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Original Article

Poor Quality of Sleep in Patients on Chronic Hemodialysis

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Abstract

Introduction: Sleep disorders (SD) are common in patients with renal failure, particularly in those on dialysis. This can impair their daily quality of life and worsen their cardiovascular prognosis. **Objective:** Our work aimed to describe the prevalence and risk factors of SDs among chronic hemodialysis patients in the Nephrology and Dialysis Department of the Rabat Military Hospital, Morocco. **Patients and Methods:** The trial was designed as a prospective single-center study and included all hemodialysis patients in the nephrology department of the Rabat Military Hospital. For each patient, we assessed four SDs: insomnia, sleep apnea, restless legs syndrome, and excessive daytime sleepiness**. Results:** We included 52 patients; the mean age of the patients was 50 ± 17 year (range 24–76); male:female ratio was 1.1. SDs were found in 40 patients with a predominance of insomnia and sleep apnea syndrome (SAS), and multivariate logistic regression was used to identify factors associated with different SD Insomnia was correlated with anemia, excessive daytime sleepiness, and inflammation; SAS was correlated with age ≥50 years, obesity and excessive daytime sleepiness. Restless legs syndrome was associated with advanced age, excessive daytime sleepiness and presence of a biological inflammatory syndrome. **Conclusions:** Sleep disorders have a considerable impact on the quality of life of patients on dialysis, so it is essential to look for them and especially to determine the associated factors to control them.

Keywords: Excessive daytime sleepiness, hemodialysis, insomnia, restless legs syndrome, sleep apnea, sleep disorders

Introduction

Patients with chronic renal disease, and in particular chronic hemodialysis patients, are prone to various sleep disorders (SDs) that may affect their daily quality of life and contribute to increased their cardiovascular morbidity and mortality.[1] In comparison to the general population, the prevalence of SDs in patients with renal impairment is significantly increased due to the presence of usual risk factors such as age, gender, obesity and other factors specific to uremia and dialysis (anemia, uremic toxins, inflammation, side effects of drugs).[2]

Sleep disorders appear very early during stages 1 and 2 of chronic renal failure and may worsen with decreasing renal function.[2]

It's reported in other studies that up to 80% of dialysis patients complain of poor quality of sleep.[3]

Insomnia, sleep apnea, restless legs syndrome and excessive daytime sleepiness are the most commonly reported SDs.[4] Besides, studies have shown that SDs may increase the risk of cardiovascular death in patients with chronic renal failure.[3]

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Patients and Methods

The study was designed as prospective observational single-center study conducted in the renal nephrology and renal transplant department of the Mohammed V Military Training Hospital in Rabat. All the 52 chronic hemodialysis patients were recruited for this study. The inclusion criteria were: adult dialysis patients (over 18 years of age), chronic hemodialysis patients for more than 1 year, three sessions per week, 4 h each. In the included patients, the SDs studied were: Insomnia, sleep apnea syndrome (SAS), restless legs syndrome and excessive daytime sleepiness.

We conducted this study using a questionnaire in French and/or translated into dialectal Arabic, and based on the Insomnia Severity Index questionnaire which contains seven questions (difficulty falling asleep, difficulty staying asleep or

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waking too early in the morning etc.) whose answers are noted from 0 to 4, the sum of the scores obtained forming a score that can vary between 0 and 28. The risk of SAS was estimated with the non obstructive sleep apnea syndrome (NoSAS) score, which represents the weighted sum of the points attributed to the following five parameters: The choker, the body mass index, the snoring, the age, and the male sex. The maximum score is 17 points, and a threshold of ≥8 is associated with a high risk of sleep-disordered breathing.[4]

Restless Legs Syndrome (RLS) was assessed by the abridged version of the Cambridge-Hopkins RLS questionnaire analyzing 13 symptom intensity and frequency.[5] Excessive daytime sleepiness is evaluated by the Epworth Sleepiness Scale, which is a simple way to detect pathological daytime sleepiness and has eight questions, a total of more than 10 points suggesting the presence of pathological somnolence.[4]

In addition, clinical parameters (age, sex, medical history, smoking and alcohol consumption, underlying renal disease, blood pressure, temperature, dry weight), biochemical measurements (creatinine, urea, hemoglobin, fasting glucose, albumin C-reactive protein, calcemia, phosphatemia, and PTH 1–84) and dialysis metrics (frequency and duration of the dialysis session, dry weight, interdialytic weight gain, mean Kt/v) were collected from the medical records of the patients.

