Sleep Disorders in ESRD Patients Undergoing Hemodialysis

Mohammad Reza Abassi[1], Amin Safavi[3], Masoumeh Haghverdi[3], and Babak Saedi[2]

[1] *Nephrology Research Center, Tehran University of Medical Sciences, Tehran, Iran*

[2] *Department of Otolaryngology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran*

[3] *Department of Medicine, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran*

Received: 04 Jul. 2014; Received in revised form: 02 Jan. 2015, Accepted: 08 Jun. 2015

Abstract- Kidney failure affects different aspects of normal life. Among different manifestations, sleep problem can be considered as a common complaint of ESRD (End Stage Renal Disease) patients. In this study, we aimed to investigate the interrelationship between sleep disorders in ESRD patients and their characteristics. Through a cross-sectional study (2010-2011), 88 ESRD patients undergoing maintenance hemodialysis thrice weekly were recruited to enter the study. We used a self-administered questionnaire into which the data were reflected. The patients selected their specific sleep disorders using a nine-item scale while the Epworth Sleepiness Scale (ESS) determined both the presence and severity of sleep disorders. The data was finally analyzed with their baseline characteristics, dialysis characteristics, medication/stimulants use, and clinical and biochemical parameters. Over 95% of the patients had, at least, one specific sleep disorder while the ESS revealed 36.36% of patients as normal, 59.09% as having mild sleep disorders, and 4.54% as having moderate to severe sleep disorders. Sleep disorders were significantly correlated with older ages (P=0.035), dialysis dose (P=0.001), blood creatinine levels (P=0.037), upper airways obstruction (P=0.035), hepatomegaly (P=0.006), hepatic failure (P=0.001), higher blood TSH levels (P=0.039), history of hypothyroidism (P=0.005), and the use of levodopa (P=0.004), anti-hypertensive medications (P=0.006), benzodiazepines (P=0.006), Eprex (Erythropoietin) (P=0.001), Venofer (Iron Sucrose Injection) (P=0.013), and phosphate-binders agents (P=0.018). Sleep disorders are common findings among ESRD patients and seem to be a more complicated issue than a simple accumulation of the wastes products in the body. Whatever the causes of sleep disorders are, disorder-specific treatments should be considered.

Acta Med Iran, 2016;54(3):176-184.

Keywords: Sleep disorder; Hemodialysis; ESRD; Excessive daytime sleepiness; Sleep apnea; Renal disease

Introduction

Kidney failure affects different aspects of normal life. Among different manifestations, sleep problem can be considered as a common complaint in ESRD (End Stage Renal Disease) patients. Logically, this condition is also quite frequent in ESRD patients with no functional kidneys, even while regularly undergoing maintenance dialysis (1-6). In ESRD patients, sleep disorders usually present as insomnia, restless leg syndrome (RLS), obstructive sleep apnea syndrome (OSAS) or sleep apnea-hypopnea syndrome (SAHS), excessive daytime sleepiness (EDS), narcolepsy, sleepwalking, nighttime waking, nightmares, rapid eye movement behavioral disorder (RBD), periodic limb movements (PLM) in sleep, and poor concentration (1-5,7,8) which sometimes are ascribed to the uremic state itself (8), while improvements to the uremic state, either by dialysis or renal transplant could not necessarily ameliorate the sleep disorders (2,9). This implicates more complicated processes causing sleep disorders in ESRD patients which are not fully understood yet.

Whatever the causes of sleep disorders are, the shortage of sleep and its low quality in ESRD patients make the nighttime rest insufficient for their physiologic needs and subsequently keeping them sleepy, exhausted and low concentrated during daily activity. Furthermore, the disease and dialysis co-morbidities in addition to sleep disorders significantly lower their quality of life (3,8,10) putting more stress on them while these patients have been reported having higher illness intrusiveness and worse self-perceived health, (3) and also apt to more severe depression; (4) even significant psychological problems have been reported being associated with sleep

Corresponding Author: B. Saedi
Otolaryngorhinology Research Center, Imam Khomeini Hospital Complex, Tehran University of Medical Sciences, Tehran, Iran
Tel: +98 21 66581628, Fax: +98 21 66581628, E-mail address: saedi@tums.ac.ir

disorders in ESRD patients (9). With all these, sleep health of ESRD patients sometimes is obscured from the attention of their nephrologists (2) despite there are some treatments for some specific sleep disorders (3).

