Sleep science

SLEEP DISTURBANCES AND GENDER DIFFERENCES IN SCHIZOPHRENIA

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Running Title: *Sleep in schizophrenia*

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ABSTRACT

Objective: The objective of this study was to evaluate sleep disorders and their relationship to clinical variables in schizophrenia. Subjects and Methods: In this cross-sectional study with ambulatory patients suffering from schizophrenia, sleep quality was evaluated with the Pittsburgh Sleep Quality Index (PSQI), and excessive daytime sleepiness by the Epworth Sleepiness Scale (ESS). Results: Eighty-two patients (42 male and 40 female) aged 17 to 59 years (mean age 32.2±9.8) were studied. Poor sleep quality (PSQI>6), exhibited by 41 patients (51.3%), was independently associated with the female gender (OR=2.98; CI=1.13-7.83). Excessive daytime sleepiness (ESS>10) was found in 20 patients (24.7%), and ESS scores tended to correlate with treatment duration (P=0.07). Conclusion: In schizophrenia, poor sleep quality, present in 50% of the patients studied, is associated with the female gender. We suggest that physical and cognitive-behavior therapy to improve sleep quality should be initiated intensively in women with schizophrenia.

Keywords: Sleep; Schizophrenia; Epworth Sleepiness Scale.

INTRODUCTION

Sleep is an active state vital for physical, mental, and emotional well-being, and is important for optimal cognitive functioning (1). Sleep problems are described as difficulty in falling or staying asleep, in staying awake, or in adhering to a consistent sleep-wake schedule. Poor sleep quality and excessive daytime sleepiness are known to occur in both schizophrenia (2) and Parkinson's disease (3), suggesting that dopamine may play a role in regulating the sleep-wake cycle (4). Administration of antipsychotic drugs that have effects on neurotransmitter systems, including histamine, acetylcholine, serotonin, norepinephrine and dopamine, might play a role in the sleep-wake cycle. Antipsychotic therapy in schizophrenia can minimize sleep problems. Conversely, sedative effects associated with these medications have the ability to disrupt sleep and wake patterns. Randomized controlled trials comparing the effects of these medications upon sleep have rarely been conducted (5).

It has already been shown that sleep quality is related to quality of life (6), and altered sleep has been associated with a failure to consolidate learning (7). Although the characteristics of sleep in patients with schizophrenia have been described (8), subjective sleepiness (previously associated with deficits in pre-frontal activation (9) can potentially affect cognition and has rarely been investigated. Other relevant aspects of the relationship between sleep disorders and clinical variables, particularly gender differ-

ences, have not been studied.

Although schizophrenia affects both genders with the same frequency, women tend to have a better clinical pre-morbid state, develop the disease at a later age, and show a different symptom profile, with less florid psychotic symptoms (10,11). These findings have been attributed to different structural brain abnormalities. A better response to typical antipsychotic drugs in patients undergoing the premenopausal phase has been associated with the presence of estrogen (12). Understanding gender differences in schizophrenia is critical to guide therapeutic decisions.

The purpose of this study was to evaluate sleep quality, excessive daytime sleepiness and its relationship to the severity of comorbidity among patients with schizophrenia.

SUBJECTS AND METHODS

Study design

This was a cross-sectional study involving a sample of 82 ambulatory schizophrenia patients consecutively recruited from an outpatient hospital-based clinic. Assessment included the Structured Clinical Interview from the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV). All subjects met the DSM-IV criteria for schizophrenia (13), and had not undergone recent hospitalizations or changes in medication in the preceding three months. Mini-Mental State (MMSE) (14) above 18 was required to join the study. None of the subjects were using sleep-promoting drugs, such as benzodiazepines or antidepressants. The antipsychotic treatment as well had not undergone any changes during the preceding three months. All data were collected simultaneously during a four-month period. The pertinent protocol was approved by the local Research Ethics Committee, and written informed consent was obtained from all patients involved.

Assessment procedures

A socio-demographic and clinical questionnaire was applied by a medical staff comprising three professionals. Clinical data were further confirmed by a chart review. Subjective sleep quality was evaluated by the Pittsburgh Sleep Quality Index (PSQI) (15). The PSQI has seven components, each one dealing with a major aspect of sleep: 1) subjective sleep quality; 2) sleep onset latency; 3) sleep duration; 4) sleep efficiency; 5) presence of sleep disturbances; 6) use of hypnotic-sedative medication; and 7) presence of daytime disturbances, as an indication of daytime alertness. Component six always scored zero because the patients who used hypnotic-sedative medication were not included in the study. Individuals showing total PSQI scoring six or above were considered poor sleepers.

Excessive daytime sleepiness (EDS) was assessed by the Epworth Sleepiness Scale (ESS), a validated questionnaire containing eight items that query about dozing expectation in eight hypothetical situations. Dozing probability ratings range from zero (no probability) to three (high probability) (16). An ESS scoring 10 or above indicates EDS.

Statistical analysis

Data were examined for normality using the Kolmogorov-Smirnov test. ANOVA and Mann-Whitney test were used to assess gender differences. Pearson's correlation test was used to compare scores of behavior and clinical variables. A logistic regression analysis was performed to estimate the effect of clinical variables in the presence of poor sleep quality (PSQI>6) and excessive daytime sleepiness (ESS>10). Further adjustments were made using variables derived from the bivariate analysis (P<0.1). The statistical analysis was done with the Statistic Package for Social Sciences (SPSS- Norusis, 1993) software for Windows. The level of significance was set at p<0.05.

