Original Article

Sleep Quality and Its Correlates in HIV Positive Patients Who Are Candidates for Initiation of Antiretroviral Therapy

Fatemeh Dabaghzadeh, Pharm.D[1]
Hossein Khalili, Pharm.D [1,2]
Padideh Ghaeli, Pharm.D[1]
Abbas Alimadadi, MSc[3]

1 Department of clinical pharmacy, Faculty of Pharmacy, Tehran University of Medical Sciences, Tehran, Iran.
2.Faculty of Pharmacy, Kerman university of Medicai Sciences, Kerman, Iran
3 Psychiatry and psychology Research center, Roozbeh Hospital, Tehran University of Medical Sciences, Tehran, Iran

Corresponding author:
Padideh Ghaeli, Pharm.D. Faculty of Pharmacy (Tehran University of Medical Sciences), Roozbeh Psychiatric Hospital, South Kargar Ave, Tehran, Iran.
Tel: +98-21-55412222
Email: pghaeli@sina.tums.ac.ir
.

Objective: Based on Pittsburg Sleep Quality Index, it has been reported that most human immunodeficiency virus (HIV) positive patients suffer from various degrees of sleep problems. Sleep disorders can affect quality of life, physical and social functioning and can also cause chronic fatigue. Some psychological and physiological factors are related to sleep quality. The purpose of the present study was to evaluate sleep quality and its related psychological and physiological factors in Iranian human immunodeficiency virus positive patients who were candidates for initiation of antiretroviral therapy .
Method: This was a cross- sectional study of 59 HIV positive out-patients in stages 2 or 3 of HIV disease who were candidates for initiation of antiretroviral therapy. Pittsburg Sleep Quality Index (PSQI), Hamilton Depression Rating Scale (HDRS), Hamilton Anxiety Rating Scale (HARS) and Somatization Subscale of Symptom Checklist 90 (SCL-90) were used to assess the patients' sleep quality, depression, anxiety and physiological factors, respectively. SPSS software version 12 was used for data analysis. The Pearson correlation coefficient was utilized to analyze the correlation between PSQI and other quantitative variables.
Results: Based on the sleep quality assessment, 47.5 % of the patients had PSQI > 5 that was defined as sleep disturbances. A significant correlation was found between sleep quality and HDRS ($r = 0.531$, $p = 0.0001$), HARS ($r = 0.627$, $p = 0.0001$) and somatization subscale of SCL-90 ($r = 0.36$, $p = 0.05$).
Conclusion: This study showed that human immunodeficiency virus positive individuals suffer from sleep disorders at least as same as the general population, and that psychological variables including depression and anxiety and physiological variables including physical morbidities in different systems of the body lead to sleep disturbance in this population.

Key words: *Human immunodeficiency virus, Sleep quality*

Iran J Psychiatry 2013; 8:4: 160-164

Sleep disorders are common problems and have been reported in 10% to 40% of the general population (1). These problems can affect quality of life, physical and social functioning and can also cause chronic fatigue (1). It seems that HIV (human immunodeficiency virus) infected individuals are more vulnerable to sleep disturbances (2). Based on Pittsburg Sleep Quality Index, it has been reported that 73 % to 100% of HIV positive patients suffer from various degrees of sleep problems (3-4). Normal sleep architecture can be changed (1-2), and slow wave sleep may be increased significantly in HIV positive individuals (5-7). Greater sleep onset latency, early morning awakening, more frequent awakenings during the night, and reduced sleep efficiency have been reported in this population (8-11). Anxiety and depression are psychological factors that affect sleep quality (1, 12-13). Sleep disturbance is a common symptom of depression (13). Patients with anxiety disorders have delayed sleep onset and reduced total sleep time (12). HIV positive patients with higher levels of depression or anxiety showed more sleep disturbances than HIV positive individuals without depression and anxiety symptoms (8). Physical symptoms such as pain, abdominal cramping, diarrhea, incontinence, itching, burning, fever, night sweats, cough and dyspnea can also cause sleep disturbances in HIV positive patients (8). Some studies have suggested an inverse correlation between immune system and sleep quality in HIV positive patients (14-15), but others did not show this relationship (5, 16-17). The frequency of sleep disturbances was evaluated in different populations such as general population (35.2%) (18), renal transplant (62%) (19), dialysis (73.8%) (20), multiple sclerosis (87.2%) (21) and cancer patients (71.7%) (18). Sleep quality and its correlated factors have not been evaluated in the Iranian HIV positive individuals. The aim of this study was to evaluate the sleep quality

