VERSITA

Cent. Eur. J. Med. • 7(1) • 2012 • 112-117
DOI: 10.2478/s11536-011-0115-0

Central European Journal of **Medicine**

Insomnia severity in chronic kidney disease patients with various therapies

Research Article

Marinela Z. Knezevic[1]*, Vladimir V. Djordjevic[2], Ivana C. Bivolarevic[1], Jelena J. Jovic[3], Vidojko M. Djordjević[4]

[1]*Medical Faculty, University of Kragujevac, Svetozara Markovica 69, Kragujevac 34 000, Serbia*

[2]*Clinic of Mental Health Protection, Clinical centre Nis, Zorana Djindjica 48 , Nis 18 000, Serbia*

[3]*Health Center Uzice, Primary Health Care Center, Jug Bogdanova 4, Uzice 31 000, Serbia*

[4]*Clinic of Nephrology, Clinical centre Nis, Zorana Djindjica 48, Nis 18 000, Serbia*

Received 22 May 2011; Accepted 28 August 2011

Abstract: The prevalence of insomnia is greater in end-stage renal disease. The aim of our study was to determine the frequency of insomnia and subclinical insomnia in patients with various dialysis therapy and kidney transplant recipients, in order to assess the severity of insomnia and examine whether there is a difference in severity among groups. In cross-sectional study, we evaluated 120 patients with terminal renal failure. Based on therapy, patients were divided into four groups: hemodiafiltration, standard bicarbonate dialysis, peritoneal dialysis and kidney transplant recipients. The severity of insomnia was evaluated through the use of the Insomnia Severity Index (ISI). Most patients who reported any kind of insomnia problems with ISI were on conventional dialysis (80%), followed by hemodiafiltration (76.7%) and peritoneal dialysis (63.3%). Transplant recipients had least difficulties with insomnia (46.7%). Insomnia Severity Index showed that insomnia in end-stage renal patients is not very severe. Most of the patients had "no clinically significant insomnia". Our findings indicate that patients on hemodiafiltration and transplant recipients have a significantly lower score on Insomnia Severity Index. Patients with end-stage renal disease have high frequency insomnia problems. However, our study shows that insomnia in these patients is not severe. Insomnia is the most frequent and severest in patients on standard bicarbonate dialysis.

Keywords: *Insomnia • Insomnia severity index • Dialysis • Kidney transplantation*

1. Introduction

Insomnia is characterized by: trouble falling asleep, maintaining sleep, or non refreshing sleep. Disturbances in sleep occur at least three times per week for at least one month; sleep disturbance results in marked personal distress or interference with personal functioning in daily living [1].

The prevalence of insomnia is greater in dialysis patients than in general population [2,3]. Studies have been reported to range from 45% to 90% [4-11]. Insomnia occurs at an early stage chronic kidney disease (CKD), too [12,13]. Its frequency in early CKD is 62.9% [12]. Much less information is available about the prevalence of insomnia in transplant patients [14,15].

Researches suggest that insomnia has an effect on physical, mental and social functions [16,17]. "Poor sleep" in dialysis patients is associated with lower quality of life [8,18,19]. Also there is no study that examines the severity of insomnia in patients with various dialysis therapy and kidney transplant recipients.

The aim of our study was to determine the frequency of insomnia and subclinical insomnia in patients on hemodiafiltration (HDF), bicarbonate hemodialysis (BHD),

* *E-mail: marinela.knezevic@gmail.com*

peritoneal dialysis (PD) and transplant kidney recipients, to assess the severity of insomnia by Insomnia Severity Index (ISI) and examine whether there is a difference among groups in severity. We also examined what kind of insomnia is the most common in these groups (initial, transitory, terminal or mixed).

