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BRIEF REPORT

Prevalence and Risk Factors of Sleep Disturbance in a Large HIV-Infected Adult Population

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Abstract This cross-sectional study evaluates the prevalence and factors associated with sleep disturbances in French adult HIV-infected outpatients. Patients fullfilled a self-administered questionnaire on their health behavior, sleep attitudes (Pittsburgh sleep quality index, PSQI), quality of life and depression; 1354 patients were enrolled. Median sleeping time was 7 h. Poor sleep quality was observed in 47 % of the patients, and moderate to serious depressive symptoms in 19.7 %. Factors significantly associated with sleep disturbances were depression, male gender, active employment, living single, tobacco-smoking, duration of HIV infection, nevirapine or efavirenz-including regimen. Prevalence of poor sleepers is high in this HIV adult outpatient population. Associated factors seem poorly specific to HIV infection and more related to social and psychological status. Taking care of these disturbances may prove to be an effective health management strategy.

Resumen Este estudio transversal evalúa la prevalencia y los factores asociados con los trastornos del sueño en adultos franceses pacientes en ambulatorio infectados por el VIH. Los pacientes completan un auto-cuestionario sobre su comportamiento de salud, las actitudes del sueño (Pittsburgh Sleep Quality Index, PSQI), la calidad de vida y la depresión; 1354 pacientes fueron incluidos. La mediana del tiempo de sueño fue de 7 horas. La malacalidad del sueño se observó en el 47 % de los pacientes, y moderados a graves síntomas depresivos en 19,7 % de los pacientes. Los factores asociados significativamente con las alteraciones del sueño son: la depresión, el sexo masculino, trabajador activo, viviendo solo, fumador, la duración de la infección VIH, tratamiento nevirapina o efavirenz. La prevalencia de los trastornos del sueño es alta en esta población de pacientes adultos VIH en ambulatorio. Los factores asociados parecen poco relacionados a la infección VIH y más relacionados con el estatus social y psicológico. El cuidado de estos trastornos puede ser una estrategia eficaz en la gestión de la salud.

Keywords Sleep disturbance · Insomnia · Depression · HIV infection

Introduction

Sleep disturbances are common in HIV populations, estimated as occurring in as many as 70 % in some studies, most of them performed early in the HIV epidemic [1]. In the HIV population, anxiety regarding a potential fatal illness, financial concerns, stigmatization, depression, and

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unemployment are frequent and can interfere with physical, mental, and emotional functioning and consequently affect the quality of sleep [2–4].

The availability of new antiretrovirals with higher and prolonged efficacy and limited adverse effects lead to an increased life expectancy in HIV individuals. Sleep disturbances impaired quality of life and cognitive function that could lead to a poor medication adherence. To prevent potentially arising complications it seems important to screen sleep disturbances as part of routine HIV care due to the potentially negative effects of insomnia on health, including HIV disease progression [5]. We aimed to determine the prevalence of sleep disturbances and their associated factors in a HIV-infected adult population.

Material and Methods

We performed a cross-sectional study in the "Pays de la Loire" region, North-West of France, which has an HIV population of 3,736 persons. Between November 2012 and May 2013, all HIV-infected patients over 18 years of age presenting for routine care at HIV clinic in the 6 centres of "Pays de la Loire" (Nantes, Angers, La Roche sur Yon, Saint Nazaire, Le Mans, Laval) were offered to participate in the study. Patients were excluded if they refused to complete the questionnaire or if they were under legal guardianship. The ethics committee approved this research and each participant gave informed consent. Each participant was self-administered a questionnaire on sleep disturbances, the Pittsburgh Sleep Quality Index (PSQI), a questionnaire on quality of life (WHO QOL HIV BREF questionnaire) and depression (Beck depression Inventory (BDI)-II questionnaire [6, 7]. PSQI is a 19-item questionnaire which enquires about sleep over the past month and assesses sleep components including sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of hypnotics, and daytime dysfunction. Sleep disturbances was defined as a global score >5 (sensitivity of 90 % and specificity of 87 %). In the BDI-II questionnaire, depression was defined as a BDI score ≥19. Socio-demographic data, educational level, employment status, self-reported substance abuse (tobacco, alcohol, and illicit drugs) and marital status were obtained and documented. Medical and treatment history, current antiretroviral therapy and immuno-virologic data were also obtained from the medical records.