So, the vast problems coming from sleep disorders in ESRD patients raise the need for studies in more details for the scope of the neuromuscular impairments to be fully figured out, and for new treatments to be discovered. We conducted a cross-sectional investigation where the presence and the severity of sleep disorders in ESRD patients are determined and analyzed with multiple variables including the patients' and dialysis characteristics, clinical and laboratory findings and specific medications and stimulants they may have been using.

Materials and Methods

The Study was conducted in dialysis center of Imam Khomeini Hospital (an academic affiliated hospital of Tehran University of Medical Sciences) between 2010 and 2011. With the aim to investigate the presence and severity of sleep disorders among ESRD patients and the factors impacting on these disorders, we designed a cross-sectional study and recruited 88 consecutive ESRD patients undergoing maintenance hemodialysis thrice weekly. Entrants to this study agreed to participate by signing our printed informed consent forms while we were obliged to keep their personal information confidential. A self-administered questionnaire with several sections was used for data collection; some fields were filled by the patients and some by the medical staff. The following subjects were the questioned areas in the questionnaire:

Patients' Baseline Information

As filled in by the patients, they determined their age, gender, and marital status. Weight and height were also acquired to calculate their body mass index (BMI).

Determination of Sleep Disorders

A nine-item problem-specific sleep disorder scale was used to determine the patients' specific sleep disorders; this scale was based on the five-item Insomnia Index (11) which was modified with four extra items from other studies. For this item patients had no limitations, and they could mark as many items as they wanted. Marking of at least one item was considered as having a sleep disorder. On the other hand, both the presence and the severity of sleep disorders in these patients were determined using the Epworth Sleepiness Scale (ESS), a 24-score scale which asks the patients likelihood to doze or fall asleep in the eight following conditions: 1.sitting and reading; 2.watching TV; 3.sitting inactive in a public place (e.g. theatre or meeting); 4.as a passenger in a car for an hour without a break; 5.lying down to rest in the afternoon; 6.sitting and talking to someone; 7.sitting quite after a lunch without alcohol; and 8.in a car while stopped for a few minutes in traffic. The score for each item ranges from 0 to 3 while the 0 score goes to no chance to doze, score 1 to a slight chance, 2 to moderate and 3 to high. (12) Based on the ESS, scores of 0 to 8 were considered as normal, 9 to 12 as a mild sleep disorder, and 13 to 24 as moderate to severe disorders. Accordingly, the nine-item scale represented the diversity of problems among the ESRD patients while the ESS scores measured both the presence and the severity of sleep disorders. The ESS categorizations were used for bivariate and multivariate analysis with other variables.

Dialysis Characteristics

Dialysis dose and shift were the two variables taken into account here. Dialysis dose was defined as in Kt/V formula, in which K stands for dialyzer clearance of urea, t for dialysis time and V for the volume of distribution of urea; while dialysis shift referred to the morning, afternoon or evening shifts when the patients were undergoing hemodialysis. By the way, dialysis duration (mean time of being connected to the dialyzer) and weight loss during dialysis were taken into account.

Clinical and Laboratory Findings

A thorough ENT examination was performed looking for facial skeletal deformities, nasal structural abnormalities, nasal discharge or inflammation, glossopharyngeal malformations (e.g. macroglossie, long uvula, the excessive tissue of soft palate, hanging and hypertrophy of tonsillar folds, webbing), airways obstruction, and neck circumference. These were mostly the causes potentially and anatomically affecting the respiration. On the other hand cardiac and respiratory examinations took the chest deformities, cyanosis, clubbing, rales, wheezes, hepatomegaly, jugular vein pressure (JVP), arrhythmias, edema and ascites into account, while the past medical history unveiled possible positive histories for concomitant cardiovascular diseases, diabetes, hepatic failure, renal diseases other than the cause leading to ESRD, respiratory diseases, gastroesophageal reflux disease (GERD), or endocrine malfunctions. Simultaneously, recent lab values of the patients (including fasting

plasma glucose, and blood levels of hemoglobin, phosphorus, calcium, creatinine, urea, Albumin, triglycerides, cholesterol, and thyroid hormones) were screened to evaluate the latest status of the patients.