2. Materials and methods

2.1. Subjects

Our observation cross-sectional study was conducted between December 2010 and January 2011 at the Clinic of Nephrology, Clinical centre Nis. We evaluated 120 patients with chronic renal failure. Patients were divided into four groups: hemodiafiltration (group 1), patients on standard bicarbonate dialysis (group 2), peritoneal dialysis (group 3) and kidney transplant recipients (group 4). All patients who were receiving dialysis therapy or whose health conditions were regularly monitored during the mentioned period participated in the research. The study was approved by the local Ethics Committee. The criteria for including patients in the study were: age >18 years, without communication barrier and provided informed consent. All patients in our study were stabile dialysis/ transplant patients without significant comorbidity. We excluded patients with psychiatric disorders and cognitive dysfunctions.

BHD patients were treated three times weekly, about 4.5 hours per session. HDF patients were treated three times weekly as well, for about 4.5 hours per session. PD was done as CAPD (continuous ambulatory peritoneal dialysis). All HD patients were in daily shifts and had adequate dialysis (Kt/V > 1.2).

Insomnia Severity Index (ISI). The Insomnia Severity Index has seven questions which demonstrate following issues in patients: the severity of their problem with falling asleep, staying asleep, waking up too early, satisfaction with their current sleep pattern, how much the patients' sleep problems are noticeable to others, how much the patients are worried about their current sleep problem and whether these problems influence their daily functioning. Each question score ranged from 0 to 4. The seven answers are added up to get a total score. A higher score indicates severe insomnia. The ISI is a reliable and valid instrument to quantify perceived insomnia severity [20].

2.2. Statistical methods

Data were expressed as mean ± standard deviation and frequency (%). The Kolmogorov-Smirnov test was used for testing variable's normality. After we had given non-normally distributed variables the statistical significance among the study groups was assessed by using the non-parametric Kruskal-Wallis Test (three or more categories) and Mann-Whitney Tests (two categories). Chi-square test was applied to compare percentage. Linear regression analysis was used to determine factors affecting ISI. Analyses were performed using SPSS, version 13.0. P-value ≤ 0.05 was considered statistically significant.

3. Results

We evaluated 120 patients (74 males and 46 females) who were divided into four groups: hemodiafiltration (HDF), patients on standard bicarbonate dialysis (BHD), peritoneal dialysis (PD) and kidney transplant recipients. Sociodemographic and clinical characteristics of the patients included in the study are present in Table 1. As shown in table, there were no statistically significant differences in gender, marital status, educational status, employment status, economic status, lifestyle characteristics (smoking and alcohol intake), diabetes and duration of the therapy among groups. The mean duration of time on therapy was: 47.2 ± 50.0 (HDF), 30.9 ± 31.5 (BHD), 35.3 ± 27.5 (PD) and 30.9 ± 37.9 (transplantation) months. The time on therapy in transplant group relates to transplantation period (no total replacement therapy period). We found statistically significant difference among groups regarding age and presence of ischemic hearth disease.

Most patients who reported any kind of insomnia symptoms with ISI were on BHD (80%), then HDF (76.7%) and PD (63.3%). Transplantation recipients had least difficulties with insomnia (46.7%) (Figure1). Insomnia symptoms were considered to be: difficulty falling asleep, difficulty staying asleep and problems with waking up too early.

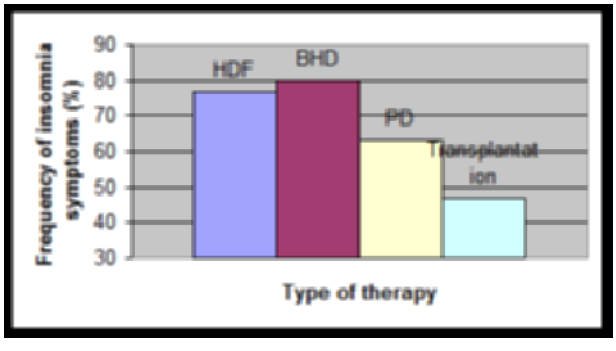

Figure 1. Frequency of insomnia symptoms among patients on HDF, BHD, PD and transplantation recipients.

Table 1. Sociodemographic and clinical characteristics for the study patients.

