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PRN (As-Needed) Psychotropic Medication Use in Borderline Patients and Other Personality-Disordered Subjects over 14 Years of Prospective Follow-up

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Abstract

The use of PRN (as-needed) psychotropic medication in borderline patients has not been well characterized. This study had three purposes: (i) to describe the prevalence of PRN psychotropic medication use among borderline patients and other personality-disordered comparison subjects over 14 years of prospective follow-up; (ii) to examine the rates reported by ever-recovered and never-recovered borderline patients; and (iii) to examine the reasons for taking PRN medication reported by these patients. Overall, the prevalence of PRN psychotropic medication use was initially approximately 3 times higher among borderline patients than other personality-disordered comparison subjects, with a significant one-third decline in the use of PRN medication reported by borderline patients over time. In analyses restricted to borderline patients, never-recovered borderline patients were about twice as likely to use PRN medication than ever-recovered borderline patients over time. In terms of reasons for use, the rates of PRN medication use to decrease agitation for both diagnostic groups declined significantly over time, although they remained significantly higher among borderline patients. Likewise, never-recovered borderline patients reported higher use of PRN medication to decrease agitation than ever-recovered borderline patients over time. The results of this study indicate that PRN psychotropic medication is widely used for the treatment of borderline patients, particularly those who have not achieved a recovery in both the symptomatic and psychosocial realms. They also suggest that borderline patients use proportionally more PRN medication to decrease agitation than other personality comparison subjects, with lower proportional use to reduce agitation found among recovered borderline patients.

Introduction

Clinical experience suggests that a high percentage of individuals with borderline personality disorder (BPD) receive *pro re nata* (PRN) or as-needed psychotropic medication, despite no evidence of its efficacy. Among hospitalized psychiatric patients with a variety of diagnoses, the prevalence of PRN use ranges from 23%¹ to 97%², and the diagnosis of any personality disorder is associated with a higher use of PRN per day than those with a diagnosis of depressive episode, brief psychotic episode, schizophrenia, and bipolar affective disorder.²

PRN medication for borderline patients is used to relieve symptoms such as sleep disturbance, agitation, anxiety, impulsivity, anger, heightened emotional lability, and transient psychosis³. When a patient has such symptoms, the decision of when to administer the PRN medication is left to the nurse, caregiver, or patient, under a previously prescribed medication regimen. The drugs typically administered PRN include antipsychotic, anxiolytic, and hypnotic agents, and can be given orally or by intramuscular injection.⁴ An early prescription of standing medication may be avoided with the initial use of PRN medication to treat acute symptoms before they worsen⁵. Additionally, a judicious use of PRN medication can be helpful in evaluating the need to change the standing medication plan³. For instance, in borderline patients whose anxiety problems demand constant PRN use, a reevaluation of the standing medication dose may be needed.

However, there are no studies comparing the effects of regularly scheduled medication to PRN medication for BPD. In fact, there is evidence that PRN medications used to treat psychiatric disorders in general are associated with increased risks of morbidity, unwanted side effects, pharmacological interactions between regular and PRN drugs, polypharmacy, and physical addiction⁶. Furthermore, greater PRN administration may result in higher than recommended dosages, complicated assessment of efficacy of regular scheduled medicines, and be a cause of non-adherence with regular medication⁷. Drug-seeking behavior and externalization of responsibility may be reinforced by forming an association, on the part of the patient, between an undesirable behavior and taking an extra pill. In addition, PRN use may expose borderline patients to unnecessary psychotropic medications⁸. Finally, we must take into account the importance of placebo effect on PRN medications, making effectiveness difficult to determine⁹.

The study reported here, which is part of the McLean Study of Adult Development (MSAD), is the first to describe over 14 years of prospective follow-up the rates of PRN psychotropic medication use reported by a well-defined sample of borderline patients and other personality-disordered comparison subjects. In addition, the differences between borderline patients who ever-recovered and never-recovered in their use of PRN drugs were assessed. Finally, we examined the reasons for taking PRN medication reported by these diagnostic groups and by borderline personality disorder recovery status. We hypothesized that PRN use would be more prevalent among borderline patients than comparison subjects over time. We also hypothesized that ever-recovered borderline patients would use less PRN medication than patients who never-recovered from BPD. This study focuses on PRN medication taken on an outpatient basis.