and its related psychological and physiological factors in the Iranian HIV positive patients who were candidates for initiation of antiretroviral therapy.

Material and Methods

This cross-sectional study was conducted in the HIV Clinic of Imam Khomeini Hospital Complex in Tehran, Iran during a one year period. Fifty nine (42 males and 17 females), 18 to 55 year old HIV positive patients were included in this survey. The stages of HIV infection were determined according to 1993 revised classification of centers for disease control and prevention (CDC) definition. The stages A, B and C are based on patients' clinical condition related to HIV infection. The stages 1, 2 and 3 are based on patients' CD4 cells count. The CD4 cell counts for stages 2 and 3 are 200/µl to 499/µl and below 200/µl, respectively (22). All the participants had CD4 cell counts of less than 350/µl and were candidates for initiation of antiretroviral therapy. The patients' demographic and laboratory data were collected. Pittsburg Sleep Quality Index (PSQI), the validated Persian versions of Hamilton Depression Rating Scale (HDRS), Hamilton Anxiety Rating Scale (HARS) (23) and Somatization Subscale of Symptom Checklist 90 (SCL-90) (24, 25) were used to assess the patients' sleep quality, depression, anxiety and physiological factors, respectively. It should be explained that PSQI is a self measured, 7-component questionnaire including subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medications and daytime dysfunction during the last month. The validated Persian version of PSQI (Cronbach's alpha= 0.77) was utilized in the present study (26); PSQI of greater than 5 was considered as sleep disturbance (11). An expert interviewer completed the HDRS and HARS questionnaires. The HDRS is a 17-item scale, and it is categorized from 0 to 4 (27). The HARS evaluates 14 anxiety related parameters, with scores of 0 to 4 (28). Somatization dimension of SCL-90 represents physical morbidity. This self- reported questionnaire includes 12 items. This subscale represents distress in different systems of the body such as cardiovascular, gastrointestinal, respiratory, autonomic systems and is rated from 0 (none) to 4 (extreme) (29). SPSS software version 12 was used for data analysis. Normal distribution of the variables was assessed according to Kolmograph-Smirnov test. The Pearson correlation coefficient was used to analyze the correlation between PSQI and other quantitative variables. The patients were assigned into two groups: patients with normal sleep and patients with sleep disturbance (PSQI score > 5). The Chi-square test was used to determine the relationship between these two groups and the stages of HIV infection. P value of less than 0.05 was considered as statistically significant.

Result

Fifty nine HIV positive patients (42 males and 17 females) with the mean ± SD age of 36.9 ± 9.8 were included in the study. The patients' demographic data were summarized in Table 1. In this study, 42.4% of the patients had a high-school diploma, 55.9% were married and 52.5% were self-employed. The most common routes of HIV transmission were sexual contacts (35.6 %) and injection drug use (33.9 %). Oral candidiasis (10.2 %) and chronic hepatitis C (23.7%) were the most common opportunistic infection and concomitant disease in the patients .

The patients' mean ± SD of PSQI, HDRS, HARS and Somatization Subscale of SCL-90 scores were 5.88 ± 4.22, 12.58 ± 7.18, 8.58 ± 5.78 and 11.29 ± 7.45, respectively. The classification of these scores is demonstrated in Table 2.