Data were analysed using SAS version 9.2. Continuous variables are presented as median and interquartile (IQR) and comparison between groups was made using Wilcoxon rank sums test. Categorical variables are presented as frequencies (%) and group differences using χ^2 test with a level of significance at <0.05. A logistic regression model was performed to identify variables associated with sleep disturbances. Variables with a P value <0.20 in univariate analysis were included in the logistic regression model. Associations were assessed using odd ratios (ORs) and 95 % Confidence Intervals (CIs).

Results

From November 2012 to May 2013, 1354 HIV-infected adult outpatients were enrolled in the study. Patients characteristics are presented in Table 1. Patients were mainly males born in France, in the late fourties. The great majority of participants were on antiretroviral therapy, for a median of almost 10 years, with virologic suppression and CD4 >500/μL. Presence of a co-morbid condition was present in 37.2 % of participants, the most frequent being dyslipidemia, high blood pressure, lipodystrophy and diabetes, in 20.0, 15.1, 11.8 and 3.0 % of the patients, respectively. During the previous month, 8.5 % and 7.7 % of the patients had taken sleeping pills and anxiolytic drugs, respectively; 38.7 % were tobacco smokers, 8.7 % were excessive drinkers defined as drinking >20 g alcohol per day and 18 % were regular or occasional drug users (marijuana 11.7 %, poppers 8.2 %, cocaine 1.6 %, ecstasy 0.4 %, heroin 0.1 % and other drugs 1.0 %). The median duration of nighttime sleep was 7 h (interquartile IQR 6; 8). According to PSQI, 47.0 % (486/1036) of the patients were considered poor sleepers based on a PSQI score >5, more frequently in female than in male (56.4 vs. 43.9 %, $P < 0.05$). In multivariate analysis, being a female, a tobacco smoker, living single, being unemployed or moderately or seriously depressed were significantly associated with poor sleep quality (Table 1). Among HIV-related factors, duration of known HIV infection >10 years was positively associated with poor sleep quality, while efavirenz- or nevirapine-containing regimens were negatively associated (Table 1). Nadir CD4 cell counts, age, BMI, education level, HIV transmission risk group, CDC stage C, hepatitis B or C coinfection, other co-morbidities, other antiretrovirals and center were not associated factors. The course and natural sleep/wake disorders were evaluated in Question 5 of PSQI: 41 % of the subjects cannot get to sleep within 30 min three or more times a week and 22 % one or two times a week, 57 % wake up at the middle of the night or early morning three or more times a week, and 33 % and 31 % of the subjects had bad dreams and pain at least once a week, respectively. According to BDI-II evaluation, 19.7 % of the patients reported moderate to serious depressive symptoms. Compared to patients without poor sleep quality, quality of life was significantly impaired in poor sleeper patients (PSQI > 5), in all the six

Table 1 Patients characteristics and factors associated with sleep disturbances in univariate and multivariate analysis