Materials and Methods

This study is part of the McLean Study of Adult Development (MSAD)¹⁰. All participants were initially inpatients at McLean Hospital (Belmont, Mass.).

After the study procedures were explained, participants provided written informed consent. Master's-level interviewers, blinded to the patient's clinical diagnoses, used four semi-structured interviews to assess each patient: the Background Information Schedule (BIS)¹¹, the Structured Clinical Interview for DSM-III-R Axis I Disorders (SCID-I)¹², the Revised Diagnostic Interview for Borderlines (DIB-R)¹³ and the Revised Diagnostic Interview for DSM-III-R Personality Disorders (DIPD-R)¹⁴.

At each of eight follow-up waves separated by 24 months, our diagnostic battery was readministered as well as the Revised Borderline Follow-Up Interview¹⁵, which is the follow-up analog to the BIS administered at baseline. We added in the follow-up waves more detailed questions about the use of PRN psychotropic medication(s) to alleviate symptoms such as insomnia, anxiety, and agitation. We defined anxiety as a psychological state of intense fear and apprehension accompanied with physical symptoms of autonomic arousal such as sweating and palpitations that become maladaptive in the absence of real threat and significantly impact functioning; and agitation as a state of poorly organized and aimless psychomotor activity that stems from physical or emotional unease, with symptoms such as motor restlessness, irritability, and uncooperative behavior.

Good to excellent follow-up (within a generation of raters) and longitudinal (between generations of raters) inter-rater reliability were maintained throughout the course of the study for variables pertaining to treatment use¹⁶. Good to excellent follow-up and longitudinal inter-rater reliability were also maintained for diagnoses of both axis I and II disorders^{17, 18}.

To be considered recovered, the borderline patient, besides achieving symptomatic remission for two years, must have achieved concurrent good social and vocational functioning (at least one emotionally sustaining relationship with a friend or partner and work consistently and competently on a full time basis).

Statistical Analyses

Data pertaining to PRN medications over the 14 years of follow-up were assembled in panel format (i.e., multiple records per patient, with one record for each assessment period for which data were available). The binary outcome of interest at each assessment period was an indicator (yes versus no) of PRN medication taken for 1 month or more. The prevalence of PRN medication use over time, and its relation to diagnostic group, was assessed using log-linear longitudinal regression modeling methods. In this modeling framework, the generalized estimating equations (GEE) approach was used to appropriately account for the correlation among repeated measures on the same patient. The log-linear regression models included the effects of diagnostic group and time; in addition, to allow the pattern of change in the prevalence of PRN medication use over time to differ between groups, interactions between diagnosis and time were examined and included as necessary. A similar analytic

approach was used in analyses restricted to borderline patients, where the regression models included the effects of recovery status and time (and, possibly, their interaction). Results of these analyses are presented in terms of relative risk ratios (RRR) and their 95% confidence intervals (CI).

Results

At baseline, a total of 290 patients met criteria for borderline personality disorder according to both the Revised Diagnostic Interview for Borderlines and DSM-III-R, and 72 met DSM-III-R criteria for at least one non-borderline axis II disorder (but neither criteria set for borderline personality disorder). Baseline demographic data have been reported previously¹⁰.

At two year follow-up, when we started to study the use of PRN medication, 81.1% (N=223) of borderline patients were women, and 86.9% (N=239) were Caucasian. Their mean age was 29 years (SD=8.0), their mean socioeconomic status rating¹⁹ was 3.5 (SD=1.39) (1=highest and 5=lowest), and their mean GAF score was 46.2 (SD=13.2). For subjects with other personality disorders, 67.2% (N=45) were women, and 86.6% (N=58) were Caucasian. Their mean age was 29 years (SD=5.8), their mean socioeconomic status rating was 3.0 (SD=1.25) (1=highest and 5=lowest), and their mean GAF score was 57.9 (SD=13.2). Significant between-group differences were found for gender ($p=0.01$), socioeconomic status rating ($p=0.01$) and Global Assessment of Functioning score ($p<0.001$). More specifically, borderline patients were more likely to be female, come from a lower socioeconomic background, and have a lower GAF score.

In terms of continuing participation, 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 patients with other personality disorders (OPD), with 82.9% (N=58/70) of surviving patients in this group (one died by suicide, and one died of other causes) being reassessed at all eight follow-up waves.

