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Sedative-Hypnotic Use in Patients with Borderline Personality Disorder and Axis II Comparison Subjects

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Abstract

Sleep disturbance is a common, yet poorly understood, phenomenon in borderline personality disorder (BPD). We examined the use of sedative-hypnotic medication in BPD, as part of a larger naturalistic study. In comparison to other personality disorder (OPD) comparison subjects, a significantly higher percentage of BPD subjects than OPD subjects used both as needed (prn) and standing medications to help them sleep. Specifically, over the course of the study, BPD subjects were approximately 4 times more likely to have used prn (OR = 4.27, 95% CI: 2.22–8.22) and standing sleeping medications (OR = 3.81, 95% CI: 1.88–7.72). When adjusted for differences in depression, anxiety, and age among BPD and OPD subjects, BPD subjects were approximately 3 times more likely to have used prn (adjusted OR = 3.38, 95% CI: 1.73–6.61) and standing sleeping medications (adjusted OR = 2.81, 95% CI: 1.33–5.95). These results indicate that sedative-hypnotic use is greater among BPD than OPD subjects. They also confirm clinical observations that subjective sleep disturbance is a significant problem in BPD.

Introduction

Sleep disturbance is a common phenomenon seen across the spectrum of psychiatric illness. A significant literature exists examining the role of sleep abnormalities in mood, psychotic, and anxiety disorders (Krystal, Thakur, & Roth, 2008; Mellman, 2006). Less attention has been paid to the role of sleep disturbance in borderline personality disorder (BPD), although clinically patients with BPD frequently complain of sleep disturbance. Given that both insomnia and BPD are significant causes of morbidity, investigation into the nature of sleep disturbance in BPD is warranted (Buysse, Germain, Moul, & Nofzinger, 2005; Gunderson & Zanarini, 1987).

The vast majority of studies examining sleep in BPD have focused on objective findings using polysomnography (PSG). Objective PSG findings in BPD including shortened rapid-

eye movement (REM) latency, increased REM density, slow-wave sleep (SWS) abnormalities, and sleep continuity disturbance have all been reported (Akiskal, Yerevanian, Davis, King, & Lemmi, 1985; Asaad, Okasha, & Okasha, 2002; Battaglia, Ferini Strambi, Bertella, Bajo, & Bellodi, 1999; Bell, Lycaki, Jones, Kelwala, & Sitaram, 1983; Benson, King, Gordon, Silva, & Zarcone, 1990; De la Fuente, Bobes, Vizuite, & Mendlewicz, 2001; De la Fuente et al., 2004; Lahmeyer et al., 1988; McNamara et al., 1984; Reynolds et al., 1985). However, interpretation of the literature is complicated by the fact that several studies failed to control for co-morbid psychiatric disorders (e.g. depression) and similar PSG findings occur in myriad psychiatric disorders (Benca, Obermeyer, Thisted, & Gillin, 1992). Furthermore, even when co-morbid depression is accounted for in the study design, objective PSG findings in BPD are not consistent across studies. More recently, a comparison of never-depressed BPD subjects to healthy controls failed to find significant differences in REM or SWS variables (Philipsen et al., 2005). Although BPD subjects did not exhibit significant differences in standard objective measures of sleep during the study, they did exhibit increased delta power in non-REM and REM sleep as determined by spectral analysis, and reported significantly worse sleep using subjective measures both during and prior to the study, consistent with other reports of subjective sleep complaints in BPD patients without co-occurring depression (Asaad et al., 2002; Philipsen et al., 2005; Semiz, Basoglu, Ebrinc, & Cetin, 2008). These results suggest there may be a discrepancy between objective and subjective measures of sleep disturbance in BPD.

Although the literature suggests that patients with BPD may have associated objective and/or subjective sleep disturbance, little is known about the management (e.g., use of sedative-hypnotic medications) or evaluation of sleep disturbance in BPD populations. When examining the first six years of the McLean Study of Adult Development (MSAD), a significantly higher percentage of non-remitted BPD patients than remitted borderline patients used daily sleep medication, suggesting that sleep disturbance may be a marker of or perpetuating factor for continued illness in BPD (Frankenburg & Zanarini, 2004). Beyond this, to our knowledge, there have been no studies examining the use of medications for sleep in BPD, and thus this post hoc study examines the use of sedative-hypnotic medications among BPD subjects in a naturalistic setting. Given that BPD subjects have frequent sleep complaints, we hypothesized that BPD subjects would have a higher frequency of use of sedative-hypnotic medications than axis II comparison subjects.