Medications and Stimulants Use

Stimulants like cigarette smoking or beverages like tea, coffee, and alcohol in addition to opium use, which may have an impact on sleep were also reflected in the sheets. By the way, the role of specific medications - administered for ESRD patients - on sleep was also taken under investigation; these medications were: calcitriol, L-Dopa, benzodiazepines, anti-hypertensive medications, clonidine, antiplatelets, antidiabetic agents, Eprex (erythropoietin), Venofer (iron sucrose injection), vitamin supplements, and phosphate binders.

Ethical approval

The protocol of this study was approved by the Institutional Review Board of the Tehran University of Medical Sciences. Detailed information about the study was given to the participants, and a written informed consent was obtained from each one. All aspects of the study were conducted according to the Declaration of Helsinki.

Statistical Methods

Descriptive and comparative analysis of the data was done using SPSS (version11.5). T-test, ANOVA, and logistic regression analysis test were used to compare the results. The values were evaluated using descriptive statistical methods (mean ± SD) and the results were expressed at a significance level of $P < 0.05$.

Results

A total of 88 ESRD patients who were regularly undergoing maintenance hemodialysis thrice weekly entered to the study. Fifty-four (61.36%) patients were male, making a 1:0.62 male to female ratio. Mean age was calculated as 56.88 ± 7.63 years (ranging from 24 to 93). The mean body mass index was also 24.52 ± 3.67 kg/m2 ranging from 16.40 to 34.85. Among these participants, 64 patients (72.72%) were married, 16 (18.18%) were single but not living alone, and eight (9.09%) were single and living alone. Table 1 outlines patients' baseline characteristics in sleep-disorder-severity groups.

Table 1. Patients' baseline information in sleep-disorder-severity groups

Baseline Information		Amount in Sleep-Disorder-Severity Groups (%)		
		Normal	Mild	Moderate to Severe
Age	Mean	52.78	53.31	59.50
	SD	3.85	2.98	4.02
	Range	30 to 93	24 to 83	40 to 74
Gender	Male	17 (19.31)	35 (39.77)	2 (2.27)
	Female	15 (17.04)	17 (19.31)	2 (2.27)
Body Mass Index (BMI)	Mean	24.42	24.58	24.51
	SD	6.54	6.23	5.93
	range	19.72 to 29.13	16.40 to 34.85	20.32 to 27.88
Marital Status	Single and alone	3 (3.40)	5 (5.68)	0
	Singlebut not alone	8 (9.09)	8 (9.09)	0
	married	21 (23.86)	39 (44.31)	4 (4.54)

The nine-item problem-specific sleep disorder scale revealed that 84 patients (95.45%) had marked at least one item, and 64 (72.72%) had marked more than one. Table 2 displays the frequency of sleep problems the patients have been suffering from, with the early waking in the morning as the most frequent problem. Based on the ESS, 32 patients (36.36%) were considered as "normal," 52 (59.09%) as having "mild" sleep disorders, and 4 (4.54%) as having "moderate to severe" problems.

Table 2. Sleep disorder frequencies

Sleep Disorder	Frequency (%)
Frequent waking during night	39 (44.31)
Morning headache	14 (15.90)
Loud snoring	25 (28.40)
Daytime dozing and lack of concentration	35 (39.77)
Nocturnal urine frequency	5 (5.68)
Daytime sleepiness	34 (38.63)
Having problems going to sleep while in bed	35 (39.77)
Waking very early in the morning	57 (64.77)
Nighttime waking and having problems going to sleep again	39 (44.31)

Comparative Analysis

Sleep Disorders versus Patients' Baseline Characteristics

Patient's age was a factor of statistical significance, showing that older patients had more severe sleep disorders. (P=0.035). However, it can be defined as a confounding factor because of the high prevalence of confounding factors in the elderly group. That's while sex was neither significantly correlated with the presence of sleep disorders (P=1.000) nor with their severity (P=0.440). Despite the greater number of married patients in this case series, marital status also had not a significant role in the presence of sleep disorders (P=0.214), nor had an impact on the severity of the disorder (P=0.730). BMI also had the same story (P=0.653).