RESULTS

Eighty-two subjects of both genders (42 male) aged 17 to 59 years (mean age 32.2±9.8 years) with schizophrenia were evaluated. Patients were either in use of traditional antipsychotic medication (haloperidol or fluphenazine) or atypical antipsychotic medication (risperidone or olanzapine). Therapy duration ranged from 3 to 72 months (mean duration 4.96±4.99). Clinical and demographic data are depicted in Table 1. Women were of older age, had undergone treatment for longer periods, and had lower levels of education (Table 1). Poor sleep quality (PSQI>6) could be observed in 41 (51.3%) of the cases, and prevailed among female patients (mean 7.08±2.86); mean among male patients was 5.15±2.67 (Mann-Whitney, P= 0.002).

Table 1: Demographic data of 82 patients with the diagnosis of schizophrenia according to gender

		Male N=42	Female N=40	Test, p value
Age (y)	Range Mean±SD	18-59 31.81±9.90	17-56 38.95±9.86	ANOVA, 0.002**
Treatment duration (m)	Range Mean±SD	3-20 5.57 ±5.42	4-72 10.14 ±13.27	ANOVA, 0.008**
Years of education (y)	Range Mean±SD	1-5 3.56 ±1.42	1-5 2.56 ±1.68	ANOVA, 0.04*
PSQI	Range Mean±SD	1-12 5.15 ±2.67	2-12 7.08± 2.86	Mann-Whitney, 0.002**
ESS	Range Mean±SD	0-18 6.83± 5.06	0-15 5.83 ±4.18	Mann-Whitney, 0.48

Abbreviations: y=years; m=months; PSQI=Pittsburgh Sleep Quality Index; ESS=Epworth Sleepiness Scale.

The patient's age was directly correlated with treatment duration and inversely to years of education (Table 2). PSQI scores were inversely correlated with level of education, indicating that patients with a higher level of education had better sleep quality. ESS scores showed a trend of correlation with treatment duration (p=0.07).

Table 2: Pearson correlation test between clinical variables and scores of behavioral scales in 82 patients with schizophrenia

	Age	Treatment duration	Years of education	PSQI
Treatment duration	r=0.359** p= 0.001			
Years of education	r=-0.250* p=0.03	r=-0.150 p= 0.20		
PSQI scores	r=0.113 p=0.31	r=0.088 p=0.44	r=-0.356** p=0.002	
ESS scores	r=-0.081 p=0.47	r=-0.204 p=0.07	r=0.058 p=0.62	r=0.010 p=0.92

Abbreviations: PSQI= Pittsburgh Sleep Quality Index; ESS= Epworth Sleepiness Scale. *=p<0.05; **=p<0.01

Poor sleep quality was associated with the female gender (OR= 2.79; CI= 1.12-6.90) and remained so after controlling for years of education (OR= 2.98; CI= 1.13-7.83) (Table 2). Excessive daytime sleepiness (ESS>10) was found in 20 patients (24.7%), and was not associated with any of the measures studied (Table 3).

Table 3: Logistic regression analysis between clinical variables, poor sleep quality (PSQI>6) and excessive daytime sleepiness (ESS>10)

	PSQI>6 N=41 (51.3%)	ESS>10 N=20 (24.7%)
Gender	2.79 (1.12-6.90)*	0.60 (0.21-1.68)
Age	1.00 (0.96-1.05)	0.99 (0.95-1.04)
Treatment duration	1.02 (0.97-1.07)	1.00 (0.96-1.05)
Years of education	0.66 (0.49-0.90)	1.09 (0.79-1.52)

Abbreviations: PSQI= Pittsburgh sleep quality index; ESS= Epworth sleepiness scale.

DISCUSSION

The results of our study show that poor sleep quality is frequent and independently associated with the female gender in patients with schizophrenia. According to our data, a more vigorous therapy, particularly the use of physical therapy or cognitive behavior therapy for sleep disorders, could be used in female patients. Gender differences in schizophrenia have been extensively described. It has been observed that male cases tend to develop earlier, and severe forms of the disease cause greater deterioration (17). In contrast, schizophrenia onset in the female sex occurs later and presents more severe positive and affective symptoms (11). Anxiety-depressive symptoms and low self-perception have also been described in association with the female gender in schizophrenia (18). Our findings related to poor sleep quality in women may be explained by the presence of increased mood behavior disorders in such patients. Interestingly, sleep quality was not correlated with age and treatment duration, but was correlated with the level of education. In this study, women were older and had a lower level of education. Lower school performance levels among women can be explained by lower pressure for educational achievement, particularly due to different cultural pressures exerted upon men and women. It has been previously demonstrated that lower school performance levels predict poor outcomes (19). As sleep quality was not related to age or to comorbidity severity, two factors frequently associated with sleep disorders, we postulate that sleep disorders commonly found in schizophrenia are directly connected to mental illness.

We found that nearly a quarter of patients presented excessive daytime sleepiness. In our study, a trend of association between therapy duration and excessive daytime sleepiness was found, so it is possible that chronic antipsychotic therapy contributes to sleepiness. Personality disorders have already been identified as an important clinical factor that determines excessive daytime sleepiness (20). Establishing causes for daytime sleepiness may be a difficult task, considering that in other medical situations it has been demonstrated that several clinical conditions, such as diabetes (21), sleep apnea syndrome and daily social activities (22), can interfere with the sleep-wake cycle. To our knowledge, studies on the prevalence of sleepiness and its association with clinical factors or therapeutic measures in schizophrenia are still missing. This is an important subject, and modafinil, a drug that reduces sleepiness, has been associated with general schizophrenia improvement (23).

In short, poor sleep quality, shown by half of patients studied, prevails among female patients. We suggest that physical and cognitive-behavior therapy with the purpose of improving sleep quality should be initiated intensively in women with schizophrenia.

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