Methods

Subjects

The current study utilized data generated by the McLean Study of Adult Development (MSAD), a longitudinal study of the course of BPD. The MSAD design and methodology are described in detail elsewhere (Zanarini, Frankenburg, Hennen, & Silk, 2003). In brief, subjects were initially identified while inpatients at McLean Hospital in Belmont, Massachusetts. Initial screening criteria included that subjects: be 18 to 35 years of age; have a known or estimated IQ greater than or equal to 71; have no prior or current symptomatology of schizophrenia, schizoaffective disorder, bipolar I disorder, or an organic etiology that could cause psychiatric symptoms; and be fluent in English. At the initiation of the study, a total of 362 subjects were enrolled: 290 meeting study criteria for BPD, 72 subjects meeting criteria for other personality disorders (OPD). Attrition was low throughout the course of the study: 91%, 88%, and 86% of original BPD subjects and 88%, 85%, and 83% of original OPD subjects completed follow-up at years 6, 8, and 10 respectively. At the year 10 assessment, 18 BPD subjects had died (12 by suicide; 6 by other causes) and 1 OPD subject died (by suicide). Overall, 91% (N=309) of surviving subjects were re-interviewed at all five follow-up waves.

Procedures

After study procedures were explained at baseline, written informed consent was obtained. Each subject met with a masters-level interviewer who conducted a comprehensive diagnostic assessment when blinded to the subject's clinical diagnoses. Three semi-structured diagnostic interviews were administered: the Structured Clinical Interview for DSM-III-R Axis I Disorders (SCID-I), the Revised Diagnostic Interview for Borderlines (DIB-R), and the Diagnostic Interview for DSM-III-R Personality Disorders (DIPD-R) (Spitzer, Williams, Gibbon, & First, 1992; Zanarini MC, Gunderson JG, Frankenburg FR, Chauncey DL, 1989; Zanarini, Frankenburg, Chauncey, & Gunderson, 1987). Inter-rater and test-retest reliability of these three measures have been found to be good to excellent (Zanarini & Frankenburg, 2001; Zanarini, Frankenburg, & Vujanovic, 2002).

At each follow-up wave 24 months apart, axis I and II psychopathology was reassessed by staff members blind to baseline diagnoses. Informed consent was obtained again in each case, and the aforementioned diagnostic battery was re-administered. The follow-up inter-rater and follow-up longitudinal reliability of these three measures have also been found to be good to excellent (Zanarini & Frankenburg, 2001; Zanarini et al., 2002). At 6-year follow-up and each follow-up thereafter (8-year and 10-year), the Medical History and Services Utilization Interview (MHSUI), was administered to assess the health of patients, lifestyle issues related to physical health, and health care utilization (Frankenburg & Zanarini, 2004).

Within the follow-up at years 6, 8, and 10, two separate questions regarding the use of sedative-hypnotic medications were asked of subjects. One question (in the Revised Borderline Follow-Up Interview; BFI-R) asked whether subjects had taken an as needed (*pro re nata*; prn) medication to help them sleep for at least a month; a separate question (in the MHSUI) inquired whether in the last two years, subjects had taken a medication to help them sleep on a regular (standing) basis. Both questions were included in the analysis to prevent self-report bias due to omission (e.g., a sedative-hypnotic medication could be reported as a standing, but not a prn medication, and vice-versa).

Two additional sleep-related questions were considered of secondary interest. As part of the MHSUI, subjects were asked if they had been referred for a sleep study (polysomnography; PSG) in the previous two years. As part of the BFI-R subjects were asked if one of their standing medications (excluding medications prescribed specifically to help them sleep) was found to be most helpful because of its soporific effects.

Data Analysis

Marginal logistic regression modeling, using the generalized estimating equations (GEE) approach, was conducted to determine if the use of sedative-hypnotics differed between subjects with BPD as compared to other personality disorder (OPD) comparison subjects. Analyses included the effects of diagnostic group (BPD versus OPD) and time of measurement (prior analyses indicated that there were no significant interactions between diagnostic group and time). Analyses were conducted with and without adjustment for potential confounding variables. Due to sparseness of data and limitations of sample size, three sets of potential confounders were separately adjusted for in the analyses to determine if their inclusion altered the crude (or unadjusted) analyses in a discernible way: co-occurring depression or anxiety disorder, sex, and age. The three anxiety disorders included in the analysis were generalized anxiety disorder, panic disorder, and post-traumatic stress disorder, as these are the primary anxiety disorders most frequently associated with sleep disturbance (Mellman, 2006). To allow for a possible non-linear relationship between sedative-hypnotic use and age (e.g., insomnia burgeoning at age-related events such as

menopause), we included both age and age-squared in these analyses. Because adjustment for sex did not alter the crude or unadjusted analysis, it was excluded from the final analysis, however major depressive episode, anxiety disorder, age, and age-squared were all included in the final analysis as potential confounders. Statistical significance was fixed at $\alpha = 0.05$ and effects are reported in terms of (un)adjusted odds ratios (OR) comparing BPD subjects to OPD subjects.