Sociodemographic and clinical variables	HDF (n=30)	BHD (n=30)	PD (n=30)	Transplantation (n=30)	p-value
Age (mean ± SD)	56.4±11.1	54.5±16.4	56.1±13.1	41.3±7.7	**<0.05**
Male (% (n*))	70% (21)	70% (21)	43.3% (13)	63.3% (19)	0.109
Married (% (n))	83.3% (25)	80% (24)	73.3% (22)	63.3% (19)	0.292
Educational status (% (n))					0.086
Elementary school	13.3% (4)	26.7% (8)	43.3% (13)	13.3 (4)	
High school	80% (24)	70% (21)	50% (15)	83.3% (25)	
University education	6.7% (2)	3.3% (1)	6.7% (2)	3.3% (1)	
Employment status (% (n))					0.083
Employed	16.7% (5)	10% (3)	0% (0)	20% (6)	
Unemployed	6.7% (2)	20% (6)	23.3% (7)	26.7% (8)	
Retired	76.7% (23)	70% (21)	76.7% (23)	53.3% (16)	
Economic status (% (n))**					0.417
< 100 €	26.7% (8)	46.7% (14)	33.3% (10)	30% (9)	
100 – 300 €	56.7% (17)	50.0% (15)	50% (15)	60% (18)	
> 300 €	16.7% (5)	3.3% (1)	16.7% (5)	10% (3)	
Lifestyle caracteristics (% (n))					
Smoker	20% (6)	30% (9)	20% (6)	33.3% (10)	0.528
Alcohol	6.7% (2)	0% (0)	3.3% (1)	0% (0)	0.288
Comorbidity (% (n))					
Ischemic hearth disease	30% (9)	43.3% (13)	36.7% (11)	0% (0)	**0.001**
Diabetes	20% (6)	10% (3)	30% (9)	10% (3)	0.126
Duration of therapy (months) (mean ± SD)	47.2±50.0	30.9±31.5	35.3±27.5	30.9±37.9	0.328

**n=number of patients; **monthly income per member of patient's family*

Table 2. Type of insomnia problem*.

Sleeping problem (% (n**))	HDF (n=30)	BHD (n=30)	PD (n=30)	Transplantation (n=30)
No problem	23.3% (7)	20% (6)	36.7% (11)	53.3% (16)
1) Difficulty falling asleep	3.3% (1)	13.3% (4)	10% (3)	3.3% (1)
2) Difficulty staying asleep	23.3% (7)	0% (0)	3.3% (1)	0% (0)
3) Problems waking up too early	3.3% (1)	0% (0)	0% (0)	0% (0)
4) Mixed	46.7% (14)	66.7% (20)	50% (15)	43.3% (13)

** chi-square test was used for comparison, p = 0.019, Cramer's V = 0.287*
*** n = number of patients*

Table 3. Insomnia Severity Index among patients on HDF, BHD, PD and transplantation recipients*.

Severity of insomnia (% (n**))	HDF (n=30)	BHD (n=30)	PD (n=30)	Transplantation (n=30)
No clinically significant insomnia	76.7% (23)	40% (12)	56.7% (17)	60% (18)
Subthreshold insomnia	16.7% (5)	26.7% (8)	20% (6)	23.3% (7)
Clinical insomnia (moderate)	6.7% (2)	33.3% (10)	20% (6)	13.3% (4)
Clinical insomnia (severe)	0% (0)	0% (0)	3.3% (1)	3.3% (1)

** chi-square test was used for comparison, p = 0.181, Cramer's V = 0.187;*
*** n = number of patients*

The most frequently recorded type of insomnia problem was mixed night-time waking, trouble falling asleep and early morning waking (Table 2).

The total score ISI showed that most patients have "no clinically significant insomnia" (Table 3).

Kruskal-Wallis Test indicated statistically significant differences in insomnia severity among the study groups (p=0.040). Additional Mann-Whitney tests found statistically significance difference in insomnia severity between BHD and HDF (p=0.002) and between BHD and transplant recipients (p=0.048) (Table 4).

