Nephrol Dial Transplant (2004) 19: 95–99
DOI: 10.1093/ndt/gfg423

Nephrology
Dialysis
Transplantation

Original Article

Quality of sleep in patients with chronic kidney disease

Eduard A. Iliescu, Karen E. Yeates and David C. Holland

Department of Medicine, Queen's University, Kingston, Ontario, Canada

Abstract

Background. Sleep disorders are common in patients with renal failure on dialysis; however, the prevalence of 'poor sleep' in patients with chronic kidney disease (CKD) not yet on dialysis is not known. This study aimed to measure the prevalence of 'poor sleep' in CKD patients and to examine the association between quality of sleep and the degree of renal impairment in this population.

Methods. Quality of sleep was measured using the Pittsburgh Sleep Quality Index (PSQI) in 120 prevalent CKD patients.

Results. Sixty-three subjects (53%) had 'poor sleep' defined as a global PSQI score > 5. There was no statistically significant relationship between the global PSQI score and the blood urea nitrogen level (BUN), serum creatinine level or calculated creatinine clearance, but the sleep efficiency component score correlated with BUN ($r = 0.19$, $P = 0.04$) and serum creatinine ($r = 0.20$, $P = 0.03$). A history of depression was the only independent predictor of 'poor sleep' (global PSQI > 5).

Conclusions. 'Poor sleep' is common in CKD patients. Quality of sleep decreases in the early stages of CKD and does not appear to be associated with the subsequent degree of renal failure. Large prospective longitudinal studies of quality of sleep in CKD patients are needed to confirm the high prevalence of impaired quality of sleep in this population and examine the association between renal function and quality of sleep while controlling for potential confounding variables.

Keywords: chronic kidney disease; chronic renal failure; depression; pre-dialysis; questionnaire; sleep disorders

Introduction

Decreased quality of sleep is common in dialysis patients and is associated with decreased health-related quality of life [1,2]. The reported prevalence of 'poor sleep', including sleep-wake complaints, sleep-disordered breathing and excessive sleepiness, in dialysis patients is in the range of 45–80% [1–10]. The prevalence of 'poor sleep' in patients with chronic kidney disease (CKD) not yet on dialysis is not known. The objectives of this study were to measure the prevalence of 'poor sleep' in a prevalent population of CKD patients and to examine the association between quality of sleep and the degree of renal impairment in this population.

Subjects and methods

This was a cross-sectional study of prevalent patients attending the CKD clinic at Kingston General Hospital (KGH). The end-stage renal disease (ESRD) programme at KGH is the only provider of renal replacement therapy (RRT) for the region of south-eastern Ontario, Canada. The CKD programme at KGH is a component of the ESRD programme. The primary objectives of the CKD programme are to retard progression of CKD and to prepare CKD patients for timely initiation of RRT when ESRD is reached. To enter the CKD programme, patients usually have an irreversible elevation in the serum creatinine > 250 μmol/l ($\times 0.85$ for females), but this degree of elevation in the serum creatinine is not an absolute requirement. The study subjects were recruited consecutively during the regular CKD clinic visits over a 3 month period. The quality of sleep, renal function and the other variables were measured concurrently at the time of enrolment. Patients were excluded if they were < 18 years of age, if they were unable to understand English or if they were not competent to give informed consent. The Queen's University Research Ethics Board approved the protocol.

Renal function

The measurements of renal function were the blood urea nitrogen level (BUN), the serum creatinine level and the

Correspondence and offprint requests to: Eduard A. Iliescu, 2058 Etherington Hall, Queen's University, Kingston, Ontario, Canada. Email: eai1@post.queensu.ca

estimated creatinine clearance calculated using the Cockcroft–Gault equation [11]. For categorical analysis the subjects were separated, based on creatinine clearance, into five groups corresponding to the five stages of the K-DOQI classification of CKD [12].