Table 1 shows PRN use over time for borderline patients and other personality-disordered comparison subjects. Results of the log-linear regression analyses indicate that the pattern of change in PRN use over time differs between the diagnostic groups. Specifically, borderline patients were approximately 3 times (RRR=3.22; 95% CI: 1.91, 5.44) more likely to use any PRN medication than other personality-disordered comparison participants at the start of the follow-up period. The significant interaction between diagnosis and time (0.37) indicates that the relative decline in the prevalence of PRN medication use is 34% (i.e., $[1 - [0.37 \cdot 1.77]] \cdot 100\% = 34\%$) for borderline patients, in contrast to the 77% nonsignificant (i.e., $[1.77 - 1] \cdot 100\% = 77\%$) increase for the comparison group over time.

Considering the reasons to use PRN medication among PRN-medicated patients, there were no significant differences in the prevalence of PRN use to improve sleep or to decrease anxiety between borderline and other personality-disordered comparison subjects, but the prevalence of PRN medication use to decrease agitation was 28% (i.e. $[1.28 - 1] \cdot 100 = 28\%$) higher in borderline patients than other personality-disordered comparison subjects (over the

duration of follow-up). Taking borderline and other personality-disordered individuals together, the prevalence of PRN use to improve sleep or to decrease anxiety did not change significantly over time, although there was a significant reduction of 18% (i.e., $[1 - 0.82] * 100\% = 18\%$) in PRN use to decrease agitation over time. No interactions between diagnostic group and time were found for the reasons to use PRN among PRN-medicated patients.

Table 2 shows the PRN use over time for ever-recovered versus never-recovered borderline patients. Those who have never-recovered were about twice as likely (i.e., $1/0.55 = 1.81$) to use PRN medication than ever-recovered borderline patients (over the duration of follow-up). Over time, for both groups taken together, there was a significant 31% reduction (i.e., $[1 - 0.69] * 100 = 31\%$) in use of PRN medication. No interaction between recovery status and time was found.

Considering the reasons to use PRN medication between PRN-medicated ever-recovered and never-recovered borderline patients, there were no significant group differences in the prevalence of PRN use to improve sleep and to decrease anxiety, but ever-recovered borderline patients were 16% (i.e., $[1 - 0.84] * 100 = 16\%$) less likely to use PRN to decrease agitation than never-recovered BPD patients. Taking borderline patients together, the prevalence of PRN use to improve sleep or to decrease anxiety did not change significantly over time, yet there was a reduction of 20% (i.e., $[1 - 0.80] * 100\% = 20\%$) in PRN use to decrease agitation over time. No interaction between recovery status and time was found for any of the three reasons to use PRN medication.

Finally, in exploratory analyses of the relationship between use of psychotropic standing medication(s) and PRN medication(s), a positive association was found both for borderline patients (RRR: 1.12; 95% CI: 1.09–1.15) and other personality-disordered comparison subjects (RRR: 1.32; 95% CI: 1.18–1.49). When analyses are adjusted for use of standing medications, there were no discernible differences in the results (data not shown).

Discussion

Four main findings have emerged from this study. The first is that borderline patients reported significantly greater use of psychotropic PRN medication than other personality-disordered comparison subjects in our naturalistic study. The fact that nearly one-third of our borderline patients consistently used PRN medication over 14 years of follow-up highlights the necessity of evaluating its clinical effectiveness and risks. There are no available evidence-based medical protocols for prescribing PRN psychotropic medication(s) for borderline patients. Indeed, a recent systematic review published by Yoshida et al²⁰ concluded that psychotropic PRN as a clinical intervention does not have a robust evidence-base for any psychiatric disorder. Moreover, the positive association between PRN and standing medications found in our study points out the necessity of careful consideration of the risks of drug interactions and polypharmacy⁶. Researchers have found benzodiazepines to be significantly associated with behavioral dyscontrol in borderline patients²¹, including hostile outbursts, and worsening of impulsive behaviors²², suggesting that clinicians should use PRN benzodiazepines with particular caution.