Dialysis Dose

Dialysis dose and the presence of sleep disorders were significantly correlated (P<0.001), and as displayed in Figure 1, patients with more severe sleep disorders had received higher dosages of dialysis. By the way, dialysis duration and weight loss during dialysis also had not a significant correlation between the severity of sleep disorder (P=0.701 and P=0.757, respectively.

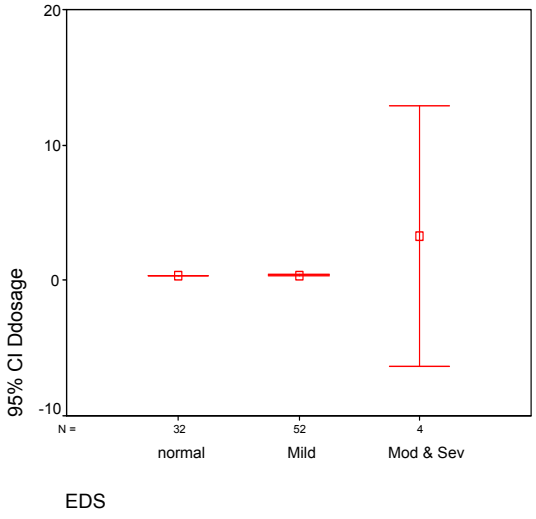

Figure 1. Dialysis dosage and sleep disorder severity

Dialysis Shifts

Morning, afternoon, or evening dialysis shifts neither had a significant role in the presence of sleep disorders (P=0.118) nor in the severity of the disorder (P=0.187) in this study.

Sleep Disorders versus Clinical and Laboratory Findings

ENT examination

Having an ENT abnormality was not significantly correlated with the presence of a sleep disorder, except for airways' obstructions (*P*=0.035); while the ENT abnormalities could not significantly impact on the severity of sleep disorder (*P*=0.68). On the other hand, sleep disorders were significantly more severe in those without ENT abnormalities (*P*=0.014).

Cardiovascular and Respiratory Examinations

No physical finding was significantly correlated with the presence of sleep disorder while the only finding which could signify a correlation with the severity of sleep disorder was hepatomegaly (*P*=0.006).

Systemic Diseases

No systemic disease was correlated with the presence of a sleep disorder, while as summarized in Table 3 hepatic failure was significantly correlated with the severity of sleep disorder. On the other hand, the presence of sleep disorders was also significantly correlated with positive histories of hypothyroidism (*P*=0.005). History of renal diseases other than the leading cause of ESRD also had not a significant association to the presence of a sleep disorder (*P*=0.356).

Table 1. The role of concomitant organic diseases with ESRD in sleep-disorder-severity groups

Organic disease	Sum of the disease (%)	Amount in Sleep-Disorder-Severity Groups (% in group)			*P*-Value
		Normal	Mild	Moderate to Severe	
Cardiovascular	72 (81.81)	24 (75)	44 (84.61)	4 (100)	0.339
Diabetes	33 (37.5)	8 (25)	23 (44.23)	2 (50)	0.182
Hepatic	6 (6.81)	0	4 (7.69)	2 (50)	0.001*
GERD	35 (39.77)	8 (25)	24 (46.15)	3 (75)	0.053
Respiratory	13 (14.77)	3 (9.37)	8 (15.38)	2 (50)	0.095
Renal**	25 (28.40)	5 (15.62)	18 (34.61)	2 (50)	0.107

*significant; **renal diseases here refer to those other than the leading cause of ESRD

Laboratory Findings

Blood levels of hemoglobin, phosphor, calcium, thyroid hormones, fasting plasma sugar, urea, albumin, triglycerides, and cholesterol were not significantly correlated with the presence of sleep disorders; except for creatinine which patients with sleep disorders had a significantly lower means of blood creatinine levels (*P*=0.037); whilst they had higher maximums of blood creatinine levels than the rest entrants. Blood TSH levels also signified a correlation with sleep disorders (*P*=0.039) (Figure 2).