Table 4. Insomnia Severity Index among groups.

Kind of therapy	N	Mean ± Std.Deviation	Median
1 HDF	30	4.60 ± 4.336	3.00
2 BHD	30	10.10 ± 7.155	11.00
3 PD	30	7.23 ± 7.108	6.00
4 Transplantation	30	6.17 ± 7.076	2.50
Total	120	7.03 ± 6.756	5.00

The ischemic hearth disease is significantly and independently associated with insomnia severity index (Table 5). There was no significantly association between insomnia severity score and age, smoking, alcohol intake and diabetes.

4. Discussion

We compared socioeconomic conditions among the groups in order to eliminate differences of socioeconomic factors among the groups which can have influence on the severity of insomnia. Except in age and presence of ischemic hearth disease, there is no statistical significant difference in other sociodemographic and clinical characteristics among groups. The mean age of patients was: 56.4 ± 11.1 (HDF), 54.5 ± 16.4 (BHD), 56.1 ± 13.1 (PD) and 41.3 ± 7.7 (transplantation). Patients in standard bicarbonate dialysis, hemodiafiltration and peritoneal dialysis have approximately the same age, but transplant patient are younger. It is because kidney donation typically occurs in younger chronic renal failure patients. In our patients it is the most common living donation between relatives. Frequency of ischemic hearth disease is the lowest in transplant patients which is according to expectations, because they are the youngest.

Insomnia is a great problem in end-stage renal patients. The prevalence of insomnia in these patients ranges widely in various studies. This is most likely due to different diagnostic criteria [1,21] and certain limitations of using subjective tests in detecting sleep problems [22]. Patients in our study reported high frequency insomnia problems. Values obtained correspond with the results of previous researches [5,7,9,10,23,24]. However, the main aim of our study was to assess whether there is a difference in frequency and severity of insomnia among various dialysis therapies.

Patients from all groups complained about difficulty falling asleep, difficulty staying asleep and early morning waking, but most had a mixture of problems. Night-time waking and difficulty falling asleep were reported mostly. These data match the reports of previous studies [11].

The fact is that there are many studies of the prevalence of insomnia, but there are almost no studies that examine the severity of insomnia in end-stage renal patients. Therefore, this is the first study that has attempted to determine how clinically significant these insomnia problems, which the patients without doubt have, really are. The results we obtained using a questionnaire Insomnia Severity Index show that insomnia in end-stage renal patients is not very severe (Table 3).

Previous researches have shown that the psychological and physical cases contribute to insomnia in end-stage renal disease patients. Insomnia correlated with the presence of depression, anxiety, anemia, primary sleep disorders such as restless legs syndrome, metabolic [23,25] and immunology distress [26]. It is questionable how dialysis therapy influences, directly or indirectly (through the co-morbidites state), the onset of insomnia in these patients.

While some studies found a connection between insomnia and biochemical parameters of dialysis efficiency [6,23], others don't [27].

Table 5. Relationship between ISI (dependent variable) and independent determinants.

Predictive variables	Unstandardized	Standard error	Standardized B coefficients	t	P value
Age	B coefficients	0.049	-0.070	-0.700	0.485
Smoking	-0.034	1.408	-0.031	-0.337	0.736
Alcohol intake	-0.475	3.862	-0.142	-1.581	0.117
Ischemic hearth disease	-6.106	1.520	0.333	3.298	**0.001**
Diabetes	5.013	1.646	0.001	0.006	0.995

The main finding of this study is that patients in BHD have a higher rate of insomnia symptoms than patients in HDF. The frequency and severity of insomnia is slightly higher in BHD patients than in HDF patients. This result was partly known [9] and expected because HDF treatment reflects an improved blood clearance on uremic toxins.