Based on the sleep quality assessment, 47.5 % of the patients had PSQI > 5 that was defined as sleep disturbances. A significant correlation was found between sleep quality and HDRS ($r = 0.531$, $p = 0.0001$), HARS ($r = 0.627$, $p= 0.0001$) and Somatization Subscale of SCL-90 ($r = 0.36$, $p = 0.05$) (Table 3). The frequency of PSQI > 5 of the patients in different stages of HIV infection are displayed in Table 4. The correlation between the patients' HIV infection stages and PSQI scores was significant , ($X2 (1) = 5.732$, $p = 0.017$). There was not any significant correlation between the patients' laboratory data and their sleep quality except neutrophil percentage ($r = 0.309$, $p = 0.023$).

Discussion

Although sleep disorders are common problems in the general population, the prevalence of sleep disorders is more common in the HIV positive population than the general population, and it can affect the quality of life of these patients (1). The correlation between the severity of HIV infection and its progression to advanced stages of this disease has been reported in several studies (8, 14-15). We detected sleep disturbances in 47.5 % of the Iranian HIV positive individuals who were candidates for antiretroviral therapy. Sleep disorders have been reported in 63% to 100% of other HIV positive populations (2, 8, 11).

Wibbeler et al. Reported that 63.9 % of the HIV positive patients could be classified as poor sleepers based on the PSQI score (11). In another study, Robbins et al. found that all their HIV infected participants suffered from sleep disturbance (8).

In our patients, the prevalence of sleep disorders was similar to 10% to 40% of the Iranian general population and to other countries (2, 19, 30).

Table1: Demographic data of the patients

Characteristics		Frequency (percent) or Mean± SD
Sex	Male	42 (71.2 %)
	Female	17 (28.8 %)
Age		36.9 ± 9.8
Weight		65.9 ± 12.7
Period between diagnosis and treatment		19.14 ± 25.23
CD_4 count		157.91 ±117.23
Education	Illiterate	4 (6.8 %)
	Elementary	9 (15.3 %)
	Guidance school	13 (22.0 %)
	High school	25 (42.4 %)
	More than Diploma	8 (13.6%)
Transmission	IV drug injection	20 (33.9 %)
	Sex	21 (35.6 %)
	Needle	1 (1.7 %)
	IV drug injection and sex	11 (18.6 %)
	Unknown	4 (6.8 %)
	Blood	2 (3.4 %)
Job	Self-employed	31 (52.5 %)
	House-hold	9 (15.3 %)
	Employee	4 (6.8 %)
	Student	3 (5.1 %)
	Taxi driver	4 (6.8 %)
	Unemployed	6 (10.2 %)
	Engineer	1 (1.7 %)
	Medical staff	1 (1.7 %)
Opportunistic Infection	TB	1 (1.7 %)
	CMV	2 (3.4 %)
	Candidiasis	6 (10.2 %)
	None	47 (79.7 %)
	Zoster	2 (3.4 %)
	TB and Candidiasis	1 (1.7 %)
Concomitant disease	Diabetes	1 (1.7 %)
	Depression	1 (1.7 %)
	HBV	2 (3.4 %)
	HCV	11 (18.6 %)
	GI disease	3 (5.1 %)
	None	38 (64.4 %)
	HBV and HCV	3 (5.1 %)
State of marriage	Single	19 (32.2 %)
	Married	33 (55.9 %)
	Divorced	7 (11.9 %)

The patients' demographic data including age, sex, duration of HIV infection, CD4 count, HIV transmission rout , education, job and baseline diseases and concomitant infections.
IV: Intravenous, TB: Tuberculosis, CMV: Cytomegalovirus, HCV: Hepatitis C virus, HBV: Hepatitis B virus, GI: Gastrointestinal, SD: Standard deviation

Table2: Classification of the patients' depression, anxiety and sleep quality status