Our second finding is that recovery in borderline patients is associated with a lower prevalence of PRN use. Non-recovered borderline patients may be more likely to need PRN medication due to the severity of their symptoms. In a previous study²³, we found that a mechanism of defense called emotional hypochondriasis (transformation of unbearable feelings of rage, sorrow, shame and/or terror into unremitting attempts to get others to pay attention to the enormity of the emotional pain that one feels) is one of the symptoms that predicts time to recovery in BPD patients. As a consequence of this persistent symptom, the non-recovered patient may complain about his/her psychopharmacologist who cannot cure her/his insomnia, anxiety or agitation, putting pressure on the clinician to “do something”²⁴. This “something must be done” pressure is difficult to withstand and may lead to excessive PRN medication prescribing, instead of trying first to help the patients to place their symptoms in a meaningful historical context and to teach them a range of mentalization, mindfulness, self-validation, distress tolerance, and emotion regulation skills²⁵. Additionally, the inconsistent use of PRN medication may hinder the possible benefits of consistent use of standing medications in decreasing the severity of overall borderline symptomatology.²⁶

For panic disorder, the use of PRN medication can inhibit positive outcomes of cognitive behavioral therapy, decreasing the ability to cope with anxiety symptoms²⁷. The same mechanism may occur in borderline patients, with the excessive use of PRN medication in individuals in distress hampering their ability to face challenges that provoke distress and not teaching them the coping skills required to have a better level of functioning in the community²⁸. This problem is especially relevant for borderline patients when we consider that most of those who fail to recover do so due to difficulties in attaining and maintaining a good vocational adjustment²⁹, for which it is necessary to possess abilities to deal with internal distress and flexibility in interpersonal relationships.

Therefore, before prescribing a PRN medication for borderline patients, the following eight suggestions made by Hilton et al³, and Baker et al⁴ may be helpful: i) a clear focus about the purpose of the PRN medication, ii) a time-limited prescription of PRN medication, with regular review, stopping the use of PRN if it is not helpful, iii) consideration of side effects and drug interactions, iv) limit the number of PRN medications to the minimum required, v) specify medication doses and/or maximum daily dose, vi) non-pharmacological treatments, such as de-escalation, counseling, time-out, reality testing, cognitive behavioral therapy should be always considered prior to the use of PRN medication, vii) reasons for deciding that PRN medication is more appropriate than alternative approaches must be carefully recorded in the patient’s clinical record, viii) clinical outcome of PRN medication must be assessed and documented, including feedback from the patient’s experience of using PRN medication.

The third finding is that the prevalence of the use of PRN medication declined significantly over time for patients with borderline personality disorder. Even though the prevalence of PRN medication is still high after 14 years of follow-up, the decline of approximately one-third in PRN medication use over time reflects our previous findings that overall borderline patients have become less symptomatic over time³⁰, asking for progressively less PRN medication.

The fourth finding of the current study is that a proportionally higher use of PRN medication to decrease agitation is found in borderline patients than in other-personality-disordered comparison subjects, with lower proportional use of PRN to reduce agitation found among recovered borderline patients. Previous studies concerning the subsyndromal phenomenology of BPD have demonstrated that some of the symptoms of BPD seem to be acute in nature and others seem to be temperamental in nature^{31, 32}. Borderline temperamental symptoms, such as feelings of chronic anger, emptiness, nondelusional paranoia, intolerance to aloneness may lead to overwhelming agitation, which in turn may require the use of PRN medication for borderline patients, especially for those who have not achieved recovery.

The most important limitation of the current study is that all the participants were initially inpatients. To what extent these results would generalize to never-hospitalized patients is unclear. Another limitation is that our data were obtained by self-reports that cannot be verified, raising the possibility that subjects may have inaccurately reported the reasons for the prescription of PRN drugs. Additionally, no systematic rating scales were applied to evaluate clinical effectiveness, safety, and dose- response relationships for PRN medication(s). Finally, the naturalistic nature of the current study also limits what can be inferred about the effect of PRN medication(s) on borderline symptomatology.

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Table 1

PRN (As-needed) Psychotropic Medication Taken for 1 Month or More by Patients with Borderline Personality Disorder (BPD) and Other Personality Disorders (OPD) over 14 Years of Prospective Follow-up