Results

Table 1 presents the clinical variables of interest at the 6-year follow-up of the MSAD for BPD and OPD subjects. The proportion of BPD subjects who were female was significantly greater than in the OPD comparison subjects. Similarly, rates of panic disorder, PTSD, and depression were significantly greater among BPD than OPD subjects.

Table 2 presents the primary and secondary sleep-related variables of interest in BPD and OPD subjects, including adjusted and unadjusted comparisons between the two groups. Over the course of the study, rates of use of prn sleeping medications among BPD subjects ranged from 23.9–29.8% compared to 3.2–11.5% among OPD subjects. Similarly, rates of standing sleeping medication use ranged from 17.3–31.4% among BPD subjects compared to 5.0–9.5% among OPD subjects. BPD subjects were significantly more likely to have used prn and standing sleeping medications compared to OPD subjects in the unadjusted analysis. Specifically, over the course of the study, the BPD subjects were approximately 4 times more likely to have used prn (OR = 4.27, 95% CI: 2.22–8.22) and standing sleeping medications (OR = 3.81, 95% CI: 1.88–7.72). When adjusted for differences in depressive episode, anxiety disorder, and age, there was some attenuation of the magnitude of these effects; however, the use of both prn and standing sleep medications remained significantly higher among BPD than OPD subjects. Specifically, when adjusted for depressive episode, anxiety disorder, and age, BPD subjects were approximately 3 times more likely to have used prn (adjusted OR = 3.38, 95% CI: 1.73–6.61) and standing sleeping medications (adjusted OR = 2.81, 95% CI: 1.33–5.95).

In regards to secondary outcome measures of interest, BPD subjects did not significantly ($Z=1.44$, $p = 0.15$) report that their standing medications (excluding sleeping medications) were most helpful due to their soporific effects (adjusted OR = 1.8, 95% CI: 0.81–4.02). However, BPD subjects were significantly ($Z=2.44$, $p = 0.015$) more likely to be referred for a sleep study compared to OPD subjects (unadjusted OR = 4.32, 95% CI: 1.33–13.99). Due to the relatively low frequency of sleep study referrals as compared to sedative-hypnotic use, adjustment for the potential confounders was not made for the sleep study referral data.

Discussion

This study demonstrates that BPD subjects report significantly greater use of sedative-hypnotic medications than OPD comparison subjects in a naturalistic study. In many ways, the results of this study are not surprising since sleep disturbance is a common clinical complaint faced by practitioners in the treatment of patients with BPD. That the significantly higher use of sedative-hypnotic medications remains despite controlling for other major comorbidities that cause insomnia (e.g., depressive and anxiety disorders) and common risk factors for sleep disturbance (e.g., increasing age), suggests that the sleep disturbance in BPD may be a distinct entity present among BPD patients. Alternatively, BPD may be a risk factor for the development of other causes of sleep disturbance that were not controlled for in this study (e.g., pain syndromes, urinary urgency, etc.). In particular, nightmares may be more common in BPD than the general population, even in the absence of PTSD, and thus

patients in our study may have self-reported sleeping medications that included those prescribed specifically to manage nightmares (Semiz et al., 2008).

Another potential explanation of these results is that increased sedative-hypnotic use in patients with BPD may reflect a greater tendency to report a sleep complaint in patients with BPD, rather than truly increased rates of sleep disturbance in this population. Subjects with BPD may be more sensitive to transient sleep disruptions, and thus, more likely to report a complaint. Also, BPD subjects may have had more frequent visits to prescribing clinicians than OPD subjects, increasing the likelihood that an insomnia complaint would be treated pharmacologically.

