

Sleeping Disorders in Early Chronic Kidney Disease

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Studies in patients on maintenance hemodialysis have disclosed a high prevalence of sleeping disorders, which have been linked to various factors including blood urea levels, creatinine levels, parathyroid hormone levels, anemia, systolic and diastolic blood pressure, quality of life, disease intrusiveness, and comorbidities. In contrast, few studies have been performed in patients with chronic kidney disease (CKD), who represent the target of the present study. A group of 52 CKD patients were enrolled after characterization of their renal function. Comorbidities were evaluated by means of the Charlson Comorbidity Index. Sleep disorders were evaluated by means of the Sleep Disorder Questionnaire (SDQ), a 26-item questionnaire providing a hierarchic classification for relevant insomnia, relevant hypersomnia, subclinical disorders, or absence of sleep complaints. Results indicate that, in the early stages of CKD, at a time the comorbidity index is low, sleep disorders are present in 80.7% of patients. This finding, which needs to be confirmed in a larger cohort of patients, indicates that sleep disorders affect the lives of CKD patients as soon a diagnosis of disease potentially progressing to end-stage renal disease was made. *Semin Nephrol* 26:64-67 © 2006 Elsevier Inc. All rights reserved.

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Several studies in the past 30 years have shown that uremic patients are at great risk for disordered sleep. Sleep disorders have been reported in 47% to 70% of hemodialysis patients on maintenance hemodialysis and in 50% of peritoneal dialysis patients, compared with 12% of healthy controls.¹⁻⁹ The most prominent sleep disorders among patients with end-stage renal disease are insomnia, restless leg syndrome, periodic limb movement disorders, and sleep apnea-hypopnea syndrome.

A multitude of causes including anemia, blood urea levels, plasma creatinine levels, parathyroid hormone (PTH) concentrations, increased blood pressure, quality of life, and illness intrusiveness may contribute to sleep disturbances in patients on maintenance hemodialysis. Furthermore, there is a positive correlation between sleep disturbances and increased morbidity and mortality related to cardiovascular disease and infectious complications, the 2 major causes of death in hemodialysis patients.

Patients on maintenance hemodialysis have comorbid conditions. Their role has been recognized since the early

days of uremia therapy with maintenance hemodialysis.^{10,11} Recently, comorbidities have emerged as the crucial problem in uremia prevention and therapy. There is evidence that adequate treatment of some comorbidities may postpone initiation of dialysis. We now know that comorbidities affect patients' outcome. Various indices have been proposed to evaluate the impact of comorbidities on the clinical outcome of patients with end-stage renal disease.¹²⁻¹⁶ Finally, the Charlson Comorbidity Index (CCI), proposed in 1987, emerged as the most valid, thus providing a method to classify prognostic comorbidities in various diseases,¹⁷ and in patients on maintenance hemodialysis.¹⁸⁻²¹

Studies have focused on patients on maintenance hemodialysis, whereas patients with mild/moderate chronic kidney disease (CKD) have been neglected. In fact, only a few studies on this category of patients are available, and include patients with various degrees of plasma creatinine levels, from mild to severe.²²⁻²⁴ Therefore, this study was devised to evaluate the prevalence of sleep disturbances in early stages of CKD patients and to examine the relationship of sleep disorders to renal function and to comorbidities.

Methods

Patients

A group of 52 (31 M and 21 F) early CKD patients with a mean age of 61.2 ± 19.3 years (mean \pm SD), were enrolled

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for a cross-sectional study 2 months after CKD was diagnosed. Twenty-eight of the patients were retired, 12 patients worked full-time, 2 patients were students, 3 patients were unemployed, and 7 patients were housewives.

Systolic blood pressure averaged 138 ± 19 mm Hg, diastolic blood pressure averaged 79 ± 10 mm Hg, mean hemoglobin concentration averaged 11.7 ± 2.3 g/dL, plasma creatinine concentration averaged 1.9 ± 0.8 mg/dL, and blood urea level averaged 74 ± 49 mg/dL. Sleep duration averaged 6.2 ± 2.3 hours, CCI averaged 5.3 ± 2.4 . The cause of renal disease was glomerulonephritis in 6 patients, interstitial nephritis in 8 patients, vascular disease/hypertension in 10 patients, diabetic nephropathy in 5 patients, and polycystic kidney disease in 2 patients. No cause was found for 22 patients. Thirty-nine patients were on angiotensin-converting enzyme inhibitors, 17 were on calcium channel blockers, 7 were on vasodilators, 19 were on diuretics, and 4 were on other antihypertensive drugs. A total of 13 patients (25%) needed sleeping pills. At the time of enrollment no patient received erythropoietin.