			Univariate analysis				Multivariate analysis			
	N = 1354	%	Parameter	OR[a]	95 % CI[a]	P[b]	OR[a]	95 % CI[a]	z score[b]	P[b]
Baseline characteristics										
Age (years), med.(IQR)	47 (40–54)		[18;40]	1.06	[0.78;1.43]	0.72				
			≥55	1.21	[0.89;1.64]	0.24				
			[40;55]			ref.				
Male	995	73.5		0.61	[0.45;0.81]	0.001	0.7	[0.50;0.95]	−2.3	0.02
BMI, med. (IQR)	23.5 (21–26.2)		≤18.5	1.24	[0.74;2.09]	0.42				
			>25	1.04	[0.80;1.36]	0.76				
			[18.5;25]			ref.				
Country of birth										
France/Africa/Other	1122/199/33	82.9/14.7/2.4	France	0.79	[0.56;1.11]	0.18				
			Africa/Other			ref.				
Living single	645	48	Yes vs. no	1.81	[1.42;2.32]	<0.0001	1.5	[1.18;2.01]	3.1	0.002
Active employment	768	56.7	Yes vs. no	0.56	[0.44;0.72]	<0.0001	0.7	[0.55;0.95]	−2.3	0.02
HIV transmission risk										
Homosexual	656	48.4		0.78	[0.60;1.02]	0.07				
Heterosexual	515	38.0				ref.				
Others	183	13.5		0.99	[0.67;1.48]	0.98				
Education level										
Primary/no diploma	131	9.7		0.93	[0.73;1.17]	0.53				
School-leaving diploma	789	58.3		0.99	[0.87;1.13]	0.91				
High school level	427	31.5				ref.				
HIV characteristics										
Duration HIV infection (years), med.(IQR)	12.4 (6.2–19.8)		≥10 vs. <10	1.44	[1.13;1.85]	0.004	1.5	[1.15;1.97]	2.9	0.003
Nadir CD4 (/μL), med.(IQR)	207 (95–309)			0.99	[0.88;1.12]	0.88				
CD4 cell counts (/μL), med. (IQR)	604 (434–784)		≤200	1.58	[0.84;2.99]	0.16				
			>500	1.22	[0.93;1.61]	0.15				
			[200;500]			ref.				
CDC stage C	279	20.6	Yes vs. no	1.09	[0.80;1.47]	0.60				
HCV and/or HBV co-infection	182	13.4	Yes vs. no	1.13	[0.23;5.64]	0.88				
Comorbidities[c]	504	37.2	Yes vs. no	1.17	[0.91;1.51]	0.22				
Current ART	1275	94.2	Yes vs. no	0.82	[0.48;1.39]	0.45				
Duration of ART (years), med.(IQR)	9.5 (4.2–15.8)									
HIV RNA <50 copies/mL	1105	86.7	<50 vs. ≥50	0.76	[0.56;1.05]	0.10				
Occasional or regular drug user[d]	243	18.0	Yes vs. no	1.56	[0.90;2.72]	0.0504				

Table 1 continued

			Univariate analysis				Multivariate analysis			
	N = 1354	%	Parameter	OR[a]	95 % CI[a]	P[b]	OR[a]	95 % CI[a]	z score[b]	P[b]
Regular coffee/tea drinker	813	78.5		0.85	[0.63;1.15]	0.3				
Excessive alcohol drinker[e]	117	8.7		0.84	[0.66;1.06]	0.15				
Tobacco smoker	524	38.7	Yes vs. no	1.4	[1.09;1.80]	0.008	1.3	[1.03;1.76]	2.1	0.032
Sport	513	37.9	Yes vs. no	0.76	[0.59;0.99]	0.04				
Depression (BDI-II score ≥19)	251	19.7		5.45	[3.77;7.89]	<0.0001	4.6	[3.16;6.78]	7.9	<0.0001
ARV-including regimen										
NRTI										
Abacavir	357	26.4		1.08	[0.82;1.44]	0.58				
Lamivudine	398	29.4		1	[0.76;1.31]	0.98				
Tenofovir	758	56.0		0.98	[0.76;1.25]	0.85				
Emtricitabine	735	54.3		0.95	[0.75;1.22]	0.70				
NNRTI										
Nevirapine	401	29.6		0.8	[0.61;1.06]	0.12	0.7	[0.52;0.95]	−2.3	0.023
Efavirenz	179	13.2		0.48	[0.33;0.69]	<0.0001	0.5	[0.30;0.68]	−3.8	0.0002
PI										
Darunavir	296	21.9		1.27	[0.94;1.70]	0.11				
Atazanavir	154	11.4		1.17	[0.79;1.74]	0.43				
INI (Raltegravir)	189	14.0		1.29	[0.91;1.82]	0.15				
Other ARVs	293	21.6		1.09	[0.81;1.47]	0.56				

ART antiretroviral therapy, *ARV* antiretroviral, *NRTI* nucleoside reverse transcriptase inhibitor, *NNRTI* non nucleoside reverse transcriptase inhibitor, *PI* Protease Inhibitor, *INI* integrase inhibitor

[a] OR odds ratios and 95 % CI confidence intervals

[b] z score and P value based on Wald-test of logistic regression

[c] Dyslipidemia, high blood pressure, lipodystrophy, diabetes

[d] Marijuana, cocaine, ecstasy, heroin, poppers

[e] >20 g per day

domains: physical, psychological, level of independence, social relations, environment, and spiritual/religion ($P < 0.0001$ for each domain).

