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Rates of Psychotropic Medication Use Reported by Borderline Patients and Axis II Comparison Subjects over 16 Years of Prospective Follow-up

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Abstract

The purpose of this study was to assess the classes and types of psychotropic medication reported by borderline patients and axis II comparison subjects over 16 years of prospective follow-up. Medication use was assessed at baseline using a semistructured interview of proven reliability and validity as well as its follow-up analog at eight contiguous two-year follow-up periods. A significantly higher percentage of borderline patients than axis II comparison subjects reported taking an antidepressant, an anxiolytic, an antipsychotic, and a mood stabilizer over time. They also reported more commonly taking seven of the ten more specific types of medication studied (i.e., all but tricyclic antidepressants, monoamine oxidase inhibitor antidepressants [MAOIs], and atypical antipsychotics). The rates over time of taking antipsychotics and mood stabilizers were stable, while there was a significant decline in the rates of antidepressants and anxiolytics from baseline to eight-year follow-up (but not from eight to 16-year follow-up) reported by those in both study groups. In terms of specific medications, rates of atypical antidepressants and anticonvulsants were the most stable. In contrast, nonbenzodiazepine anxiolytics declined the most steadily over time, while rates of atypical antipsychotics increased significantly over the 16 years of prospective follow-up. Taken together, the results of this study suggest that a substantial percentage of borderline patients continue to use the major classes of medication over time. They also suggest that the declining rates of use tend to stabilize less than a decade after index admission.

Introduction

Pharmacotherapy is a very common form of treatment for those with borderline personality disorder (BPD). However, only eight naturalistic studies have documented this clinical practice.[1-8] Five of these studies are cross-sectional in nature.[1-5] In general, they found that

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rates of taking standing psychotropic medications were high for patients with BPD and often discriminating for the disorder.

Two of these cross-sectional studies prospectively followed the psychiatric treatment received by their subjects.[6-8] Bender et al. conducted a two-year follow-up study[6] of borderline patients and comparison subjects. Some of the subjects in this study—the Collaborative Longitudinal Study of Personality Disorder (CLPS)--were initially inpatients, others were outpatients, and some were seeking treatment. It was found that patients with borderline personality disorder were significantly more likely than patients with major depressive disorder and no serious personality pathology to have had a medication consultation session over time.

Zanarini et al.[7] studied the classes and types of medication reportedly taken by 290 borderline patients and 72 axis II comparison subjects who were initially inpatients over six years of prospective follow-up. They found that taking any standing medication and polypharmacy involving 2-5 concurrent medications was significantly more common among borderline patients than axis II comparison subjects. They also found that all four classes of medication studied (i.e., antidepressants, anxiolytics, antipsychotics, and mood stabilizers) were reported by a significantly higher percentage of borderline patients than axis II comparison subjects. However, for those in both study groups, use of each of these classes of medication declined significantly over time at about the same rate.

Hörz and colleagues[8] also studied time-to-stopping taking standing psychotropic medication in this sample over 10 years of prospective follow-up. It was found that 44% of borderline patients were able to stop taking these medications for at least one two-year follow-up period. However, 67% of those who stopped later resumed taking standing psychotropic medications.

The current study builds upon these two earlier longitudinal studies from the McLean Study of Adult Development (MSAD) in three important ways. First, it returns to the inclusive list of classes and types of medication assessed in the earlier of these two studies. Second, it adds an additional decade of prospective follow-up to the study of this inclusive list of classes and types of psychotropic medication. Third, it assesses time trends encompassing the first and second eight years of follow-up separately— allowing us to determine the significance of short and midterm declines in use vs. further long-term declines in participation in the 14 forms of pharmacotherapy studied.

Materials and Methods

As noted above, the current study is part of the McLean Study of Adult Development (MSAD), a multifaceted longitudinal study of the course of borderline personality disorder. The methodology of this study, which was reviewed and approved by the McLean Hospital Institutional Review Board, has been described in detail elsewhere.[9] Briefly, all subjects were initially inpatients at McLean Hospital in Belmont, Massachusetts. Each patient was screened to determine that he or she: 1) was between the ages of 18-35; 2) had a known or estimated IQ of 71 or higher; 3) had no history or current symptomatology of schizophrenia,

schizoaffective disorder, bipolar I disorder, or an organic condition that could cause serious psychiatric symptoms (e.g., lupus, MS); and 4) was fluent in English.