Parameter	Score	Frequency (%)	Mean± SD
Depression	Normal (0-7)	12 (20.3 %)	12.58 +/- 7.18
	Mild Depression (8-13)	22 (37.3 %)	
	Moderate Depression (14-18)	11 (18.6 %)	
	Severe Depression (19-22)	8 (13.6 %)	
	Very Severe Depression (≥ 23)	6 (10.2 %)	
Anxiety	Normal (0-13)	46 (78 %)	8.58 +/- 5.78
	Mild Anxiety (14-17)	11 (18.6 %)	
	Moderate Anxiety (18-24)	1 (1.7 %)	
	Severe Anxiety (25-30)	1 (1.7 %)	
Sleep quality	Patient with normal sleep	31 (52.5 %)	5.88 +/- 4.22
	Patient with sleep disturbance	28 (47.5 %)	

The patients' depression, anxiety and sleep quality were assessed and categorized based on the Hamilton Depression Rating Scale (HDRS), Hamilton Anxiety Rating Scale (HARS) and
Pittsburg Sleep Quality Index (PSQI) respectively

Table3: Correlation between sleep quality and neuropsychiatric scales

Scales	Correlation coefficient	p value
HDRS	0.531	0.0001
HARS	0.627	0.0001
Somatization subscale of SCL90	0.36	0.05

HDRS: Hamilton Depression Rating Scale, HARS: Hamilton Anxiety Rating Scale, SCL90: Symptom Checklist 90

Table 4: Data of stages of HIV infection and patients with and without sleep disturbance

Stage of HIV infection	Patients with normal sleep, frequency (%)	Patients with disturbed sleep, frequency (%)	P value
2	16 (27.1 %)	6 (10.2 %)	0.017
3	31 (25.4 %)	22 (37.3 %)	
A	25 (42.4 %)	22 (37.2 %)	
B	4 (6.8 %)	4 (6.8 %)	0.981
C	2 (3.4 %)	2 (3.4 %)	

Stage of HIV infection was determined according to 1993 revised classification of centers for disease control and prevention (CDC) definition. The Chi-square test was used to determine the relationship between these two groups and stages of HIV infection

Sleep disorders were reported in 32.1 % of the Austrian general population (31). In a random sample study of an Iranian urban population, sleep disturbances were detected in 37% of the participants (30). Nearly equal prevalence of sleep disturbances in our HIV positive individuals and the general population may be attributed to our inclusion criteria of the study. We evaluated HIV positive out-patients with CD4 count of lower than 350/µl. These patients did not receive antiretroviral therapy and did not complain about serious concomitant diseases or opportunistic infections. Predisposing factors for sleep disturbances in this population have been reported as antiretroviral, complications of concomitant diseases and opportunistic infections including general pain, abdominal cramping, diarrhea, incontinence, itching, burning, fever, night sweats, cough and dyspnea (8). In white et al. study, no difference was observed between HIV positive patients with CD4 counts of less than 400 and seronegative controls in sleep disturbance frequency (7) .

A significant correlation was found between the stages of HIV infection and sleep disturbances in the present study. In previous studies, it was reported that the quality of sleep will be worsen along with disease progression in HIV positive individuals (8, 14-15). Darko et al. reported that sleep disturbances was related to CDC stages of HIV infection (15). The risk of opportunistic infections and an indication for antibiotic prophylaxis will increase with HIV infection progression in this population. Opportunistic infections can produce various symptoms including pain, fever, night sweet, pain, cough and dyspnea that can disturb patients' sleep (8) .

Our findings showed that both psychological and physiological factors can affect sleep quality. We found a direct correlation between sleep disturbance and depression, anxiety and physical morbidity as measured by HDRS, HARS and Somatization Subscale of SCL- 90. These findings are in line with the results of other studies (2, 8, 11). Depression is the most important factor that affects sleep quality (11); physiological factors such as pain and psychological factors such as psychological stressors in HIV positive patients can also affect their sleep quality (1). We used the HDRS and HARS to assess depression and anxiety, and we found they are correlated with sleep quality (8). Depression and anxiety are frequent depression and anxiety status in our patients. These questionnaires have been used to evaluate these mental disorders in HIV positive patients in another study (16). HIV positive individuals with anxiety have problems in falling asleep, decreased slow wave sleep and more non REM sleep (2, 8). In this study, physical morbidity in HIV infected patients was assessed based on Somatization Subscale of SCL- 90. This questionnaire has been used in HIV positive population in another study in Iran (24). Physical morbidities including pain, abdominal cramping, diarrhea, incontinence, itching, burning, fever, night sweats, cough and dyspnea are common problems in HIV infected patients. These morbidities can cause problems in falling asleep and may diminish sleep efficiency (8). Also, pain may cause non-restorative sleep in HIV positive individuals (1).