Quality of sleep

Quality of sleep was measured using the Pittsburgh Sleep Quality Index (PSQI) [13]. This self-administered questionnaire assesses quality of sleep during the previous month and contains 19 self-rated questions yielding seven components: subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, use of sleep medications and daytime dysfunction. Each component is scored from 0 to 3, yielding a global PSQI score between 0 and 21, with higher scores indicating lower quality of sleep. The PSQI is useful in identifying 'good sleepers' and 'poor sleepers'. A global PSQI score >5 indicates that a person is a 'poor sleeper' having severe difficulties in at least two areas or moderate difficulties in more than three areas [13].

Other variables

Age, sex, cause of renal disease, living alone, post-secondary education, employment, depression, haemoglobin, erythropoietin dose, serum albumin (bromcresol purple method), serum total calcium and serum phosphorus were determined from interview and chart review. Comorbidity was measured using the modified Charlson Comorbidity Index (CCI) [14]. Age was not included in the index, in order to examine the influence of age on quality of sleep independent of comorbidity. Depression was defined as depressed mood, as confirmed by a previous diagnosis of depression.

Statistical analysis

The analysis was performed using statistical software SAS® System for Windows release 6.12 (SAS Institute Inc., Cary, NC, USA). The prevalence of 'poor sleep' was determined by the proportion of subjects with global PSQI >5. Student's *t*-test was used to compare the means of normally distributed variables between groups and the Mann–Whitney *U*-test was used for variables that were not normally distributed. Differences among categorical variables were analysed using the chi-square test or the two-tailed Fisher's exact test, as appropriate. The level of significance was $\alpha = 0.05$ for all comparisons. Multiple logistic regression with forwards stepwise selection ($\alpha = 0.05$) was performed to identify factors independently associated with 'poor sleep' (PSQI >5).

Results

Univariate analysis

One-hundred and thirty subjects were eligible to enter the study during the study period. Ten subjects were excluded: three language barrier, six refused and one recovered renal function and had a normal serum creatinine. One-hundred and twenty subjects were included in the study. There were missing values for weight due to wheelchair use (three subjects) and for albumin (two subjects), calcium (three subjects) and phosphate (four subjects) due to absent, insufficient or inadequate blood samples. Complete data are available for all other variables. The characteristics of the 120 subjects are shown in Table 1. One subject was Asian, one was African Canadian, two were Native Canadian and the remainder were Caucasian. The causes of renal disease were glomerulonephritis (14 patients), diabetic nephropathy (30), vascular/hypertension (39), obstruction (2), interstitial nephritis (12), polycystic kidney disease (7) and unknown (16). The mean (SD) and range of the global and component PSQI scores are shown in Table 1. Sixty-three (53%) subjects were 'poor sleepers' (global PSQI >5). Sleep disturbance was the component of PSQI with the greatest degree of abnormality, followed by sleep latency. The distribution of subjects among the five K-DOQI classes of CKD severity was: 0 subjects in Stage 1, 2 in Stage 2, 15 in Stage 3, 66 in Stage 4 and 34 in Stage 5. Three subjects had missing values for weight and creatinine clearance.

Table 1. Characteristics of the 120 subjects included in the study

Variable	*n* (%)	Mean (SD)	Range
Age (years)		68.14 (14.13)	20.0–94.0
Females (*n*)	51 (42.5)		
Living alone (*n*)	31 (25.8)		
Employed (*n*)	13 (10.8)		
Post-secondary education (*n*)	32 (26.7)		
Depressed (*n*)	26 (21.7)		
Charlson comorbidity index		5.63 (2.83)	2–13
Haemoglobin (g/l)		116.7 (14.3)	85.0–163.0
Erythropoietin ($\times$ 1000 U/week)		1.62 (2.48)	0–14.0
Serum albumin (g/l)		37.85 (3.98)	26.0–45.0
Serum total calcium (mmol/l)		2.27 (0.18)	1.82–2.94
Serum phosphorus (mmol/l)		1.42 (0.32)	0.86–2.34
BUN (mmol/l)		20.49 (7.11)	6.60–44.00
Serum creatinine (μmol/l)		352 (135)	133–809
Creatinine clearance (ml/min)		20.96 (10.93)	6.65–61.29
Quality of sleep			
Global PSQI		6.57 (4.13)	1–17
Subjective sleep quality		0.91 (0.77)	0–3
Sleep latency		1.05 (1.06)	0–3
Sleep duration		0.53 (0.88)	0–3
Sleep efficiency		0.97 (1.17)	0–3
Sleep disturbance		1.53 (0.63)	0–3
Use of sleep medications		0.65 (1.16)	0–3
Daytime dysfunction		0.93 (0.75)	0–3

