia.

Additionally, Table 1 shows the results of t-tests comparing the variables of subjects with and without insomnia. The normal group included 63 subjects, and the insomnia group included 75 subjects. Total PSQI score and scores of C2, C3, C5, C6, and C7 showed significant differences between the two groups, although scores of C1 and C4 did not show significant differences.

Similarly, the SF-8 score and CES-D score showed significant differences between the two groups; the insomnia group showed significantly higher SF-8 and CES-D scores than the normal group. There were no significant differences in demographic variables or other clinical variables.

Comparison between subjects with a short and a long HD duration
Table 2 shows the results of t-tests comparing the variables of the short HD duration group and long HD duration group. The subjects in the short HD duration group had an HD duration ≤4 years. The subjects in the long HD duration group had an HD duration ≥5 years. The short HD duration group included 72 subjects, and the long HD duration group included 66 subjects.

Table 1 Demographic and clinical data of all the subjects and comparison of subjects with and without insomnia

Variables	Total (n=138)	Normal (n=63)	Insomnia (n=75)	P-value
Age (years)	66.8±11.9	67.4±12.5	66.4±11.5	0.608
Sex (male:female)	96:42	46:17	50:25	0.419[a]
HD time (hours)	3.8±0.4	3.8±0.4	3.8±0.4	0.955
HD duration (years)	6.5±6.2	6.0±6.3	6.9±6.1	0.413
BUN (mg/dL)	64.6±16.9	65.8±16.7	63.6±17.1	0.466
Cre (mg/dL)	10.4±3.1	10.4±3.2	10.4±3.0	0.934
SF-8	15.8±6.2	14.2±4.6	17.2±7.0	0.003*
CES-D	8.2±7.2	6.0±6.5	9.9±7.4	0.002*
Depression, n (%)	21 (15.2%)	7 (11.1%)	14 (18.7%)	0.218[a]
RLS, n (%)	26 (18.8%)	15 (23.8%)	11 (14.7%)	0.171[a]
PSQI				
C1 – quality	0.8±0.9	0.3±0.6	1.3±0.9	0.195
C2 – latency	1.5±1.2	0.7±0.9	2.1±1.0	0.000*
C3 – duration	0.4±0.8	0.1±0.4	0.6±0.9	0.000*
C4 – efficacy	0.0±0.3	0.0±0.1	0.1±0.4	0.279
C5 – disturbances	0.7±0.5	0.6±0.5	0.9±0.4	0.001*
C6 – medication	1.0±1.4	0.4±1.0	1.5±1.5	0.000*
C7 – daytime dysfunction	0.5±0.8	0.2±0.5	0.7±0.9	0.000*
PSQI total score	4.9±3.0	2.4±1.4	7.0±2.2	0.000*
Insomnia, n (%)	75 (54.3%)	–	–	–

Notes: Data presented as mean ± standard deviation unless stated otherwise. "–" indicates not applicable. [a]Chi-square test. *P<0.01.
Abbreviations: HD, hemodialysis; BUN, blood urea nitrogen; Cre, creatinine; SF-8, Short Form 8 Health Survey; CES-D, Center for Epidemiologic Studies Depression Scale; RLS, restless legs syndrome; PSQI, Pittsburgh Sleep Quality Index.