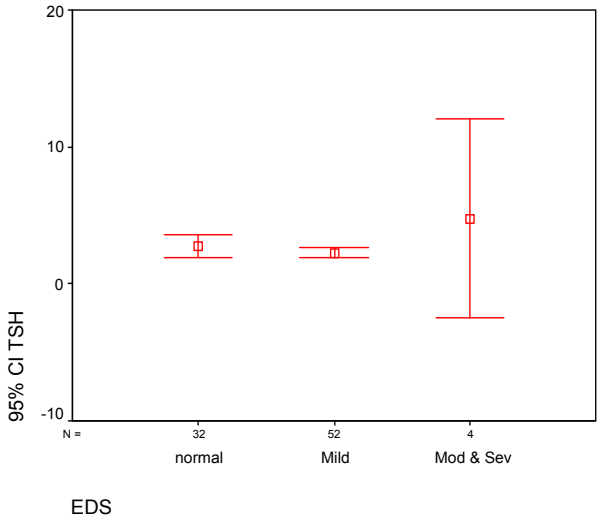

Figure 2. blood TSH levels and sleep disorder severity

Sleep Disorders versus Medications and Stimulants Use

Table 4 shows the frequency of medications and stimulants use among the patients. No specific stimulant, including cigarette smoking (*P*=0.726), tea (*P*=0.256), coffee (*P*=0.359), alcohol (*P*=1.000), and opium (*P*=0.450) could significantly correlate with the presence of sleep disorders, nor impact on sleep disorder severity. But, for the six drugs in the Table reaching the significance level, L-Dopa use was lower in patients experiencing sleep disorders, and anti-hypertensive medications use precipitated in lower rates of sleep disorders,

Table 2. Drug and stimulants consumption rates in patients

Drug or Stimulant	Total Number of Users (%)	Amount in Sleep-Disorder-Severity Groups (% in group)			*P*-value
		Normal	Mild	Moderate to Severe	
Tea	84 (95.45)	30 (93.75)	50 (96.15)	4 (100)	0.793
Coffee	12 (13.63)	2 (6.25)	9 (17.3)	1 (25)	0.284
Alcohol	3 (3.40)	0	3 (5.76)	0	0341
Opium	4 (4.54)	1 (3.12)	3 (5.76)	0	0.772
Calcitriol	52 (59.09)	17 (53.12)	32 (61.53)	3 (75)	0.601
L-Dopa	9 (10.22)	0	7 (13.46)	2 (50)	0.004*
Benzodiazepines	21 (23.86)	3 (9.37)	15 (28.84)	3 (75)	0.006*
Clonidine	5 (5.68)	0	4 (7.69)	1 (25)	0.072
Anti platelet	24 (27.27)	4 (12.5)	19 (36.53)	1 (25)	0.056
Anti diabetic agents	19 (21.59)	5 (15.62)	13 (25)	1 (25)	0.589
Eprex	78 (88.63)	23 (71.87)	51 (97.08)	4 (100)	0.001*
Venofer	65 (73.86)	18 (56.25)	43 (82.69)	4 (100)	0.013*
Vitamins	84 (95.45)	30 (93.75)	50 (96.15)	4 (100)	0.793
Phosphate binders	59 (67.04)	16 (50)	41 (78.84)	2 (50)	0.018*
Anti hypertensives	62 (70.45)	16 (50)	43 (82.69)	3 (75)	0.006*

*: significant

Discussion

Sleep disorders are a common occurrence among ESRD patients (1-6). The current study showed over 95% of patients to have at least one sleep disorder. These problems add to ESRD patients' co-morbidity and worsen their quality of life. The management of sleep disorders is hence of great benefit to ERSD patients. It is a process whose details require better understanding.

In this study, a relatively large group of ESRD patients regularly undergoing thrice-weekly hemodialysis was recruited. A variety of factors were involved in the selection process. These included patients' demographic data, clinical and laboratory findings, past medical histories, and different uses of medications and stimulants. This was done to cover most of the suspected variables which may have a role in the development of sleep disorders in ESRD patients.