After the study procedures were explained, written informed consent was obtained. Each patient then met with a masters-level interviewer blind to the patient's clinical diagnoses for a thorough psychosocial and treatment history as well as diagnostic assessment. Four semistructured interviews were administered: 1) the Background Information Schedule (BIS), which assesses lifetime psychiatric treatment history,[5] 2) the Structured Clinical Interview for DSM-III-R Axis I Disorders (SCID I),[10] 3) the Revised Diagnostic Interview for Borderlines (DIB-R),[11] and 4) the Diagnostic Interview for DSM-III-R Personality Disorders (DIPD-R).[12] The interrater reliability of the BIS was carefully assessed in a sample of 45 personality-disordered patients and was found to be good-excellent.[5] As a measure of validity, we compared self-report of treatment history according to the BIS with the medical records of 15 patients who had received all of their psychiatric care at McLean Hospital. Convergent validity was also found to be good-excellent[5]. In addition, the inter-rater and test-retest reliability of all three diagnostic measures have been found to be good-excellent.[13,14]

The psychotropic medications used by borderline patients and axis II comparison subjects over the years of follow-up were assessed using the treatment section of the Revised Borderline Follow-up Interview[15]—the follow-up analog to the Background Information Schedule. This measure, as well as our diagnostic battery, was readministered every two years over 16 years of prospective follow-up by raters blind to previously collected information. The follow-up interrater reliability (within one generation of follow-up raters) and follow-up longitudinal reliability (from one generation of raters to the next) of these four interviews have also been found to be good-excellent.[7,13,14]

The vast majority of our two-year follow-up interviews were conducted within several months of the date of each subject's last interview. However, two subjects who were unavailable for interview at 12 and 14-year waves of data collection provided six years of data at 16-year follow-up. A third subject who was unavailable for interview at 8, 10, 12, and 14-year waves of data collection provided 10 years of data at 16-year follow-up. All told, eight of 2881 interviews (or 0.3%) assessed a longer time period than our typical two years.

Statistical Analyses

Data on psychotropic medications were assembled in panel format (i.e., multiple records per patient, with one record for each follow-up period for which data were available). Generalized estimating equations (GEE), appropriately accounting for repeated measures on the same patients, were used to fit loglinear regression models assessing the role of diagnostic group (BPD vs. OPD or other personality disorder) on the prevalence of medication use over time. Specifically, these analyses modeled the log prevalence as a piecewise-linear function of time, with separate slopes for the change from baseline to 8 year follow-up and for the corresponding change from 8 to 16 year follow-up; the models also included the effect of diagnostic group. Preliminary tests of diagnostic group by time

interactions were also conducted to assess whether the pattern of change in prevalence differed by diagnostic group. As there was no evidence of interaction, main effects of diagnostic group and time are reported; results of these analyses yielded an adjusted relative risk ratio (RRR) and 95% confidence interval (95%CI) for diagnostic group and the two time trends. Given the large number of comparisons for the 14 classes or types of medication studied, we applied the Bonferroni correction for multiple comparisons to the analysis of each class or type of medication, resulting in the following adjusted alpha level: 0.0036 (0.05/14).

Results

The sample and its diagnostic characteristics have been described before.[9] Two hundred and ninety patients met both Revised Diagnostic Interview for Borderlines and DSM-III-R criteria for borderline personality disorder and 72 met DSM-III-R criteria for at least one nonborderline axis II disorder (and neither criteria set for borderline personality disorder). Of these 72 comparison subjects, 4% met DSM-III-R criteria for an odd cluster personality disorder, 33% met DSM-III-R criteria for an anxious cluster personality disorder, 18% met DSM-III-R criteria for a nonborderline dramatic cluster personality disorder, and 53% met DSM-III-R criteria for personality disorder not otherwise specified (which was operationally defined in the DIPD-R as meeting all but one of the required number of criteria for at least two of the 13 axis II disorders described in DSM-III-R).

Baseline demographic data have also been reported before.[9] Briefly, 77.1% (N=279) of the subjects were female and 87% (N=315) were white. The average age of the subjects was 27 years (SD=6.3), the mean socioeconomic status was 3.3 (SD=1.5) (where 1=highest and 5=lowest), and their mean GAF score was 39.8 (SD=7.8) (indicating major impairment in several areas, such as work or school, family relations, judgment, thinking, or mood).

In terms of continuing participation, which has also been described before,[16] 87.5% (N=231/264) of surviving borderline patients (13 died by suicide and 13 died of other causes) were reinterviewed at all eight follow-up waves. A similar rate of participation was found for axis II comparison subjects, with 82.9% (N=58/70) of surviving patients in this study group (one died by suicide and one died of other causes) being reassessed at all eight follow-up waves.