Discussion

This study is one of the largest and most recent to date study evaluating the prevalence of sleep disturbances in an HIV outpatient cohort. The studied population is representative of the total HIV population from the region "Pays de la Loire" as 44.8 % of the patients in care at time of the study were included with no significant differences in terms of demographic data between the two populations (data not shown). The rate of 47 % of sleep disturbances in our population is high but within the range of that seen in recent studies which assessed sleep quality using the PSQI, one of the most widely used standardized measures to assess subjective sleep quality [2].

A study published in 2012 on the evaluation of total sleep time and prevalence of insomnia in a French general adult population (from 15 to 85 year-old) concluded to an average sleeping time of 7 h and 13 min and a prevalence of sleep disturbance in the last 8 days of 47 % [8]. Our results are very closed to those found in the previous study. However the demographic characteristics of the 2 populations are different: median age of our HIV population was younger—47 years-old—with a narrow interquartile (40–54), and chronic co-morbid disease was observed more frequently than in the general population of similar age.

In the 1990s, sleep disturbances in HIV-infected patients were mainly associated with immunodepression, symptomatic infection and antiretroviral side effects [1, 9]. Even in the context of improved antiretroviral therapy and optimally controlled replication, patients may still continue to experience sleep disturbances indicating that they may be attributable to factors other than HIV disease, relative to social and psychological factors. In our study, gender, employment status, and marital status were significantly associated with sleep disturbances and these socioeconomic factors are known to be important determinants of sleep disturbance whatever the medical condition [9]. We have not found that single or childless women had a longer sleep duration compared to married women as it has been shown in Chapman's study [10]. The high proportion of migrant women that are frequently single and taking care of children could explain the discrepancy between the two studies in the female population. Unexpectedly, patients on efavirenz-containing regimen had significantly less sleep disturbances than patients not receiving efavirenz albeit some studies were in accordance with our results [11]. This finding is probably related to a chanelling bias, as the most frequent cause for efavirenz withdrawal are complaints related to CNS symptoms, of which insomnia and sleep disorders are the most frequent, then only patients that are not bothered by CNS symptoms remain on efavirenz. The unexpected finding of the study is the high level of moderate and serious depressive symptoms, that is even higher than in other studies [2]. A challenge with sleep research is the close correlation between sleep quality and depression. In fact, several of the items in commonly used depression scales pertain to changes in sleep pattern. Patients with depressive disorders often have high rates of sleep disturbances and depression has been reported as a frequent symptom in insomniacs [12]. Only 7.7 % of the participating subjects were treated with anxiolytic drugs evidencing probable under-diagnosed depressive symptoms. Sleep disturbances could impact daily living activities that are essential for disease management, including medication adherence. This issue is particularly concerning given that patients should strive for optimal and prolonged adherence to medications for effective viral suppression and, therefore, absence of disease progression.

Our study has some limitations. Firstly this is a cross-sectional study with no control group. The PSQI explore sleep disturbances over the past month and does not evaluate the prevalence of chronic insomnia whom definition includes sleep disturbances during a 6-month period. Some data that can impact sleep duration have not been collected in our study i.e. number of children, painful neuropathy and chronic pain. However in question 5i of PSQI, one third of the patients answered that they suffered from pain at least once a week during nighttime but with no characteristic on the kind of pain. It could have been useful to better describe sleep characteristics and patterns to add others validated diagnostic tools such as polysomnography, investigations on sleep apnea, restless legs syndrom and a validated clinical sleep interview [13, 14]. We cannot establish the sequence of events or determine causality. Migrant and illiterate patients, who are frequently affected by psychosocial issues were not included in the study, which could lead to an underestimation of the sleep disturbance prevalence.

Conclusions

Nevertheless this report provides a valuable description of an unselected HIV adult outpatient population, with long-term HIV disease and antiretroviral therapy and good immuno-virologic status, in France. Clinicians should be alerted on the high frequency of poor sleep quality in HIV-infected patients, assess the patient's sleep patterns, perform a differential diagnosis, to clarify the nature of the patient's sleep disturbances, provide counselling on the importance of adequate sleep hygiene, and search for

depressive symptoms, as taking care of these disturbances may prove to be an effective health management strategy.