Assessment of Sleep Disturbances

We used a 26-item self-administered questionnaire (SDQ) that identifies sleeping disturbances according to Diagnostic and Statistical Manual of Mental Disorders, 4th edition, (DSM-IV™) criteria. The SDQ was developed by Violani et al²⁵ and was used in many previous studies in renal disease.^{21,26} The SDQ provides a hierarchic classification for relevant insomnia, relevant hypersomnia, subclinical disorders or absence of sleep complaints. The criteria adopted were the frequency, persistence, and relevance of the disturbance indicated by DSM-IV and by the International Classification of Sleeping Disorders. A specific question of the SDQ concerns hypnotics (prescription use). The questionnaire has been shown to be a sound instrument for assessing the incidence of sleep disorders in epidemiologic studies and for diagnostic screenings because of its clarity, rapidity, and inherent validity.

CCI

The CCI is a composite score of multiple comorbid conditions and age.^{24,27} Comorbid conditions are given a score of 1 to 6. The CCI assigns 1 point to myocardial infarction, congestive heart failure, peripheral vascular disease, cerebrovascular diseases, dementia, chronic pulmonary disease, connective tissue disease, peptic ulcer disease, mild liver disease, and diabetes without end-organ damage. Two points are assigned to hemiplegia, moderate or severe renal disease, diabetes with end-organ damage, tumor without metastasis, acute and chronic leukemia, and lymphoma. A total of 3 points are assigned to moderate or severe liver disease, and 6 points are assigned to metastatic solid tumors and acquired immune deficiency syndrome. Finally, for each decade more than 40 years of age, a score of 1 is added.

Statistical Analysis

Patients were divided into categories according to questionnaire responses. Means and SDs were calculated within each

Table 1 Sleep Complaints

Complaints	Percentage (%)
Sleep latency > 30 min	42.6
Frequent awakenings	62.9
Early awakenings	57.4
No refreshing sleep	50.0
Snoring	12.9
Snoring+ sleep apnea	7.4
Nightmares	29.6
Sonnambulism	7.4

subgroup for each individual parameter. Comparison between groups was performed by analysis of variance.

Results

The questionnaire identified 10 patients with no sleep disorders, 19 patients with subclinical disorders, and 23 patients with insomnia. Only 19.3% of the patients did not present with sleep disorders. Sleep complaints are detailed in Table 1.

Data in Table 2 did not disclose any difference between groups relative to body mass index, systolic blood pressure, diastolic blood pressure, levels of blood urea, plasma creatinine, uric acid, hemoglobin, plasma albumin, serum sodium, serum potassium, serum calcium, serum phosphate, PTH, or classes of antihypertensive drugs.

Patients without sleep disorders slept 8.4 ± 1.1 hours, those with subclinical disorders slept 5.9 ± 1.1 hours, and the insomniac patients slept 6.1 ± 2.2 hours ($P < .002$). Among patients needing hypnotics 2 had subclinical sleep disorders and 11 were insomniacs.

The CCI averaged 4.1 ± 1.8 in patients without sleep complaints, 5.2 ± 2.5 in patients with subclinical disorders, and 5.3 ± 1.9 in insomniacs (P value not significant).

Discussion

The study showed that sleeping disorders occur in nearly 80% of recently diagnosed CKD patients. Patients without sleep disorders slept more hours than those with subclinical disorders or insomniacs. Sleep disorders occurred in patients with a mean CCI less than 6, normal plasma albumin level, phosphate level, and PTH level. Patients who were still off erythropoietin were slightly anemic and did not reach the target for systolic blood pressure. However, hemoglobin and blood pressure did not discriminate between patients with and without sleep complaints.