Bivariate analysis

There was no significant correlation between the global PSQI score and any of the continuous variables, including BUN, serum creatinine, creatinine clearance or log transformed creatinine clearance. The sleep efficiency component score correlated with BUN (Spearman $r = 0.19$, $P = 0.04$), serum creatinine

(Spearman $r = 0.20$, $P = 0.03$) and serum calcium (Spearman $r = 0.20$, $P = 0.03$). The sleep disturbance component score correlated with serum albumin (Spearman r = 0.13, p = 0.04). There were no other significant correlations between the components of the PSQI and any of the continuous independent variables considered. Haemoglobin and the sleep disturbance score were weakly correlated (Spearman $r = 0.17$, $P = 0.06$), but this did not reach statistical significance.

The characteristics of 'good sleepers' (global PSQI ≤ 5) compared with 'poor sleepers' (global PSQI > 5) are shown in Table 2. Compared with 'good sleepers', 'poor sleepers' had a greater proportion of depressed subjects. The mean creatinine clearance was lower in 'poor sleepers' compared with 'good sleepers', but this was not statistically significant (NS). The mean PSQI among the five stages of CKD was: Stage 1, not applicable; Stage 2, 5.50; Stage 3, 4.93; Stage 4, 7.02; and Stage 5, 6.59 (NS). Given the small number of subjects in some of the CKD stages, the subjects were also separated into two groups ('group 1' and 'group 2') defined as creatinine clearance above and below 17.8 ml/min, the median creatinine clearance for the group, respectively. The quality of sleep for group 1 compared with group 2 is shown in Table 3. The scores for global PSQI, subjective sleep quality, sleep latency, sleep duration and sleep efficiency were higher, indicating lower quality of sleep, in group 2 compared with group 1, but these trends did not reach statistical significance.

Multivariate analysis

The only significant independent predictor of 'poor sleep' (PSQI > 5) in multiple logistic regression was the presence of depression (odds ratio = 3.07, $P = 0.026$). The results did not change with consideration of diabetes independent of the CCI or with consideration of all the other individual comorbidities as independent variables.

Discussion

The prevalence of 'poor sleep' in the present study was 53%. The likelihood of selection bias is low given the low non-participation rate and the fact that this is the only CKD programme in the region. There are no other

Table 2. Characteristics of 'good sleepers' compared with 'poor sleepers' among the 120 study subjects

Variable	Good sleepers (global PSQI ≤ 5) ($n = 57$)	Poor sleepers (global PSQI > 5) ($n = 63$)	*P*-value
Age (years)	66.95 (16.38)	69.22 (11.78)	0.28
Females (*n*)	20	31	0.12
Living alone (*n*)	13	18	0.47
Employed (*n*)	8	5	0.28
Post-secondary education (*n*)	12	20	0.19
Depressed (*n*)	7	19	0.02
Charlson comorbidity index	5.32 (3.04)	5.92 (2.61)	0.11
Haemoglobin (g/l)	118.1 (14.3)	115.5 (14.3)	0.33
Erythropoietin ($\times$ 1000 U/week)	1.35 (2.47)	1.86 (2.49)	0.16
Serum albumin (g/l)	38.37 (3.37)	37.36 (4.45)	0.28
Serum total calcium (mmol/l)	2.28 (0.15)	2.26 (0.20)	0.43
Serum phosphorus (mmol/l)	1.40 (0.30)	1.44 (0.33)	0.42
BUN (mmol/l)	20.08 (6.92)	20.87 (7.32)	0.52
Serum creatinine (μmol/l)	349.3 (151.1)	355.1 (120.5)	0.37
Creatinine clearance (ml/min)	22.39 (11.64)	19.64 (10.16)	0.19

Results are means (SD) unless otherwise specified.

