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Insomnia symptoms in South Florida military veterans with epilepsy☆

M.R. Lopez [a,b], J.Y. Cheng [a,b], A.M. Kanner [a,b], D.Z. Carvalho [c], J.A. Diamond [a,b], D.M. Wallace [a,b,*]

[a] Department of Neurology, University of Miami Miller School of Medicine, Miami, FL, USA
[b] Department of Neurology, Bruce W. Carter Department of Veterans Affairs Medical Center, Miami, FL, USA
[c] Sleep Laboratory, Hospital de Clínicas de Porto Alegre, Universidade Federal do Rio Grande do Sul School of Medicine, Porto Alegre, RS, Brazil

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ABSTRACT

Background: Despite the high prevalence of insomnia in veterans with epilepsy, it remains understudied. Our aim was to identify the associations of insomnia with epilepsy, comorbidities, and treatment-related variables in South Florida veterans.
Methods: We performed a cross-sectional analysis of veterans attending an epilepsy clinic over 18 months. Participants completed standardized assessments of seizure and sleep. Insomnia was defined as 1) difficulty with sleep onset, maintenance, or premature awakenings with daytime consequences or 2) sedative-hypnotic use on most nights of the previous month.
Results: One hundred sixty-five veterans (87% male, age 56±15 years) were included: 66 reporting insomnia (40%). In logistic regression analysis, insomnia was significantly associated with post-traumatic seizure etiology, lamotrigine prescription, and mood and psychotic disorders. Female gender and levetiracetam treatment were associated with lower odds for insomnia.
Conclusion: Insomnia was associated with post-traumatic epilepsy, mood/psychotic comorbidities, and antiepileptic regimen. Insomnia represents an under-recognized opportunity to improve comprehensive epilepsy care.

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1. Introduction

Insomnia, difficulty with falling or remaining asleep or experiencing premature awakenings, is one of the most common complaints reported by patients with epilepsy [1,2]. The prevalence of symptoms of insomnia in patients with epilepsy has been estimated to range from 25% to 54%, 2–4 times greater than that reported in the US general population [1–8]. Insomnia with short sleep duration has been associated with impaired health-related quality of life, increased health care costs, greater workplace injuries, and increased risk for hypertension, diabetes, and all-cause mortality in the general population [9–14]. Insomnia comorbid with epilepsy may exacerbate psychiatric problems, behavior, memory, and social functioning [6,7,15]. Furthermore, insomnia has been associated with greater seizure frequency and worse quality of life in patients with epilepsy [6,15].

There are many contributing factors to insomnia in patients with epilepsy. Choice of antiepileptic drug (AED), nocturnal seizures, and medical and psychiatric comorbidities (e.g., depression and anxiety disorders) may all result in sleep disruption [1,3,16]. With chronic sleeping difficulties, patients may also develop reactive behavioral responses perpetuating insomnia (i.e., rumination, inadequate sleep hygiene, conditioned hyperarousal to the bedroom environment) [17,18].

Although sleep disturbances and epilepsy often coexist in military veterans, none of the prior studies concerning insomnia complaints in epilepsy have examined this at-risk population. Overall, there are limited data on the effect of epilepsy, AED treatment, comorbidity-related variables, and insomnia [1–3,16]. In this study, we investigated 1) the prevalence of symptoms of insomnia in a veteran epilepsy outpatient clinic and examined their association with epilepsy-, AED-, and medical/psychiatric diagnoses-related variables and 2) the history of insomnia treatments and consultations. By characterizing the relationship between epilepsy and insomnia, we aim to increase awareness of this prevalent, treatable comorbidity in South Florida veterans.

2. Methods

This was a cross-sectional study which consisted of a review of the medical records of consecutive patients with epilepsy attending the Miami VA Healthcare System (VAHS) epilepsy clinic over 18 months (January 2010 to June 2011). The study was approved by the Miami VAHS institutional review board. A board-certified epileptologist (MRL) confirmed the diagnosis of epilepsy using the International League Against Epilepsy criteria [19].