Descriptive and deductive statistical analyzes were performed with SPSS 18.0 software (SPSS Inc. Released 2009. PASW Statistics for Windows, Version 18.0, SPSS Inc., Chicago, IL, USA). The data are expressed as mean ± standard deviation or interquartile median interval or percentage according to their nature and distribution. The prevalence of each standard deviation has been estimated. The univariate and multivariate logistic regression analysis was used to identify the risk factors associated with different disorders. Insomnia, SAS and restless legs syndrome were considered independent variables and a model was constructed for each of them to identify the co-variables associated with each SD. Excessive daily sleepiness is common consequences of these SDs and was not considered a dependent variable in the multivariate analysis. The difference is considered statistically significant for $P < 0.05$. At the end of this statistical analysis, we will highlight the factors associated with the onset of these SDs.

Results

Fifty-two patients with the mean age of patients were 50 years ± 17 years with extremes ranging from 24 to 76 years were included in this study. The sex ratio (male/female) was 1.1. Mean dialysis duration was 60 ± 17 months. Cause of end-stage renal disease was unknown in 48% of cases, glomerulonephritis in 21% of cases, a tubulointerstitial disease in 12.8%, diabetes in 10.2% of cases and vascular disease in 8% of cases.

The clinical, biochemical and dialytic characteristics of patients are shown in Table 1. SDs were found in 40 patients (76.9%) with a predominance of insomnia (52%) and SAS (43%), excessive daytime sleepiness was found in 40% of patients and restless leg syndrome in 35% of patients. SDs were more common in patients between the ages of 40 and 60 (56%), 20% of patients were between 24 and 40, and 24% of patients were over 60 years old. The causes attributed to insomnia were chronic nocturnal pain in 63% of patients with an osteoarticular and neurological origin, anxiety in 21% of cases and depression in 16% of cases.

In univariate statistical analysis, the factors statistically correlated with the onset of insomnia are anemia and excessive daytime sleepiness [Table 2]. SAS is associated with older age, obesity and excessive daytime sleepiness. Restless legs syndrome has shown a significant association with advanced age, anemia and the presence of a biological inflammatory syndrome.

However, multivariate analysis identified anemia, excessive daytime sleepiness, and inflammation as factors associated with insomnia [Table 3]. Age ≥50 years, obesity and excessive daytime sleepiness also correlated with SAS. Restless legs syndrome is associated with advanced age, excessive daytime sleepiness and the presence of a biological inflammatory syndrome. Other parameters such as sex, dialysis quality,

Table 1: Demographic, anthropometric, laboratory and dialysis characteristics of the population study

Parameters	Results
Age (years)	50±17
Gender: male/female (%)	52/48
Cause of end stage renal disease (%)	
Glomerulonephritis	21
Vascular	8
Diabetic	10.2
Tubulointerstitial	12.8
Unknown	48
Dialysis duration (months)	60±17
BMI (kg/m^2) (%)	
18.5-25.0	22
25.1-30.0	60
30.1-35.0	15
Body weight (kg)	53±26.3
Interdialytic weight gain (kg)	2.3±1.5
Kt/v (%)	
>1.2	88
<1.2	12
C-reactive protein (mg/l)	12±8.2
Serum albumin (g/dl)	38±23
Serum hemoglobin (g/dl)	9±10.1
Serum phosphate (mg/l)	48±25
Serum calcium (mg/l)	77±31
Intact PTH (*n*: 1-84 pg/ml)	508±424

Results are presented as the mean±SD or relative frequency (%). BMI: Body mass index, SD: Standard deviation, PTH: Parathyroid hormone