Table 1 details the rates of four classes of standing medications reported by borderline patients and axis II comparison subjects over 16 years of prospective follow-up. It also details the rates of 10 more specific types of medication reported by those in the two study groups over the years of follow-up. As can be seen, a significantly higher percentage of borderline patients than axis II comparison subjects reported taking an antidepressant, an anxiolytic, an antipsychotic, and a mood stabilizer over time. Specifically, the reported rates of antidepressants were approximately 30% higher (RRR=1.32, 95%CI: 1.12, 1.54) for borderline patients than axis II comparison subjects; the reported rates of anxiolytics and antipsychotics were 2.6 times higher, while the reported rates of mood stabilizers were approximately 3 times higher (RRR=2.88, 95%CI: 1.87, 4.44).

The rates for both study groups reporting taking an antidepressant and an anxiolytic declined significantly from baseline to eight-year follow-up but not from eight-year follow-up to 16-year follow-up. The rates of antipsychotics and mood stabilizers did not decline significantly in either follow-up time period for those in either study group.

In terms of the four more specific types of antidepressants, a significantly higher percentage of borderline patients than axis II comparison subjects reported taking an SSRI and an atypical antidepressant but not a tricyclic or an MAO inhibitor. Both types of anxiolytics studied—benzodiazepines and nonbenzodiazepines—were reported by a significantly higher percentage of borderline patients than axis II comparison subjects. In terms of antipsychotics, a significantly higher percentage of borderline patients reported taking a conventional but not an atypical antipsychotic. Both types of mood stabilizer studied—anticonvulsants and lithium—were reported by a significantly higher percentage of borderline patients than axis II comparison subjects

Over time, both study groups reported a significantly declining rate of taking an SSRI, a tricyclic, an MAO inhibitor, a benzodiazepine, and lithium from baseline to eight-year follow-up but not eight-year follow-up to 16-year follow-up. Those in both study groups reported a significantly declining rate of taking a nonbenzodiazepine anxiolytic and a conventional antipsychotic as well as a significantly increasing rate of taking an atypical antipsychotic at both follow-up time periods. Only the reported rates of taking an atypical antidepressant and an anticonvulsant remained stable over time for those in both study groups (i.e., did not decline significantly at either follow-up time period).

Given the complexity of these analyses, an example is presented to enhance understanding of these results. Borderline patients reported taking nonbenzodiazepine anxiolytics almost four times more commonly than axis II comparison subjects (RRR=3.99, 95%CI: 2.03, 7.85). The rate of decline for those in both groups was 49% ([1-0.51[) × 100%) during the first eight-year follow-up period and 66% ([1-0.34[) × 100%) during the second eight-year follow-up period.

Discussion

Three main findings have emerged from this study. The first is that a significantly higher percentage of borderline patients than axis II comparison subjects reported taking all four classes of medication studied as well as seven of the 10 more specific types of medication assessed. There were no discernable differences in the percentages of borderline patients and axis II comparison subjects who reported taking tricyclic antidepressants, MAOIs, and atypical antipsychotics. This is not surprising as it is generally recognized that borderline psychopathology is typically more severe than that of other types of personality disorders. It also confirms and extends similar findings from the first six years of follow-up.[7]

The second is that the rates of all four classes of medication studied remained relatively stable over time, either declining only over the first eight years of follow-up (antidepressants and anxiolytics) or not at all over the 16 years of prospective follow-up (antipsychotics and mood stabilizers). Given the naturalistic nature of this study, it is not clear what the

physicians prescribing these medications were targeting. It might have been co-occurring disorders, general psychiatric symptoms, or symptoms of BPD. For example, an atypical antipsychotic may have been prescribed for the cognitive symptoms of BPD, for severe anxiety, or to augment the effects of an antidepressant. In any case, all of these classes of psychotropic medications remained common even at 16-year follow-up. More specifically, over 50% of borderline patients reported taking an antidepressant and over 25% reported taking an anxiolytic, an antipsychotic, or a mood stabilizer. However, it should be noted that antidepressants were the class of medication most commonly reported by borderline patients throughout the study.