Limitations

The limitations of this study were the small sample size and the absence of control group. Sleep disturbances and predisposing factors should be evaluated in a prospective and well controlled study with sufficient sample size .

We suggest that treatment of depression, anxiety and physical morbidity can improve sleep quality in HIV positive patients.

Conclusion

This study showed that human immunodeficiency virus positive individuals suffer from sleep disorders at least as same as the general population, and that psychological variables including depression and anxiety and physiological variables including physical morbidities in different systems of the body lead to sleep disturbance in this population.

Acknowledgement

This study was a part of Dr. Dabaghzadeh's thesis toward graduation from post-doctoral residency in clinical pharmacy and was supported by Faculty of Pharmacy, Tehran University of Medical Sciences (grant number: 89-04-33-11884).

References

1. Reid S, Dwyer J. Insomnia in HIV infection: A systematic review of prevalence, correlates, and management. Psychosom Med 2005; 67: 260-269.
2. Phillips KD, Skelton WD. Effects of individualized acupuncture on sleep quality in

HIV disease. J Assoc Nurses AIDS Care 2001; 12: 27-39.
3. Rubinstein ML, Selwyn PA. High prevalence of insomnia in an outpatient population with HIV infection. J Acquir Immune Defic Syndr 1998; 19: 260-266.
4. Hand GA, Phillips KD, Sowell RL, Rojas M, Becker J. Prevalence of poor sleep quality in a HIV+ population of Americans. J S C Med Assoc 2003; 99: 201-205.
5. Cohen FL, Ferrans CE, Vizgirda V, Kunkle V, Cloninger L. Sleep in men and women infected with human immunodeficiency virus. Holist Nurs Pract 1996; 10: 33-43.
6. Norman S, Shaukat M, Nay KN, Cohn M, Resnick L. Alterations in sleep architecture in asymptomatic HIV seropositive patients. Sleep Res 1987; 16: 494-9.
7. White JL, Darko DF, Brown SJ, Miller JC, Hayduk R, Kelly T, et al. Early Central Nervous System Response to Hiv Infection: Sleep Distortion and Cognitive-Motor Decrements. AIDS 1995; 9: 1043-1050.
8. Robbins JL, Phillips KD, Dudgeon WD, Hand GA. Psychological and physiological correlates of sleep in HIV infection. Clin Nurs Res 2004; 13: 33-52.
9. Wiegand M, Möller AA, Schreiber W, Krieg JC, Fuchs D, Wachter H, Holsboer F. Nocturnal sleep EEG in patients with HIV infection. Eur Arch Psychiatry Clin Neurosci 1991; 240: 153-158.
10. Wheatley D, Smith K. Clinical sleep patterns in human immune virus infection. Hum Psychopharm CLIN 1994; 9: 111-115.
11. Wibbeler T, Reichelt D, Husstedt IW, Evers S. Sleepiness and sleep quality in patients with HIV infection. J Psychosom Res 2012; 72: 439-442.
12. Nokes KM, Chidekel JH, Kendrew J. Exploring the complexity of sleep disturbances in persons with HIV/AIDS. J Assoc Nurses AIDS 1999; 10: 22-29.
13. Fuller KH, Waters WF, Binks PG, Anderson T. Generalized anxiety and sleep architecture: A polysomnographic investigation. Sleep 1997; 20: 370-176.