Table 2 Comparison of subjects with a short and a long HD duration

Variables	Short HD duration (n=72)	Long HD duration (n=66)	*P*-value
Age (years)	68.9±11.3	64.6±12.3	0.032*
Sex (male:female)	49:23	47:19	0.715[a]
HD time (hours)	3.7±0.5	3.9±0.3	0.004**
HD duration (years)	1.8±1.4	11.5±5.4	0.000**
BUN (mg/dL)	65.0±16.2	64.2±17.8	0.797
Cre (mg/dL)	9.6±2.8	11.2±3.1	0.002**
SF-8	15.7±5.9	16.0±6.6	0.775
CES-D	7.5±7.1	8.9±7.4	0.241
Depression, n (%)	9 (12.5%)	12 (18.2%)	0.477[a]
RLS, n (%)	13 (18.1%)	13 (19.7%)	0.805[a]
PSQI			
C1 – quality	0.9±1.0	0.8±0.7	0.382
C2 – latency	1.4±1.2	1.6±1.1	0.309
C3 – duration	0.4±0.8	0.4±0.8	0.715
C4 – efficacy	0.0±0.2	0.1±0.4	0.512
C5 – disturbances	0.8±0.5	0.7±0.5	0.192
C6 – medication	0.8±1.3	1.2±1.5	0.130
C7 – daytime dysfunction	0.4±0.6	0.7±0.9	0.021*
PSQI total score	4.6±3.0	5.3±2.8	0.179
Insomnia, n (%)	35 (48.6%)	40 (60.6%)	0.174[a]

Notes: Data presented as mean ± standard deviation unless stated otherwise. [a]Chi-square test. *P<0.05. **P<0.01.
Abbreviations: HD, hemodialysis; BUN, blood urea nitrogen; Cre, creatinine; SF-8, Short Form 8 Health Survey; CES-D, Center for Epidemiologic Studies Depression Scale; RLS, restless legs syndrome; PSQI, Pittsburgh Sleep Quality Index.

Age was significantly higher in the short HD duration group than the long HD duration group. HD time, HD duration, and creatinine levels were significantly higher in the long HD duration group than in the short HD duration group.

There was no significant difference in the prevalence rate of insomnia between the two groups. There was also no significant difference in the total PSQI score or the scores of individual components except C7 (daytime dysfunction); the score of C7 was significantly higher in the long HD duration group than the short HD duration group.

Multiple regression analysis of the total PSQI score in subjects with a short and a long HD duration

Table 3 shows the results of multiple regression analysis of the total PSQI score in subjects in short HD duration group and long HD duration group using demographic data, the SF-8 score, depression, and RLS as dependent variables.

In the short HD duration group, no variables showed significant associations. In the long HD duration group, age and SF-8 score showed significant associations; age was negatively significantly associated with the total PSQI score, and the SF-8 score was positively significantly associated with the total PSQI score. Additionally, only the correlation between PSQI score and SF-8 found by single correlation analysis was significant.

Discussion

In the present study, we investigated the factors associated with insomnia in HD patients, with a particular focus on the HD duration of the patients. Our results showed a higher prevalence of insomnia in HD patients. There was no significant difference between the prevalence rate of insomnia in the short and long HD duration groups, while the score

Table 3 Multiple regression analysis of the total PSQI score for subjects with a short and a long HD duration

Groups	Beta coefficient	*t*-value	*P*-value
Short HD duration			
Age (years)	−0.170	−1.280	0.205
Sex	0.022	0.177	0.860
HD time (hours)	−0.042	−0.286	0.776
HD duration (years)	−0.072	−0.512	0.610
SF-8	0.191	1.354	0.180
Depression	−0.051	−0.358	0.722
RLS	0.096	0.773	0.442
Long HD duration			
Age (years)	−0.281	−2.104	0.040*
Sex	0.112	0.895	0.374
HD time (hours)	0.025	0.208	0.836
HD duration (years)	−0.126	−0.976	0.333
SF-8	0.348	2.462	0.017*
Depression	0.078	0.548	0.586
RLS	−0.183	−1.432	0.157

Note: *P<0.05.
Abbreviations: PSQI, Pittsburgh Sleep Quality Index; HD, hemodialysis; SF-8, Short Form 8 Health Survey; RLS, restless legs syndrome.

of C7 (daytime dysfunction) of the PSQI was significantly higher and the SF-8 score showed a significant association with the PSQI score in the long HD duration group. Thus, in patients with a longer HD duration, insomnia might be closely associated with QOL. This is the first report to investigate insomnia in HD patients by classifying them according to their HD duration.