The lowest frequency and severity of insomnia was found in kidney transplant recipients. Such a result is in agreement with those in other studies [15,28,29]. Sabatini et al. compared data obtained from 301 kidney transplant patients with data from patients on maintenance dialysis using Pittsburg Sleep Quality Index (PSQI). The PSQI score of the transplant patients was significantly lower, indicating better overall sleep quality than in patients on maintenance dialysis [15].

The relationship between age and sleep quality is controversial in chronic renal failure patients [6,7,10,24]. The prevalence of insomnia increases with age. In this study we didn't observe relation between prevalence of insomnia and age, we observed relation between the severity score of insomnia and age. There was no significant association. Some investigations reported that smoking and alcohol intake can be associated with sleep disorders [8], while other studies found no significant association [10,23,24]. In our study, we also found that these habits did not contribute to the insomnia severity score. A few studies have suggested that number and severity of comorbidity in hemodialysis patients can be attributed with the increase in the prevalence of sleep disorders [2,4,30]. In our study, we found that ischemic hearth disease was an independent determinant of the insomnia severity score.

Potential limitation of the questionnaire which was used in this study must also be taken into consideration. For more precise examining of the frequency of insomnia, some other questionnaires should be used. Despite these limitations this study noted some differences in the severity of insomnia problems in chronic renal disease patients on various renal replacement therapies, which was our primary goal.

What should be examined is how specific parameters of dialysis influence insomnia problems in dialysis patients.

5. Conclusion

Patients with end-stage renal disease have high frequency insomnia problems. However, our study shows that insomnia in these patients is not severe. There are statistically significant differences in the severity of insomnia between patients on hemodiafiltration and standard bicarbonate dialysis and between patients on standard bicarbonate dialysis and kidney transplant recipients.

Aknowledgements

This study was partially financed by grant No 175007 provided by the Serbian Ministry of Science and Technological Development.

The authors thank Slobodan Jankovic, professor of Medical Faculty University of Kragujevac, for the revision of the manuscript.

References

[1] World Health Organization, The ICD-10 Classification of Mental and Behavioural Disorders, Diagnostic criteria for research, Geneva, 1993

[2] Gusbeth-Tatomir P., Boisteanu D., Seica A., Buga C., Covic A., Sleep disorders: a systematic review of an emerging major clinical issue in renal patients, Int. Ur ol. Nephrol., 2007, 39, 1217-1226

[3] Noda A., Nakai S., Soga T., et al., Factors contributing to sleep disturbance and hypnotic drug use in hemodialysis patients, Intern. Med., 2006, 45, 1273-1278

[4] Musci I., Molnar M.Z., Rethelyi J., et al., Sleep disorders and illness intrusivness in patients on chronic dialysis, Nephrol. Dial. Transplant., 2004, 19, 1815-1822

[5] Williams S.W., Tell G.S., Zheng B., Shumaker S., Rocco MV., Sevick MA., Correlates of sleep behavior among hemodialysis patients. The kidney outcomes prediction and evaluation (KOPE) study, Am. J. Nephrol., 2002, 22, 18-28

[6] Adbelwhab S., Kamel M., Noshey M., Sleep disorders in hemodialysis patients, Kidney., 2010, 19, 175-181