14. Brown S, Mitler M, Atkinson H, Malone J, Chandler J, McCutchen A, et al. Correlation of subjective sleep complaints absolute T-4 cell number and anxiety in HIV illness. Sleep Res 1991; 20: 363-368.
15. Darko DF, McCutchan JA, Kripke DF, Gillin JC, Golshan S. Fatigue, sleep disturbance, disability, and indices of progression of HIV infection. Am J Psych 1992; 149: 514-520.
16. Perkins DO, Leserman J, Stern RA, Baum SF, Liao D, Golden RN, et al. Somatic Symptoms and Hiv Infection: Relationship to Depressive Symptoms and Indicators of Hiv Disease. Am J Psychiatry 1995; 152: 1776-1781.
17. Nokes KM, Kendrew J. Correlates of sleep quality in persons with HIV disease. J Assoc Nurses AIDS Care 2001; 12: 17-22.
18. Shahidi J, Khodabakhshi R, Yahyazadeh S H, Amini M Gh, Nosrati H. Quality of Sleep in Cancer Patients: Evidences from Persian Translation of Pittsburgh Sleep Quality Index. AAJC 2007; 6: 165-168.
19. Kachuee H, Ameli J, Taheri S, Assari S, Riahipour F, Khedmat H, et al. Sleep quality and its correlates in renal transplant patients. Transplant Proc 2007; 39: 1095–1097.
20. Sabet R, Naghizadeh MM, Azari Quality of sleep in dialysis patients. Iran J Nurs Midwifery Res 2012; 17: 270-274.
21. Ghaem H, Borhani Haghighi A. The impact of disability, fatigue and sleep quality on the quality of life in multiple sclerosis. Ann Indian Acad Neurol 2008; 11: 236-241.
22. From the Centers for Disease Control and Prevention. 1993 revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. JAMA 1993; 269: 729–30.
23. hams J, Gudarzi SSP, Ghorbani B, Habibi LK, Yasami MT. The Efficacy and Safety of Add-on Ginko TD (Ginkgo Biloba) Treatment for PTSD: Results of a 12-Week Double-Blind Placebo-Controlled Study. Iran J Psychiatry 2007; 2: 58-64.
24. Hedayati-Moghaddam MR, Eftekharzadeh Mashhadi I, Zibaee R, Hosseinpoor AM, Fathi-Moghaddam F, Bidkhori H. Assessment of Psychiatric Symptoms Using SCL-90-R among HIV/AIDS Individuals in Razavi Khorasan Province, Iran. Iran Red Crescent Med J 2011; 13: 58-59.
25. Mirzai R. Standardizing and validating of SCL-90-R in Iran. Arch Iran Med 2009; 12: 5-14.
26. Farrahi Moghaddam J, Nakhaee N, Sheibani V, Garrusi B, Amirkafi A. Reliability and validity of the Persian version of the Pittsburgh Sleep Quality Index (PSQI-P). Sleep Breath 2012; 16: 79-82.
27. Hamilton M. A rating scale for depression. J Neurol Neurosurg Psychiatry 1960; 23: 56-62.
28. Bruss GS, Gruenberg AM, Goldstein RD, Barber JP. Hamilton Anxiety Rating Scale Interview guide: joint interview and test-retest methods for interrater reliability. J Psychiatr Res 1994; 53: 191-202.
29. Derogatis L. Symptoms checklist-90: administration, scoring and procedures manual for the revised version. Baltimore, Minneapolis: NCS Pearson; 1994.
30. Asghari A, Farhadi M, Kamrava SK, Ghalehbaghi B and Nojomi M. Subjective Sleep Quality in Urban Population. Archives of Iranian medicine 2012; 15: 95-98.
31. Zeitlhofer J, Schmeiser-Rieder A, Tribl G, Rosenberger A, Bolitschek J, Kapfhammer G, et al. Sleep and Quality of Life in the Austrian Population. Acta neurologica Scandinavica 2000; 102: 249-257.