The major limitation of this study is that it does not use a direct measure of sleep complaints, but rather uses a surrogate marker for sleep disturbance, the use of medications to help one sleep. Another limitation of the study is that it is based on self-report data that can not be verified, raising the possibility that subjects may have inaccurately reported that medications prescribed for some other reason (e.g. mood lability, impulse control) with the desired side effect of somnolence, were reported as sleeping medications. In the case of BPD, it is quite possible that the use of sedative-hypnotics may be a component of treatment in which assistance with sleep is only one, albeit an overt, target of clinical management.

BPD subjects, in our clinical experience, often take a number of sedating medications, and occasionally, may seek to be “knocked out” or unconscious in times of heightened stress or intolerable emotional states. Often, possibly due to a confluence of transference/countertransference issues, the patient may be prescribed a sedative-hypnotic to attain this goal. In such instances, the use of a sleeping pill would not be a treatment of insomnia per se, but rather would be a treatment of the underlying emotional distress by inducing sleep. In these cases, a complaint of sleep disturbance might represent a easier problem to treat, resulting in “collusion” to treat the sleep complaint with medications, rather than addressing the underlying cause of the insomnia (Hartmann, 1978).

This study raises several important issues and potential areas of future investigation. The study design did not permit the discrimination of what types of sedative-hypnotic medications were used by subjects, and it would be of interest to know what classes of medications were used in BPD, and if they vary from OPD subjects or from trends in the general population. Furthermore, assessment of sleep complaints in BPD using standardized instruments among a large group of subjects would be useful to validate the findings of subjective sleep disturbance in previous studies that tended to have relatively small sample size. Also, it is intriguing that BPD subjects were more frequently referred for PSG, since PSG is not routinely indicated for the evaluation of insomnia, raising the possibility that rates of other primary sleep disorders (e.g. obstructive sleep apnea) may differ in BPD than OPD subjects. Finally, investigation into dysfunctional cognitions and behaviors about sleep that may be present in patients with BPD could lead to improved psychotherapeutic treatments in this population, which might obviate the need for sedative-hypnotic medications and ultimately be a better modality for management of sleep complaints in BPD patients.

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Table 1

Demographic and Clinical Characteristics of Borderline Patients and Axis II Comparison Subjects
 Clinical characteristics of BPD and OPD comparison subjects at 6 Year Follow-up of the McLean Study of Adult Development (MSAD).

	Borderline Personality Disorder	Other Personality Disorder
Total N	264	63
Mean age $\pm$ std dev	32.9 $\pm$ 5.8	33.5 $\pm$ 8.0
Sex N (%) *		
Women	213 (80.7%)	42 (66.7%)
Axis I Disorders N (%)		
GAD	19 (7.2%)	2 (3.2%)
Panic Disorder **	77 (29.2%)	7 (11.1%)
PTSD **	92 (34.8%)	3 (4.8%)
Major Depressive Episode **	162 (61.4%)	23 (36.5%)

Significant between group differences were:

* P<0.05,

** P<0.005.

Table 2

Unadjusted and adjusted comparisons of primary and secondary sleep-related outcomes in BPD versus OPD subjects. Variables included as covariates in adjusted analyses include major depressive episode, anxiety disorder (generalized anxiety disorder, panic disorder, post-traumatic stress disorder), age, and age-squared.

	Borderline Personality Disorder (%/N)			Other Personality Disorder (%/N)			Unadjusted		Adjusted	
	6 Yr FU (N=264)	8 Yr FU (N=255)	10 Yr FU (N=251)	6 Yr FU (N=63)	8 Yr FU (N=61)	10 Yr FU (N=60)	OR Diagnosis Time	95% CI Diagnosis Time	OR Diagnosis Time	95% CI Diagnosis Time
Primary Outcomes										
Pm sleep medication	23.9% 63	29.8% 76	23.9% 60	3.2% 2	11.5% 7	8.3% 5	4.27 1.08	2.22-8.22 0.78-1.48	3.38 1.30	1.73-6.61 0.91-1.85
Standing sleep medication	31.4% 83	21.2% 54	17.1% 43	9.5% 6	8.2% 5	5.0% 3	3.81 0.45	1.88-7.72 0.31-0.66	2.81 0.50	1.33-5.95 0.33-0.76
Secondary Outcomes										
Other Psychotropic Medications Help with Sleep	13.6% 36	11.0% 28	5.6% 14	4.8% 3	3.3% 2	5.0% 3	2.60 0.45	1.24-5.42 0.28-0.73	1.80 0.49	0.81-4.02 0.30-0.80
Sleep Study	8.3% 22	5.1% 13	5.6% 14	0.0% 0	0.0% 0	5.0% 3	4.32 0.78	1.33-13.99 0.40-1.54	NA	NA