[7] 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, 184-190

[8] Iliescu E.A., Coo H., McMurray M.H., et al., Quality of sleep and health-related quality of life in haemodialysis patients, Nephrol. Dial. Transplant., 2003, 18, 126-132
[9] Cengic B., Resic H., Spasovski G., Avdic E., Alajbegovic A., Quality of sleep in patients undergoing hemodialisys, Int. Urol. Nephrol., 2010, (Epub ahead of print)
[10] Eryavuz N., Yuksel S., Acarturk G., et al., Comparasion of sleep quality between hemodialysis and peritoneal dialysis patients, Int. Urol. Nephrol., 2008, 40, 785-791
[11] Sabbatini M., Minale B., Crispo A., et al., Insomnia in maintenance haemodialysis patients, Nephrol. Dial. Transplant., 2002, 17, 852-856
[12] Di Iorio B., Bartiromo M., Cesare M.C., De Santo R.M., Do sleep disorders start in dialysis or in early chronic kidney disease?, Nephrol. Dial. Transplant., 2006, 21, 1731
[13] De Santo R.M., Bartiromo M., Cesare C.M., Cirillo M., Sleep disorders occur very early in chronic kidney disease, J. Nephrol., 2008, 21, S59-65
[14] Sabbatini M., Pisani A., Crispo A., et al., Renal transplantation and sleep: a new life is not enough, J. Nephrol., 2008, 21, S97-101
[15] Sabbatini M., Crispo A., Pisani A., et al., Sleep quality in renal transplant patients: a never investigated problem, Nephrol. Dial. Transplant., 2005, 20, 194-198
[16] Leger D., Scheuermaier K., Philip P., Paillard M., Guilleminault C., SF-36: evaluation of quality of life in severe and mild insomniacs compared with good sleepers, Psychosom. Med., 2001, 63, 49–55
[17] Han S.Y., Yoon J.W., Jo S.K., et al., Insomnia in diabetic hemodialysis patients. Prevalence and risk factors by a multicenter study, Nephron., 2002, 92, 127-132
[18] Kimmel P.L., Patel S.S., Quality of life in patients with chronic kidney disease: focus on end-stage renal disease treated with hemodialysis, Semin. Nephrol., 2006, 26, 68-79
[19] Unruh M.L., Buysse D.J., Dew M.A., et al., Sleep quality and its correlates in the first year of dialysis, Clin. J. Am. Soc. Nephrol., 2006, 1, 802-810
[20] Bastien C.H., Vallières A., Morin C.M., Validation of the Insomnia Severity Index as an outcome measure for insomnia research, Sleep. Med., 2001, 2, 297-307
[21] Diagnostic Classification Steering Committee of the American Sleep Disorders Association, The International Classification of Sleep Disorders: Diagnostic and Coding Manual, Rochester, MN, 1990
[22] Perl J., Unruh M.L., Chan C.T., Sleep disorders in end-stage renal disease: 'Markers of inadequate dialysis'?, Kidney. Int., 2006, 70, 1687-1693
[23] Sabry A.A., Abo-Zenah H., Wafa E., et al., Sleep disorders in hemodialysis patients, Saudi. J. Kidney. Dis. Transpl., 2010, 21, 300-305
[24] Al-Jahdali H.H., Khogeer H.A., Al-Qadh W.A., et al., Insomnia in chronic renal patients on dialysis in Saudi Arabia, J. Circadian. Rhythms., 2010, 8, 7
[25] Pai M.F., Hsu S.P., Yang S.Y., Ho T.I., Lai C.F., Peng Y.S., Sleep disturbance in chronic hemodialysis patients: the imact of depression and anemia, Ren. Fail., 2007, 29, 673-677
[26] Chiu Y.L., Chuang Y.F., Fang K.C., et al., Higher systemic inflammation is associated with poorer sleep quality in stable haemodialysis patients, Nephrol. Dial. Transplant., 2009, 24, 247-251
[27] Holley J.L., Nespor S., Rault R., A comparison of reported sleep disorders inpatients on chronic hemodialysis and continuous peritoneal dialysis, Am. J. Kidney. Dis., 1992, 19, 156-161
[28] Molnar M.Z., Novak M., Musci I., Sleep disorders and quality of life in renal transplant recipients, Int. Urol. Nephr., 2009, 41, 373-382
[29] Kovacs A.Z., Molnar M.Z., Szeifert L., et al., Sleep disorders, depressive symptoms and health-related quality of life – a cross-sectional comparasion between kidney transplant recipients and waitlisted patients on maintenance dialysis, Nephrol. Dial. Transplant., 2011, 26, 1058-1065
[30] De Santo R.M., Lucidi F., Violani C., Di Iorio B.R., Sleep disorders in hemodialyzed patients –the role of comorbidities, Int. J. Artif. Organs., 2005, 28, 557-565