The study revealed that older patients had more severe sleep disorders that were congruent with the literature (2,5,7). Sleep disorders in older patients may be attributable to their having less efficient renal function than that of the general population. However, in ESRD patients with no renal function, and where hemodialysis adequacy levels are reached, this finding may be due to geriatric morbidities. Gender did not show a significant correlation with sleep disorders while gender dominance in sleep disorders have been reported both in females (4,13) and in males (14). Married patients were thought to have fewer sleep disorders due to spousal support, but no significant correlation was observed, ruling out family support as a contributory factor to improved sleep quality. BMI also was not considered as a factor in our study (13). However, sleep respiratory disturbances are reportedly associated with BMI (14,15), and insomnia has been associated with higher BMIs in ESRD patients (6).

The patients in this study had all been undergoing

thrice-weekly maintenance hemodialysis. None of the patients were undergoing peritoneal dialysis, and as such we were unable to investigate whether this type of dialysis plays a role in sleep disorders. Certain studies state that this is not the case (5) while others point to a poorer quality of sleep being observed in patients undergoing hemodialysis (1,10). In the present study, a significant relationship was found to exist between dialysis dose and the existence of sleep disorders. Results indicated that patients with lower doses of dialysis had more severe sleep disorders (7). This is assumed to be caused by the hypothetical accumulation of waste products in the body which are filtered out by higher doses of dialysis. However, as discussed later in this section, waste accumulation (the uremic state) does not necessarily cause sleep disorders. Differences in dialysis shift are also of importance in evaluating sleep disorders in ESRD patients. The majority of studies have shown more sleep disorders in patients undergoing morning dialysis shifts (2,5,16). A better quality of sleep has been observed after nocturnal dialysis (16). Insomnia has been associated with afternoon shifts (13). The present study, however, did not show any correlation between dialysis shifts and sleep disorders. Dialysis duration is another factor thought to have an impact on sleep disorders. However, current results indicated that both the duration of the dialysis sessions and the time of day at which they were conducted had no impact upon the presence of sleep disorders (5).

Present results showed that patients with higher doses of dialysis had more severe sleep disorders. Hypothetically, it ought to be assumed that patients with higher doses of dialysis should experience fewer sleep problems. As such, these results seem to be logically incorrect. This discrepancy can be explained, however, by considering the daily method of dialysis and the fact of patients taking routine naps in the middle of the day.

Sleep disorders are sometimes attributed to the uremic state in patients with non-functional kidneys (8). Waste solutes accumulate in the body and subsequently impact the CNS, with sleep disorders as a presentation of autonomic dysfunction. This is theoretically approved by some studies where renal transplants have ameliorated sleep disorders (16), or where sleep disorders have improved soon after afternoon dialysis shifts (16). Contrary to these findings, conventional renal replacement therapies are not reported to have a significant effect on sleep disorders in ESRD patients (8). Such patients may even experience a worse quality of sleep than those undergoing dialysis (9). This implies that sleep quality is not necessarily affected by changes in the main biochemical parameters in transplant patients (9), and also that sleep quality remains low despite well-preserved renal function (9). Accordingly, sleep disorders, in both ESRD patients undergoing regular maintenance hemodialysis and transplant patients is not necessarily associated with waste accumulation in the body, attenuating the role of the uremic state as a possible cause. On the other hand, sleep disorders in these patients may be due to causes other than those biochemical parameters routinely evaluated as a way of measuring the efficacy of dialysis. An example of this is β2 microglobulin, which is not removed by "low flow" dialysis. Since β2 microglobulin accumulates in the body, its precipitation can result in amyloid formation and amyloidosis. This is a probable cause of carpal tunnel syndrome (CTS), with amyloid precipitations in the carpal tunnel and bone cysts in the wrist being more frequently observed among dialytic patients. However, CTS can itself result in nightly pains and paresthesia, which are sometimes the cause of sleep disorders. Although chemical accumulation in the body is still thought to be the main factor involved in sleep disorders, these are sometimes ascribed to psychological problems in ESRD patients (9). Furthermore, risk factors for sleep disorders in transplant patients (e.g. obstructive sleep apnea) have been regarded as predictors of graft loss (17), suggesting that the continuation of sleep disorders, even after renal transplantation can be harmful in patients with kidney malfunction. Similarly, the individual characteristics of transplant patients – their BMI, for instance – are also reported to be risk factors for sleep disorders (15). All of the above points indicate that sleep disorders in ESRD patients undergoing dialysis or renal transplantation are due to a more complicated process that the simple accumulation of waste in the body, as patients often continue to experience sleep disturbances after regaining the full function of their kidneys.