Demographic variables were extracted from the medical record at initial evaluation for epilepsy: age, gender, medical and psychiatric

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* Corresponding author at: Bruce W. Carter Department of Veterans Affairs Medical Center, 1201 NW 16th Street, Miami, FL 33125, USA. Fax: +1 3055753210.
E-mail address: dwallace@med.miami.edu (D.M. Wallace).

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comorbidities, epilepsy subtype (focal or generalized), seizure etiology (idiopathic, post-traumatic, or secondary to other factors), seizure intractability (breakthrough seizures despite using two AEDs), and AED treatment. Medical comorbidities were weighted using the Charlson comorbidity index at the initial epilepsy evaluation [20]. Mood disorder, post-traumatic stress disorder (PTSD)/anxiety, psychotic spectrum disorders (i.e., schizophrenia, schizoaffective disorder), and substance abuse/dependence were recorded if diagnosed by a psychiatric attending physician within the last 12 months.

During the initial epilepsy evaluation, patients were asked about chronic insomnia with 2 questions: 1) "Do you have difficulty falling asleep, staying asleep, or waking up earlier than desired on most days of the last month?" and 2) "Does your sleeping difficulty cause problems for you during the day?". A positive answer to both questions or if patients reported using prescribed sedative-hypnotic medication on most days of the month fulfilled the diagnostic criteria for insomnia [21]. Medications which were prescribed primarily for sleep onset, maintenance, or premature awakenings were considered sedative-hypnotic medications. We calculated the type of sedative-hypnotic medication category prescribed, the prescribing provider (epileptologist, sleep physician, psychiatrist, primary care provider, or multiple prescribers), and the proportion of individuals who had completed formal sleep clinic consultation and polysomnography.

2.1. Data analysis

The prevalence of the above-cited variables was compared between the "insomnia" and "no insomnia" groups. Age and the Charlson comorbidity index were the only continuous variables and were reported as means ± (SD). All other variables were categorical and were reported as frequencies (%). Student *t* test was used to compare the continuous variables. Chi-square or Fisher's exact tests were used to compare the categorical variables. Multiple logistic regression analysis was performed to determine the clinical factors associated with insomnia. Variables that have been consistently associated with insomnia in prior investigations (i.e., age, gender) were included in the model a priori [4]. Variables found to be significantly different in univariate analyses were also entered as covariates in the model. We used the Hosmer–Lemeshow goodness-of-fit statistic ($p > 0.05$) to evaluate model fit. Pearson correlations between variables included in the model were checked for collinearity. For all analyses, $p \leq 0.05$ was defined as statistically significant. Statistical analyses were performed with SPSS Statistics 20.0 (SPSS, Chicago, IL).

3. Results

3.1. Demographic and epilepsy characteristics

One hundred sixty-five veterans (87% male, age 56 ± 15 years) were included in the analysis with 66 veterans (40%) meeting the criteria for insomnia (Table 1). The most common seizure etiologies were idiopathic (48%) and post-traumatic (27%) seizures. Three-fourths of the participants had focal seizures and most (61%) were treated with AED monotherapy. Compared with those without insomnia, veterans with insomnia had a significantly higher proportion of post-traumatic epilepsy (38% vs 20%, post-hoc, $p < 0.05$). There were no other significant differences in age, gender distribution, seizure subtype, proportion treated with AED monotherapy, or seizure control between those with and without insomnia complaints.

3.2. Medical and psychiatric comorbidities

The most common medical and psychiatric comorbidities for our cohort included hypertension (57%), mood disorders (55%), chronic pain (37%), and current or history of substance abuse (34%) (Table 1). The participants with insomnia had a significantly higher proportion of chronic pain conditions (55% vs 25%, $p < 0.01$) and psychiatric comorbidities compared with those without insomnia. Veterans with insomnia had a significantly higher prevalence of mood disorders (80% vs 38%, $p < 0.001$), substance abuse (44% vs 27%, $p = 0.03$), PTSD (21% vs 7%, $p < 0.01$), and psychotic disorder spectrum diagnoses (20% vs 4%, $p < 0.01$) compared with those without insomnia. There were no other significant differences in the frequencies of medical comorbidities or in the mean Charlson comorbidity index between the two groups.