The third is that the reported use of seven more specific types of medication declined significantly over time for those in both study groups. Six of these medications had significantly declining rates of use only from baseline to eight-year follow up—SSRIs, tricyclics, MAOIs, benzodiazepines, nonbenzodiazepines, and lithium. However, the reported rates of conventional antipsychotics were found to decline significantly in both follow-up periods: baseline to eight-year follow-up and eight-year follow-up to 16-year follow-up. It is not clear why borderline patients reported these declining rates of use. It may be because the severity of their borderline psychopathology was lessening.[16] It may also be because the rates of co-occurring disorders were declining.[17] However, some of the declining rates of use may have been due to changes in prescribing practices as many physicians replaced older types of medication (e.g., tricyclics, MAOIs) with newer types of medication that they believed to be more efficacious and/or to have a more benign side effect profile (e.g., atypical antidepressants, atypical antipsychotics). This pattern has been found for other disorders, including bipolar I disorder.[18]

This study has two main limitations. The first is that all of the subjects were initially inpatients. Thus, these results might not apply to those with a personality disorder who were never hospitalized. The second is that subjects in both study groups may have had trouble remembering all the medications they took during each two-year follow-up period. In that case, these percentages would be an underrepresentation of the medications taken.

Acknowledgments

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Table 1

Rates of Psychotropic Medication Reported by Borderline Patients and Axis II Comparison Subjects over 16 Years of Prospective Follow-up

	BL	2 YR FU	4 YR FU	6 YR FU	8 YR FU	10 YR FU	12 YR FU	14 YR FU	16 YR FU	RRR Diagnosis Time (0-8) Time (8-16)	95%CI Diagnosis Time (0-8) Time (8-16)	P-value Diagnosis Time (0-8) Time (8-16)
Any Antidepressant												
BPD[1]	79.7 (231)	82.6 (227)	62.8 (169)	66.7 (176)	63.5 (162)	64.7 (161)	68.0 (166)	61.3 (146)	58.4 (135)	1.32 0.76 0.98	1.12, 1.54 0.69, 0.84 0.90, 1.08	0.001 <0.001 NS
OPD[2]	56.9 (41)	73.1 (49)	39.1 (25)	46.0 (29)	41.9 (26)	45.9 (28)	50.0 (30)	45.8 (27)	51.7 (30)			
Selective Serotonin Reuptake Inhibitor (SSRI)												
BPD	67.9 (197)	64.7 (178)	43.5 (117)	50.4 (133)	45.5 (116)	47.4 (118)	48.8 (119)	38.7 (92)	35.5 (82)	1.38 0.67 0.85	1.13, 1.68 0.59, 0.77 0.73, 0.99	0.001 <0.001 NS
OPD	37.5 (27)	58.2 (39)	28.1 (18)	34.9 (22)	35.5 (22)	37.7 (23)	36.7 (22)	28.8 (17)	34.5 (20)			
Tricyclic Antidepressant												
BPD	51.4 (149)	19.6 (54)	11.2 (30)	10.6 (28)	7.1 (18)	5.6 (14)	5.7 (14)	5.0 (12)	6.1 (14)	1.56 0.08 1.31	1.08, 2.27 0.05, 0.13 0.77, 2.22	NS <0.001 NS
OPD	31.9 (23)	11.9 (8)	4.7 (3)	6.4 (4)	1.6 (1)	1.6 (1)	3.3 (2)	3.4 (2)	3.5 (2)			
Monoamine Oxidase Inhibitor (MAOI)												
BPD	11.0 (32)	4.7 (13)	1.9 (5)	0.0 (0)	0.8 (2)	0.8 (2)	0.4 (1)	1.3 (3)	0.4 (1)	1.89 0.04 1.61	0.73, 4.88 0.01, 0.11 0.28, 9.35	NS <0.001 NS
OPD	2.8 (2)	3.0 (2)	4.7 (3)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)	0.0 (0)			
Atypical Antidepressant												
BPD	31.7 (92)	39.3 (108)	31.2 (84)	34.1 (90)	32.6 (83)	28.9 (72)	32.0 (78)	33.2 (79)	32.5 (75)	1.70 0.91 1.06	1.20, 2.41 0.76, 1.10 0.88, 1.28	0.003 NS NS
OPD	11.1 (8)	26.9 (18)	14.1 (9)	14.3 (9)	16.1 (10)	14.8 (9)	23.3 (14)	23.7 (14)	22.4 (13)			
Any Anxiolytic												
BPD	46.6 (135)	37.1 (102)	29.0 (78)	28.4 (75)	28.6 (73)	25.7 (64)	23.8 (58)	26.9 (64)	26.0 (60)	2.57 0.56 1.05	1.72, 3.86 0.46, 0.68 0.86, 1.30	<0.001 <0.001 NS
OPD	15.3 (11)	19.4 (13)	9.4 (6)	11.1 (7)	4.8 (3)	11.5 (7)	11.7 (7)	11.9 (7)	8.6 (5)			
Benzodiazepine												
BPD	43.1 (125)	31.3 (86)	24.9 (67)	22.0 (58)	23.9 (61)	22.9 (57)	22.1 (54)	24.4 (58)	24.7 (57)	2.66 0.50 1.26	1.66, 4.28 0.40, 0.62 1.00, 1.57	<0.001 <0.001 NS
OPD	13.9 (10)	16.4 (11)	6.3 (4)	7.9 (5)	4.8 (3)	8.2 (5)	8.3 (5)	10.2 (6)	6.9 (4)			
Nonbenzodiazepine												
BPD	16.9 (49)	11.6 (32)	11.5 (31)	10.2 (27)	8.2 (21)	5.6 (14)	3.3 (8)	4.6 (11)	2.2 (5)	3.99 0.51 0.34	2.03, 7.85 0.34, 0.76 0.18, 0.65	<0.001 0.001 0.001
OPD	1.4 (1)	6.0 (4)	3.1 (2)	3.2 (2)	0.0 (0)	3.3 (2)	3.3 (2)	1.7 (1)	1.7 (1)			