Table 2: Univariate analysis of factors associated with sleep disorders

Variables	Insomnia		Sleep apnea syndrome		Restless legs syndrome	
	OR (CI)	*P*	OR (CI)	*P*	OR (CI)	*P*
Age ≥50 years	1.10 (0.85-3.11)	0.3	1.25 (1.06-3.89)	0.02	1.08 (0.49-2.82)	0.04
Gender (male)	1.1 (0.2-6.21)	0.5	1.45 (1.2-4.21)	0.72	1.22 (1.2-4.72)	0.38
Obesity	0.78 (0.5-1.72)	0.26	1.21 (1.07-5.12)	0.01	0.89 (0.23-1.65)	0.46
Hypertension	0.75 (0.8-1.21)	0.69	1.63 (0.83-4.16)	0.26	0.54 (0.61-1.34)	0.58
Diabetes	1.8 (0.6-4.67)	0.56	1.26 (0.61-4.21)	0.91	1.75 (0.59-3.35)	0.72
Excessive daytime sleepiness	1.1 (0.2-6.21)	0.02	1.52 (1.09-10.86)	0.03	1.29 (1.02-6.89)	0.03
Anemia	1.08 (1.06-3.48)	0.04	1.28 (0.59-7.31)	0.46	2.52 (1.21-4.98)	0.04
Biological inflammatory syndrome	1.1 (0.2-7.21)	0.06	1.05 (0.46-8.23)	0.24	1.13 (0.42-1.28)	0.02
Hypoalbuminemia	1.2 (0.5-2.25)	0.89	1.67 (0.89-2.21)	0.48	0.78 (0.66-3.12)	0.52
Low dialysis quality	0.89 (0.2-3.42)	0.56	0.96 (0.72-4.48)	0.21	0.27 (0.73-6.46)	0.72
IDWG>2.5	1.2 (0.82-1.85)	0.3	1.07 (0.18-6.03)	0.34	0.82 (0.12-4.81)	0.26

OR: Odds ratio, CI: Confidence interval, IDWG: Interdialytic weight gain

Table 3: Multivariate analysis of factors associated with sleep disorders

Variables	Insomnia		Sleep apnea syndrome		Restless legs syndrome	
	OR (CI)	*P*	OR (CI)	*P*	OR (CI)	*P*
Age ≥50 years	1.31 (0.85-2.89)	0.2	1.20 (1.11-3.87)	0.06	1.1 (0.51-2.14)	0.04
Gender (males)	1.1 (0.20-6.09)	0.5	1.24 (1.05-3.81)	0.53	1.14 (1.1-5.54)	0.43
Obesity	0.94 (0.62-1.51)	0.41	0.71 (1.07-4.22)	0.01	1.05 (0.34-1.77)	0.46
Hypertension	1.06 (0.6-1.21)	0.26	1.32 (0.83-6.13)	0.05	1.62 (0.71-1.49)	0.61
Diabetes mellitus	1.6 (0.5-4.21)	0.54	1.37 (1.21-5.21)	0.84	1.38 (0.62-4.21)	0.72
EDS	1.3 (0.2-5.21)	0.03	1.65 (1.12-9.16)	0.02	1.34 (1.1-6.21)	0.03
Anemia	1.1 (0.98-3.61)	0.02	1.22 (0.11-7.41)	0.51	2.52 (1.21-4.98)	0.04
SIB	0.87 (0.21-7.13)	0.06	1.21 (0.53-7.15)	0.28	0.97 (0.56-1.96)	0.06
Hypoalbuminemia	1.84 (0.61-2.25)	0.71	0.95 (0.89-2.24)	0.61	0.91 (0.73-3.41)	0.61
Low dialysis quality	1.2 (0.34-3.59)	0.6	1.34 (0.91-4.91)	0.18	0.24 (0.81-5.84)	0.78
IDWG>2.5	1.3 (0.9-1.74)	0.23	1.21 (0.23-6.11)	0.5	0.65 (0.12-4.63)	0.33

OR: Odds ratio, CI: Confidence interval, EDS: Excessive daytime sleepiness, SIB: Biological inflammatory syndrome, IDWG: Interdialytisc weight gain

arterial hypertension, diabetes, hypoalbuminemia, and interdialytic weight gain did not show a significant association with any of the SDs studied. None of our patients was followed or under specific treatment for these SDs.