With the exception of C1 "quality" and C4 "efficacy", there were significant differences between the PSQI component scores of the normal and insomnia groups. C1 is a subjective assessment by patients about their quality of sleep, while C4 assesses the percentage of total number of hours asleep during the total number of hours in bed. Patients diagnosed without insomnia might think that their sleep was poor or short considering their hours in bed. There has been no report discussing the differences in PSQI component scores of HD patients with and without insomnia evaluated by the PSQI, although patients might be equally influenced by their time in bed during HD and think their sleep to be poor.

We showed that the prevalence rate of insomnia in all HD patients was 54.3%. The reported range of prevalence rates of insomnia in HD patients is relatively wide. Ezzat and Mohab reported that the prevalence rate of insomnia in HD patients was 54%, a value similar to the 54.3% we have shown in the present study.[16] On the other hand, several studies of HD patients evaluated insomnia with the same method used in the present study, that is, a total PSQI score of ≥5, and reported prevalence rates somewhat different from the value shown in the present study; Parvan et al and Iliescu et al reported rates of 83.3% and 71%, respectively.[20,32] Although we used the same method to assess insomnia, differences in characteristics of the backgrounds of the patients from each hospital or the system of the hospitals might have influenced the prevalence rate. For example, more patients might have been taking hypnotics or psychotropic drugs to obtain better sleep in some hospitals, and psychiatrists or experts in insomnia treatment might have participated in sleep studies in some hospitals.

We hypothesized that the long HD duration group would show a higher prevalence of insomnia because we thought that the sleep–wake rhythm of patients might change with a longer HD duration, but there was no significant difference in the prevalence rate of insomnia between the short and long HD duration groups. The psychological reaction to HD or the introduction of HD and the practice of HD in the long HD duration group might have offset each other. In the present study, the patients were divided into two groups according to the median HD duration. Further studies using other methods

to classify patients by HD duration might obtain additional information about potential differences in the prevalence rate of insomnia in relation to HD duration.

Of the PSQI component scores, only C7 showed a significant difference between the short and long HD duration groups. C7 indicates the "daytime dysfunction" of the patient, and the questionnaire asked whether the patient had trouble staying awake during daytime activity and keeping up enthusiasm to get things done. In other words, C7 shows the influence of insomnia on whether the patient performed daytime activities without trouble, indicating that patients with higher scores on C7 might have a poorer QOL. This finding may also relate to the association between PSQI score and SF-8 score in the long HD duration group, according to the multiple regression analysis shown in Table 3 and the single correlation analysis. Particularly for patients with a longer HD duration, treatment for insomnia and psycho-education about better sleep habits and staying awake during daytime might improve the QOL.

There were some limitations to the present study. First, we did not investigate the medication of the patients; we only asked how they took medicine to help their sleep (as one question of the PSQI) but did not investigate the type or amount of medication. Indeed, we might be able to determine better prescriptions for HD patients to improve their insomnia or poor QOL associated with insomnia by investigating their medication history. Second, we did not assess comorbid diseases of the HD patients and did not investigate the method used for HD. Previous studies have reported that DM might be associated with a higher prevalence of insomnia or RLS in HD patients.[13,15] The sleep-associated activities performed by patients during HD might be influenced by the method used for HD. Thus, treatments for insomnia should likely be tailored according to comorbid diseases and the HD method. Third, we investigated only subjects who were hemodialyzed during an afternoon session. The subjects in another session might experience a suitable QOL during their HD session and might show different characteristics from those observed in the present study.

Conclusion

We investigated the differences in the characteristics of HD patients with a short or long HD duration, and the results suggest that HD patients with a long HD duration might experience an influence of insomnia on their daily activities and a potential significant association between insomnia and QOL. Therefore, we should pay greater attention to poor QOL and trouble in daily activities caused by insomnia in patients with a longer duration of HD.

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Disclosure

The authors report no conflicts of interest in this work.

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