	BL	2 YR FU	4 YR FU	6 YR FU	8 YR FU	10 YR FU	12 YR FU	14 YR FU	16 YR FU	RRR Diagnosis Time (0-8) Time (8-16)	95%CI Diagnosis Time (0-8) Time (8-16)	P-value Diagnosis Time (0-8) Time (8-16)
Any Antipsychotic												
BPD	38.6 (112)	28.7 (79)	23.1 (62)	27.3 (72)	28.6 (73)	27.7 (69)	26.2 (64)	30.7 (73)	28.1 (65)	2.61 0.74 1.20	1.64, 4.19 0.60, 0.91 0.99, 1.45	<0.001 NS NS
OPD	12.5 (9)	11.9 (8)	9.4 (6)	7.9 (5)	6.5 (4)	9.8 (6)	18.3 (11)	13.6 (8)	13.8 (8)			
Conventional Antipsychotic												
BPD	37.6 (109)	21.1 (58)	13.0 (35)	12.9 (34)	18.4 (47)	17.3 (43)	9.8 (24)	3.4 (8)	3.5 (8)	3.28 0.45 0.32	1.85, 5.80 0.34, 0.59 0.20, 0.49	<0.001 <0.001 <0.001
OPD	11.1 (8)	9.0 (6)	4.7 (3)	3.2 (2)	1.6 (1)	3.3 (2)	3.3 (2)	1.7 (1)	0.0 (0)			
Atypical Antipsychotic												
BPD	6.2 (18)	11.3 (31)	12.6 (34)	16.3 (43)	14.9 (38)	16.5 (41)	21.3 (52)	28.2 (67)	26.4 (61)	2.14 1.98 1.77	1.16, 3.95 1.36, 2.87 1.40, 2.25	NS <0.001 <0.001
OPD	2.8 (2)	4.5 (3)	4.7 (3)	4.8 (3)	4.8 (3)	8.2 (5)	15.0 (9)	11.9 (7)	13.8 (8)			
Any Mood Stabilizer												
BPD	35.9 (104)	30.2 (83)	23.4 (63)	22.0 (58)	28.2 (72)	29.3 (73)	28.3 (69)	28.2 (67)	29.0 (67)	2.88 0.73 1.25	1.87, 4.44 0.59, 0.91 1.01, 1.54	<0.001 NS NS
OPD	11.1 (8)	16.4 (11)	7.8 (5)	6.4 (4)	6.5 (4)	8.2 (5)	8.3 (5)	10.2 (6)	13.8 (8)			
Anticonvulsant												
BPD	22.1 (64)	22.2 (61)	21.6 (58)	18.2 (48)	25.9 (66)	28.5 (71)	25.0 (61)	26.5 (63)	28.1 (65)	3.17 1.14 1.21	1.86, 5.39 0.87, 1.49 0.97, 1.52	<0.001 NS NS
OPD	2.8 (2)	9.0 (6)	7.8 (5)	4.8 (3)	4.8 (3)	6.6 (4)	8.3 (5)	10.2 (6)	13.8 (8)			
Lithium												
BPD	25.9 (75)	12.0 (33)	5.6 (15)	4.9 (13)	4.3 (11)	2.8 (7)	6.2 (15)	4.2 (10)	3.9 (9)	2.97 0.13 1.54	1.63, 5.43 0.07, 0.24 0.71, 3.34	<0.001 <0.001 NS
OPD	8.3 (6)	7.5 (5)	0.0 (0)	1.6 (1)	1.6 (1)	3.3 (2)	0.0 (0)	0.0 (0)	0.0 (0)			

[1] borderline personality disorder

[2] other personality disorder