Discussion

This study confirms that SDs are widespread in chronic dialysis patients. The prevalence in our series was close to that reported in Asian or European patients ranging from 41% to 86%.[5,6] These disorders were dominated by insomnia and SAS, consistent with literature data.[4] Restless legs syndrome and excessive daytime sleepiness were present in 35% and 40% of our patients respectively, contrasting with the low frequency reported in African-American patients.[7]

Chronic insomnia (>6 months) is classified as primary and secondary. In secondary causes, for example, there are chronic pains or the syndrome of muscular impatiences of the lower limbs preventing patients from sleeping at night. This disorder may also be primary with difficulty initiating and maintaining sleep during the night without apparent cause. A condition of "hyper-arousal" that affects sleepiness and sleep maintenance is then suspected. Sleep-wake disorders are also well-known in dialysis patients and would be secondary to dysregulation of melatonin secretion.[8]

SAS is characterized by repeated stops of night breathing secondary to partial pharyngeal (hypopnea) or complete (apnea) collapse.[9] It has been selected in several studies as an independent risk factor for morbidity and cardiovascular mortality in this population.[10] Obstructive SAS is the most common type in the general population, whereas central or mixed type SAS are more common in chronic kidney disease patients.[11]

Restless legs syndrome is an imperative need to move the legs, accompanied by unpleasant sensations in the legs relieved to movement, which occur at rest, usually in the evening or at night. This syndrome is associated in 80% of the cases with periodic stereotyped and repetitive movements of the lower limbs occurring during sleep.

They can disrupt sleep and cause daytime sleepiness in severe cases.[12] It is thought to be due to dysfunction of the dopaminergic system associated with cerebral iron deficiency with a disturbance of the iron permeability of the blood-brain barrier, without a direct relationship with plasma ferritin level[13] Dialysis patients frequently fall asleep during dialysis sessions and often experience excessive sleepiness during the day.[5,14]

Many factors such as diabetes, chronic renal failure neuropathy, uremia, psychiatric disorders, malnutrition, and anemia have been identified as associated with SDs in chronic hemodialysis patients.[15-18] In some studies, the low level of physical activity has been statistically significantly associated with insomnia.[19] Besides, some authors have investigated the seasonal rhythm of SDs in hemodialysis.[20] Nevertheless, in some studies, SDs do not appear to be related to biological data or dialysis parameters suggesting the involvement of disorders. Anxio-depressive in the genesis of these SDs.[19]

In our study, anemia and inflammation were associated with SDs; advanced age and obesity were associated with SAS. Advanced age and the presence of a biological inflammatory syndrome were associated with restless legs syndrome while excessive daytime sleepiness was correlated with all other SDs.

Our results confirm previous scientific data on SDs in chronic hemodialysis patients. Some variations are not explained by the clinical and biological data they are probably due to cultural characteristics that we do not understand yet.[21]

Despite the interesting results, our study has some limitations due primarily to its small sample size, the evaluation of SDs being based on questionnaires in the absence of para-clinical exams might not be able to estimate the prevalence of these SDs, and finally, despite the associated factors, no causal effect can be formally confirmed. The development of repeated epidemiological surveys may help to better understand the prevalence of SDs in chronic hemodialysis patients in Morocco. Prevention and care programs in Morocco must take into account all relevant structural, clinical, biological, and psychosocial determinants to promote more personalized prevention programs.

Conclusions

SDs are common in hemodialysis patients. They seem to be related to clinical, biological, dialytic and psychological factors. Early diagnosis is necessary to offer multidisciplinary care between nephrologists, psychiatrists, cardiologists, and neurologists.

Author's contribution

WA: Conception and realization of the study and drafting of the article. FL, AO and DEK Critical review and revision of the manuscript. All authors approved the final version.

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Conflicts of interest

There are no conflicts of interest.

Compliance with ethical principles

Ethical approval was granted by the Research Ethics Committee of the faculty of Medicine and Pharmacy, Mohammed V University, Rabat– Morocco and all participants provided verbal informed consent.

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