Table 3. Quality of sleep for subjects with creatinine clearance above and below the median creatinine clearance for the study population

Variable	Group 1 ($n = 58$)	Group 2 ($n = = 59$)	*P*-value
Global PSQI	6.12 (4.10)	7.07 (4.21)	0.18
Subjective sleep quality	0.79 (0.74)	1.03 (0.79)	0.09
Sleep latency	0.90 (1.02)	1.24 (1.09)	0.08
Sleep duration	0.45 (0.78)	0.64 (0.98)	0.39
Sleep efficiency	0.84 (1.12)	1.07 (1.22)	0.32
Sleep disturbance	1.50 (0.63)	1.56 (0.65)	0.73
Use of sleep medications	0.69 (1.23)	0.63 (1.13)	0.97
Daytime dysfunction	0.95 (0.76)	0.90 (0.76)	0.70

Results are means (SD). Group 1, creatinine clearance > 17.8 ml/min; group 2, creatinine clearance ≤ 17.8 ml/min. Creatinine clearance could not be calculated for the three subjects with missing values for weight.

contemporary studies of quality of sleep in patients with CKD not yet on dialysis available for comparison. The prevalence of 'poor sleep' in the present study is similar to the 45–80% prevalence of sleep-wake complaints, sleep-disordered breathing and excessive sleepiness in patients with ESRD on dialysis, assessed by various means including formal polysomnography [1–10]. In a previous study we examined the quality of sleep in 89 subjects with ESRD on haemodialysis using the PSQI and found a prevalence of 'poor sleep' (global PSQI > 5) of 71% [2]. Despite the fact that the definition of depression used would have misclassified subjects with new onset of depression and treated subjects who were no longer depressed, the presence of depression was the only significant predictor of decreased quality of sleep among the independent variables considered. The association between depression and quality of sleep is well established and has been reported previously in dialysis patients and in people with normal renal function [2,13]. There was no association between the degree of renal impairment and the quality of sleep. The best evidence that renal failure can directly influence quality of sleep comes from polysomnographic studies in dialysis patients. Obstructive sleep apnoea (OSA) and periodic leg movement during sleep (PMLS) serve as a feasible model for this association. OSA is common in dialysis patients [6,7]. Slow nocturnal dialysis and transplantation improve or reverse OSA [6,15]. It has been hypothesized that OSA in dialysis patients is due to central destabilization of ventilatory control and upper airway obstruction related to acidosis and airway oedema, respectively [6]. Hanly *et al.* [5] examined daytime sleepiness with multiple sleep latency tests in 24 haemodialysis patients and found strong correlation ($r = 0.58$, $P = 0.01$) between sleep latency and BUN. A number of previous studies have examined the association between dialysis adequacy measured by small solute clearance, Kt/V urea and sleep-wake complaints and found no relationship [1–3]. In the present study there was no association between renal function and the global PSQI score, but there was an association between BUN and serum creatinine and the sleep efficiency component score (the number of hours slept *vs* the number spent in bed) in the expected direction. Given the large number of correlations these results must be interpreted with caution, but the fact that both BUN and creatinine correlated with the sleep efficiency component score decreases the likelihood that this is a chance finding.

The fact that the prevalence of 'poor sleep' in CKD was nearly as high as the prevalence of 'poor sleep' in dialysis patients suggests that quality of sleep decreases very early in CKD. One can only speculate on the factors that lead to decreased quality of sleep at early stages of renal failure. In dialysis patients, global PSQI is inversely associated with serum albumin and haemoglobin [2]. In the present study there was no association between the global PSQI and these variables, but there was an inverse relationship between the sleep disturbance component score and serum albumin level and there was a trend to higher sleep disturbance component scores with decreasing haemoglobin level. While there is biological plausibility and consistency with previous studies in dialysis patients [2], these associations demand further investigation. It seems likely that many factors that lead to decreased quality of sleep in CKD patients, such as depression, are not specific to renal failure.