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Compliance with Ethical Standards

Conflict of interest All authors report no conflict of interest.

Appendix

Study group: F. Raffi, E. Billaud, V. Reliquet, C. Allavena, C. Brunet-Cartier, B. Bonnet, P. Morineau-Le Houssine, S. Bouchez, M. Lefebvre, D. Boutoille, S. Pineau, C. Biron, M. Brière, M. Besnier, F. Sauser, P. Point, O. Aubry, O. Grossi, B. Gout, M. Colas, C. Supiot, H. Hüe, D. Brosseau, L. Larmet, J. Orain, S. Sécher-Pineau, T. Jovelin (Nantes); J.M. Chennebault, V. Rabier, P. Fialaire, Y.M. Vandamne, P. Abgueguen, S. Rehaiem (Angers); P. Perré, T. Guimard, S. Léautez, J.L. Esnault, O. Bollengier-Stragier, I. Suaud, L. Lainé, H. Durand, C. Garnier (La Roche sur Yon); H. Hitoto, L. Perez, I. Ali (Le Mans); C. Michau (Saint Nazaire); R. Vatan (Laval).

References

1. Norman SE, Chediak AD, Kiel M, Cohn MA. Sleep disturbances in HIV-infected homosexual men. AIDS. 1990;4(8):775–81.
2. Crum-Cianflone NF, Roediger MP, Moore DJ, et al. Prevalence and factors associated with sleep disturbances among early-treated HIV-infected persons. Clin Infect Dis. 2012;54(10):1485–94.
3. Gamaldo CE, Gamaldo A, Creighton J, et al. Evaluating sleep and cognition in HIV. J Acquir Immune Defic Syndr. 2013;63(5):609–16.
4. Low Y, Preud'homme X, Goforth HW, Omonuwa T, Krystal AD. The association of fatigue with depression and insomnia in HIV-seropositive patients: a pilot study. Sleep. 2011;34(12):1723–6.
5. Reid S, Dwier J. Insomnia in HIV infection: a systematic review of prevalence, correlates and management. Psychosom Med. 2005;67(2):260–9.
6. Beck AT, Steer RA, Brown GK. Manual for the beck depression inventory—II. San Antonio: Psychological Corporation; 1996.
7. Buysse DJ, Reynolds CF, Monk TH, Berman SR, Kupfer DJ. The Pittsburgh Sleep Quality Index: a new instrument for psychiatric practice and research. Psychiatry Res. 1989;28(2):193–213.
8. Beck F, Richard J, Léger D. Insomnia and total sleep time in France: prevalence and associated socio-demographic factors in a general population survey. Rev Neurol. 2013;169(12):956–64.
9. Grandner MA, Patel NP, Gehrman PR, et al. Who gets the best sleep? Ethnic and socioeconomic factors related to sleep complaints. Sleep Med. 2010;11(5):470–8.
10. Chapman DP, Wheaton AG, Perry GS, Sturgis SL, Strine TW, Croft JB. Household demographics and perceived insufficient sleep among US adults. J Community Health. 2012;37(2):344–9.
11. Clifford DB, Evans S, Yang Y, Acosta EP, Ribaudo H, Gulick RM. Long-term impact of efavirenz on neuropsychological performance and symptoms in HIV-infected individuals (ACTG 5097 s). HIV Clin Trials. 2009;10(6):343–55.
12. Morphy H, Dunn KM, Lewis M, Boardman HF, Croft PR. Epidemiology of insomnia: a longitudinal study in a UK population. Sleep. 2007;30(3):274–80.
13. Gamaldo CE, Spira AP, Hock RS, et al. Sleep, function and HIV: a multi-method assessment. AIDS Behav. 2013;17(8):2808–15.
14. Gamaldo CE, McArthur JC. The evaluation and diagnosis of "insomnia" in relation to sleep disturbance prevalence and impact in early-treated HIV-infected persons. Clin Infect Dis. 2012;55(10):1429–30;**author reply 30–1**.