In the current study, the only external factors were shown to have a role in sleep disorders were thyroid stimulating hormone (TSH) and creatinine. Higher TSH levels were significantly related to the presence of sleep disorders, as were positive histories of hypothyroidism. These findings indicate that lower thyroid function may play a role in sleep disorders both with high TSH and low T3 and T4 (clinical hypothyroidism) and with high TSH and normal T3 and T4 (subclinical hypothyroidism). We can hence conclude that thyroid function should be accurately evaluated since it has a direct impact on bodily metabolism, which sometimes is impaired in patients with renal failure. Patients in our

study experiencing sleep disorders also had significantly lower mean blood creatinine (Cr) levels. Further investigation also revealed these patients to have higher maximums of blood Cr. This finding may indicate that peak levels of blood Cr have a role in sleep disorders, perhaps relating to Cr-toxicity levels being reached, even when these patients have a lower mean blood Cr. This peaking of Cr levels was not necessarily related to poor patient control since mean Cr levels were lower than those of other similar patients. However, the higher maximums of blood Cr require further investigation.

The main cause of anemia in ESRD patients is usually low renal production of erythropoietin (EPO), although iron deficiency, inflammation, hyperparathyroidism, folate or cyanocobalamin deficiency, and sometimes aluminum toxicity are other possible causes. While blood hemoglobin (Hb) in sleep apneic patients is elevated, this may be because a higher concentration of Hb provides more oxygen binding units. These units are able to function more effectively under the low oxygen exchange rates seen in apneic patients. This is probably the reason EPO has been reported to ameliorate sleep disorders in ESRD patients (16), and why lower Hb levels have been associated with sleep disorders (4,6). Contrary to these findings, the role of hemoglobin concentration or erythropoietin administration in sleep disorders has been confirmed in some studies (5,13). In the present study, hemoglobin levels were not shown to have a significant relationship to sleep disorders, while erythropoietin administration was significantly associated with lower rates of sleep disorder.

The volume overload in CKD patients and its subsequent hypertension increase the need for anti-hypertensive treatment. Hypertension control lowers the risk of disease development since these patients have minimal renal function and antihypertensive treatment helps preserve what renal function remains. Epidemiologic studies of ESRD patients undergoing dialysis have shown that lower blood pressure is associated with a worse prognosis implying that the presence of risk factors such as hypertension are associated with better prognoses. This does not mean hypertension in ESRD patients ought to be left untreated. Its presence, however (for which the patient is taking medication) is a good prognostic indicator. In the current study, the use of anti-hypertensive medications was associated with lower rates of sleep disorder. Research into whether anti-hypertensive medication is a risk factor for sleep apnea in ESRD patients is ongoing (7). Benzodiazepines were also significantly helpful in lowering sleep disorders, although this medication has been reported as causing a lower quality of life in ESRD patients (10). Lower rates of L-Dopa were used in this study, indicating that L-Dopa can reduce the presence of sleep disorders in ESRD patients. This observation has been confirmed specifically in regard to the reduction of RLS by the use of levodopa and carbidopa (18-20). Contrary to these findings, however, it has been reported that although dopa derivatives (L-Dopa and Carbidopa) could be effective in reducing nightly leg movement, the sleep disorders in these patients remained unchanged (20). This finding may differentiate sleep disorders from autonomous dysfunctions such as RLS. The role of cigarette smoking and alcohol consumption in sleep disorders remains controversial (2,13). In the present study, we did not find a significant correlation between their consumption and both the presence and severity of sleep disorders.

This study shows that sleep disorders in ESRD patients are due to a more complicated process than the simple accumulation of waste solutes in the body. Results suggest that symptomatic treatment may also not improve sleep quality, necessitating a further and more detailed investigation into the possible mechanisms leading to sleep disorders in ESRD patients.