The main limitations of the present study are the lack of a suitable control group, absence of polysomnography and a sample size that does not permit the meaningful evaluation of the large number of variables that can influence the quality of sleep. The present study had only 60% power to detect a 20% difference (40 *vs* 60%) in the prevalence of 'poor sleep' (global PSQI > 5) between subjects in group 1 compared with group 2. There was a trend to higher PSQI scores in group 2 compared with group 1, which may have reached significance with a large sample size. Due to the cross-sectional design it was not possible to establish cause and effect in the associations examined. The prevalent study population with little ethnic diversity limits the generalizability of the results of this study to other populations, however, the fact that the prevalence of 'poor sleep' in the present study is similar to the prevalence of sleep-wake complaints in a variety of studies of dialysis patients suggests that the magnitude of sleep problems is similar among different populations.

In conclusion, the results of this study suggest that 'poor sleep' is common in CKD patients and that quality of sleep decreases in the early stages of CKD. We hypothesize that the causes of decreased quality of sleep in CKD patients are not specific to chronic renal illness and probably involve psychiatric disorders, such as depressed mood. Large prospective longitudinal studies of quality of sleep in CKD patients are needed to confirm the high prevalence of decreased quality of sleep in this population and examine the association between renal function and quality of sleep while controlling for potential confounding variables. Such studies need to start at an early stage of renal failure and include pertinent normal and chronically ill control subjects. Polysomnographic studies of CKD patients are needed to assess the prevalence of OSA and PMLS.

Conflict of interest statement. None declared.

References

1. Williams SW, Tell GS, Zheng B, Shumaker S, Rocco MV, Sevick MA. Correlates of sleep behavior among hemodialysis patients. *Am J Nephrol* 2002; 22: 18–28
2. Iliescu EA, Coo H, McMurray MH *et al*. Quality of sleep and health-related quality of life in hemodialysis patients. *Nephrol Dial Transplant* 2003; 18: 126–132
3. Holley JL, Nespor S, Rault R. A comparison of reported sleep disorders in patients on chronic hemodialysis and continuous peritoneal dialysis. *Am J Kidney Dis* 1992; 19: 156–161
4. Walker S, Fine A, Kryger MH. Sleep complaints are common in a dialysis unit. *Am J Kidney Dis* 1995; 26: 751–756

5. Hanly PJ, Gabor JY, Chan C, Pierratos A. Daytime sleepiness in patients with CRF: impact of nocturnal hemodialysis. *Am J Kidney Dis* 2003; 41: 403–410
6. Hanly PJ, Pierratos A. Improvement of sleep apnea in patients with chronic renal failure who undergo nocturnal hemodialysis. *N Engl J Med* 2001; 344: 102–107
7. Kimmel PL, Miller G, Mendelson WB. Sleep apnea syndrome in chronic renal disease. *Am J Med* 1989; 86: 308–314
8. Benz RL, Pressman MR, Hovick ET, Peterson DD. Potential novel predictors of mortality in end-stage renal disease patients with sleep disorders. *Am J Kidney Dis* 2000; 35: 1052–1060
9. Parker KP, Bliwise DL, Bailey JL, Rye DB. Daytime sleepiness in stable hemodialysis patients. *Am J Kidney Dis* 2003; 41: 394–402
10. Sabbatini M, Minale B, Crispo A *et al*. Insomnia in maintenance haemodialysis patients. *Nephrol Dial Transplant* 2002; 17: 852–856
11. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976; 16: 31–41
12. National Kidney Foundation. K/DOQI Clinical practice guidelines for chronic kidney disease: evaluation, classification and stratification. Part 4. Definition and classification of stages of chronic kidney disease. *Am J Kidney Dis* 2002; 39 [Suppl]: S46–S75
13. Buysse DJ, Reynolds CF,III, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. *Psychiatry Res* 1989; 28: 193–213
14. Beddhu S, Bruns FJ, Saul M, Seddon P, Zeidel ML. A simple comorbidity scale predicts clinical outcomes and costs in dialysis patients. *Am J Med* 2000; 108: 609–713
15. Auckley DH, Schmidt-Nowara W, Brown LK. Reversal of sleep apnea hypopnea syndrome in end-stage renal disease after kidney transplantation. *Am J Kidney Dis* 1999; 34: 739–744

Received for publication: 22.4.03
Accepted in revised form: 27.6.03