The present data should be compared with those of Iliescu et al²² who were the first to report on poor sleep in 53% of 120 grade 4 CKD patients. However, their data were obtained in patients with nearly comparable comorbidity index scores, greater impairment of renal function, higher blood urea concentrations, and requiring erythropoietin to achieve hemoglobin concentrations comparable with those present in our patients. The study by Iliescu et al²² also disclosed that sleep problems do not increase with disease progression, but dete-

Table 2 Renal Function, Sleep Duration and Comorbidities in Patients With No Sleep Disorders, With Subclinical Sleep Disorders, and Insomniacs

	All	NoSD	SSD	I	P
n	52	10	19	23	
Male, %	59	80	63	48	NS
Age, y	61.2 ± 19.3	67.7 ± 15.0	59.1 ± 21.1	67.7 ± 15.2	NS
Body mass index, kg/m ²	26.7 ± 4.7	25.6 ± 14.1	27.2 ± 5.0	26.7 ± 4.9	NS
Systolic blood pressure, mm Hg	138 ± 19	145 ± 15	139 ± 23	134 ± 7	NS
Diastolic blood pressure, mm Hg	79 ± 10	81 ± 10	80 ± 10	78 ± 9	NS
Urea, mg/dL	74 ± 49	79 ± 17	69 ± 35	76 ± 35	NS
Creatinine, mg/dL	1.9 ± 0.8	2.0 ± 0.6	1.9 ± 0.9	1.9 ± 0.8	NS
Uric acid mg/dL	6.5 ± 2.0	6.4 ± 1.2	6.3 ± 1.9	6.7 ± 2.4	NS
PTH, pg/mL	78 ± 43	70 ± 45	68 ± 46	90 ± 40	NS
Hb, g/dL	11.7 ± 2.3	11.5 ± 1.8	11.8 ± 2.8	11.8 ± 2.0	NS
Albumin, g/dL	4.3 ± 0.8	4.1 ± 0.6	4.4 ± 1.0	4.3 ± 0.8	NS
Na, mEq/L	140 ± 4	139 ± 5	140 ± 4	140 ± 3	NS
K, mEq/L	4.7 ± 0.7	4.8 ± 0.6	4.6 ± 0.6	4.8 ± 0.8	NS
Ca, mg/dL	9.5 ± 0.7	9.6 ± 0.6	9.5 ± 0.8	9.4 ± 0.7	NS
P, mg/dL	3.6 ± 0.7	3.7 ± 0.7	3.6 ± 0.5	3.6 ± 0.5	NS
Hypotensives, no.	1.6	1.6	1.8	1.4	NS
Sleep duration, h	6.20 ± 2.0	8.4 ± 1.1	5.9 ± 1.8	6.1 ± 2.3	.002
CCI	5.3 ± 2.4	4.1 ± 1.8	5.2 ± 2.5	5.3 ± 1.9	NS

NOTE. Data shown are mean ± SD. Comparison performed by analysis of variance.

All, entire study population; NoSD, no sleep disorders; SSD, subclinical sleep disorders; I, insomniacs; NS, not significant.

riorate with lower hemoglobin concentrations. However, only a minority of patients had CKD grades 1 to 3. There was no association between the degree of renal impairment and the quality of sleep. The present data strongly support the conclusions of Iliescu et al²² and extend them to the early stages of renal functional impairment.

How can it be explained that patients in the early stages of renal disease, shortly after being diagnosed with CKD, have a disrupted sleep? It might be instrumental to analyze recent preliminary data obtained by polysomnography suggesting that mechanisms for poor sleep in CKD patients might be different from those in patients on maintenance hemodialysis,²³ even when the reduction in sleep time is identical. Functional and psychologic factors may play a more prominent role in CKD, whereas intrinsic sleep disruption secondary to treatment might play a major role in HD patients. Indeed, Harris et al²⁴ also showed that CKD per se might have an impact greater than renal functional loss.

We have not analyzed cumulatively the data in patients with subclinical disorders and those with insomnia because insomnia is associated with reduced physical health, a decrease in health status, and greater functional impairment in patients with chronic illness,²⁷⁻²⁹ and also because of the sample of patients studied.

Patients enrolled for the study with early CKD diagnosis may benefit from a low-protein alimentation, and it will be important to study the long-term effect on sleeping disorders. This finding, which needs to be confirmed in a larger cohort of patients, indicates that disordered sleep affects the lives of CKD patients as soon as a diagnosis of disease potentially progressing to end-stage renal disease was made.³⁰

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