Table 1
Participant demographics and clinical characteristics.

	All (n = 165)	Insomnia (n = 66)	No insomnia (n = 99)	p-Value
Age (years)	56 ± 15	54 ± 13	57 ± 17	.25
Gender (n, %)				
Male	144 (87)	60 (91)	84 (85)	.25
Seizure characteristics (n, %)				
Seizure etiology				**.001**
Idiopathic	80 (48)	34 (52)	46 (46)	
Post-traumatic	45 (27)	25 (38)	20 (20)	
Other	40 (24)	7 (11)	33 (33)	
Seizure subtype				.51
Partial	123 (75)	51 (77)	72 (73)	
Generalized	42 (25)	15 (23)	27 (27)	
Monotherapy	100 (61)	39 (59)	61 (62)	.75
Refractory	20 (12)	7 (11)	13 (13)	.63
Comorbidities (n, %)				
Medical				
Pain	61 (37)	36 (55)	25 (25)	<**.001**
Hypertension	94 (57)	39 (59)	55 (56)	.65
Diabetes	27 (16)	8 (12)	19 (19)	.23
Heart disease	29 (18)	14 (21)	15 (15)	.32
Stroke	28 (17)	10 (15)	18 (18)	.61
Pulmonary disease	32 (19)	17 (26)	15 (15)	.09
CKD	10 (6)	5 (8)	5 (5)	.52
Liver disease	14 (8)	5 (8)	9 (9)	.73
Cancer	35 (21)	15 (23)	20 (20)	.70
Charlson index	1.6 ± 1.3	1.7 ± 1.3	1.6 ± 1.3	.55
Psychiatric				
Mood disorders	91 (55)	53 (80)	38 (38)	<**.001**
PTSD	21 (12)	14 (21)	7 (7)	<**.01**
Substance abuse	56 (34)	29 (44)	27 (27)	**.03**
Psychotic spectrum	17 (10)	13 (20)	4 (4)	<**.01**

Legend: Categorical variables are shown as frequencies (%). Frequencies are rounded to the nearest integer and may not add to 100%. Continuous variables are presented as mean ± S.D. Bolded values are significant ($p \leq 0.05$). CKD, chronic kidney disease; PTSD, post-traumatic stress disorder.

3.3. Medications and insomnia treatments

Levetiracetam, phenytoin, and valproic acid were the most commonly prescribed AEDs in our sample (Table 2). Individuals with insomnia were more commonly prescribed gabapentin (17% vs 6%, $p = 0.03$) and lamotrigine (23% vs. 9%, $p = 0.02$) and less commonly prescribed levetiracetam (21% vs. 40%, $p = 0.01$) and phenytoin (11% vs. 25%, $p = 0.02$). In addition, antidepressant, antipsychotic, and benzodiazepine medications were also more commonly prescribed to the participants with insomnia compared with those without insomnia complaints.

Sixty-eight percent of the participants with insomnia were prescribed sedative-hypnotic medications with a mean of 1 ± 0.9. Atypical antipsychotics (35%), sedating antidepressants (27%), antihistamines (15%), benzodiazepines (14%), and benzodiazepine-receptor agonists (14%) were the most commonly prescribed medication categories (Table 2). Quetiapine (20%) and zolpidem (14%) were the most prevalent individual medications prescribed for insomnia complaints. Psychiatrists prescribed the majority (92%) of the sedative-hypnotic medications in our cohort.

There were no significant differences in the proportion of individuals who had completed a sleep clinic consultation (35% vs 26%, $p = 0.24$) or