Sleep disorders are common findings among ESRD patients and seem to be a more complicated issue than the simple accumulation of waste solutes in the body. Whatever the causes of these sleep disorders, disorder-specific treatments may sometimes be effective.

References

1. Jurado-Gamez B, Martin-Malo A, Alvarez-Lara MA, et al. Sleep disorders are underdiagnosed in patients on maintenance hemodialysis. Nephron Clin Pract 2007;105(1):c35-42.
2. Merlino G, Piani A, Dolso P, et al. Sleep disorders in patients with end-stage renal disease undergoing dialysis therapy. Nephrol Dial Transplant 2006;21(1):184-90.
3. Mucsi I, Molnar MZ, Rethelyi J, et al. Sleep disorders and illness intrusiveness in patients on chronic dialysis. Nephrol Dial Transplant 2004;19(7):1815-22.
4. Pai MF, Hsu SP, Yang SY, et al. Sleep disturbance in chronic hemodialysis patients: the impact of depression and anemia. Ren Fail 2007;29(6):673-7.
5. Sabbatini M, Minale B, Crispo A, et al. Insomnia in maintenance haemodialysis patients. Nephrol Dial Transplant 2002;17(5):852-6.
6. Wei CY, Chung TC, Wu SC, et al. The subjective sleep quality and heart rate variability in hemodialysis patients.

Ren Fail 2011;33(2):109-17.
7. Chen WC, Lim PS, Wu EC, et al. Sleep behavior disorders in a large cohort of chinese (Taiwanese) patients maintained by long-term hemodialysis. Am J Kidney Dis 2006;48(2):277-84.
8. Perl J, Unruh ML, Chan CT. Sleep disorders in end-stage renal disease: 'Markers of inadequate dialysis'? Kidney Int 2006;70(10):1687-93.
9. Sabbatini M, Crispo A, Pisani A, et al. Sleep quality in renal transplant patients: a never investigated problem. Nephrol Dial Transplant 2005;20(1):194-8.
10. Kutner NG, Zhang R, Huang Y, et al. Association of sleep difficulty with Kidney Disease Quality of Life cognitive function score reported by patients who recently started dialysis. Clin J Am Soc Nephrol 2007;2(2):284-9.
11. Bastien CH, Vallieres A, Morin CM. Validation of the insomnia severity index as an outcome measure for insomnia research. Sleep Med 2001; 2(4):297-307.
12. Johns MW. Daytime sleepiness, snoring, and obstructive sleep apnea. The Epworth sleepiness scale. Chest 1993;103(1):30-6.
13. Al-Jahdali HH, Khogeer HA, Al-Qadhi, et al. Insomnia in chronic renal patients on dialysis in Saudi Arabia. J Circadian Rhythms 2010;8(1):7.
14. Argekar P, Griffin V, Litaker D, et al. Sleep apnea in hemodialysis patients: risk factors and effect on survival. Hemodial Int 2007;11(4):435-41.
15. Mallamaci F, Leonardis D, Tripepi R, et al. Sleep disordered breathing in renal transplant patients. Am J Transplant 2009;9(6):1373-81.
16. De Santo RM, Bartiromo M, Cesare MC, et al. Sleeping disorders in patients with end-stage renal disease and chronic kidney disease. J Ren Nutr 2006;16(3):224-8.
17. Szentkiralyi A, Czira ME, Molnar MZ, et al. High risk of obstructive sleep apnea is a risk factor of death censored graft loss in kidney transplant recipients: an observational cohort study. Sleep Med 2011;12(3):267-73.
18. Sandyk R, Bernick C, Lee SM, et al. L-dopa in uremic patients with the restless legs syndrome. Int J Neurosci 1987;35(3-4):233-5.
19. Trenkwalder C, Stiasny K, Pollmacher T, et al. L-dopa therapy of uremic and idiopathic restless legs syndrome: a double-blind, crossover trial. Sleep 1995;18(8): 681-8.
20. Walker SL, Fine A, Kryger MH. L-DOPA/carbidopa for nocturnal movement disorders in uremia. Sleep 1996;19(3):214-8.