	2 year FU	4 year FU	6 year FU	8 year FU	10 year FU	12 year FU	14 year FU	16 year FU	RRR Diagnosis ^a Time ^b	95%CI Diagnosis ^a Time ^b	P-value Diagnosis ^a Time ^b
Use of PRN Medication for Any Reason											
BPD % (N)	51.6 (142)	35 (94)	36.4 (96)	44.3 (113)	34.1 (85)	33.6 (82)	33.2 (79)	29.4 (68)	3.22	1.91, 5.44	<0.001
OPD % (N)	17.9 (12)	15.6 (10)	14.3 (9)	16.1 (10)	16.4 (10)	18.3 (11)	18.6 (11)	32.8 (19)	1.77 [#]	0.94, 3.32	NS
Reasons to Use PRN Among PRN-medicated Patients											
PRN to Improve Sleep											
BPD % (N)	63.4 (90)	71.3 (67)	65.6 (63)	67.3 (76)	70.6 (60)	65.9 (54)	51.9 (41)	61.8 (42)	1.09	0.88, 1.35	NS
OPD % (N)	66.7 (8)	80 (8)	22.2 (2)	70 (7)	50 (5)	54.6 (6)	63.6 (7)	47.4 (9)	0.90	0.76, 1.0	NS
PRN to Decrease Anxiety											
BPD % (N)	85.9 (122)	72.3 (68)	77.1 (74)	56.6 (64)	71.8 (61)	79.3 (65)	79.8 (63)	83.8 (57)	1.04	0.87, 1.24	NS
OPD % (N)	66.7 (8)	70 (7)	77.8 (7)	50 (5)	90 (9)	100 (11)	72.7 (8)	68.4 (13)	0.97	0.87, 1.08	NS
PRN to Decrease Agitation											
BPD % (N)	75.4 (107)	71.3 (67)	65.6 (63)	35.4 (40)	56.5 (48)	69.5 (57)	60.7 (48)	67.7 (46)	1.28	1.01, 1.62	0.035
OPD % (N)	50 (6)	50 (5)	55.6 (5)	40 (4)	20 (2)	90.9 (10)	36.4 (4)	47.8 (9)	0.82	0.70, 0.96	0.014

Abbreviations: FU= Follow-up, RRR = Relative Risk Ratio, CI = Confidence Interval, NS = Non-significant.

^a: Comparison with the two diagnostic groups (BPD and OPD) over the 14 years of follow-up.

^b: Change from 2-year follow-up to 16-year follow-up in the two groups combined.

[#]: A significant interaction between diagnosis and time was found (RRR [CI] = 0.37 [0.20, 0.72], with $p = 0.003$, indicating that the relative decline in the prevalence of PRN medication use is 34% (i.e., [1-0.37*1.77]*100% = 34%) for borderline patients, in contrast to the non-significant 77% (i.e., [1.77- 1]*100% = 77%) increase for the comparison group over time.

Table 2

PRN (As-needed) Psychotropic Medication Taken for 1 Month or More by Ever-Recovered and Never-Recovered Patients With Borderline Personality Disorder (BPD) over 14 Years of Prospective Follow-up

	2 year FU	4 year FU	6 year FU	8 year FU	10 year FU	12 year FU	14 year FU	16 year FU	RRR Recovery status ^a Time ^b	95%CI Recovery status ^a Time ^b	P-value Recovery status ^a Time ^b
Use of PRN Medication for Any Reason											
Ever-recovered BPD	% (N) 42 (63)	26.7 (40)	23.3 (35)	31.5 (46)	21.5 (31)	28 (40)	25 (35)	19.1 (26)	0.55	0.46, 0.65	<0.001
Never-recovered BPD	% (N) 63.2 (79)	45.4 (54)	53.5 (61)	61.5 (67)	51.4 (54)	41.6 (42)	44.9 (44)	44.2 (42)	0.69	0.58, 0.83	<0.001
Reasons to Use PRN Among PRN-medicated Patients											
PRN to Improve Sleep											
Ever-recovered BPD	% (N) 66.7 (42)	67.5 (27)	71.4 (25)	63.0 (29)	77.4 (24)	70 (28)	57.1 (20)	65.4 (17)	1.04	0.92, 1.17	NS
Never-recovered BPD	% (N) 60.7 (48)	74.1 (40)	62.3 (38)	70.2 (47)	66.7 (36)	62 (26)	47.7 (21)	59.5 (25)	0.91	0.76, 1.10	NS
PRN to Decrease Anxiety											
Ever-recovered BPD	% (N) 77.8 (49)	72.5 (29)	74.3 (26)	54.4 (25)	67.7 (21)	72.5 (29)	77.1 (27)	76.9 (20)	0.91	0.81, 1.01	NS
Never-recovered BPD	% (N) 92.4 (73)	72.2 (39)	78.7 (48)	58.2 (39)	74.1 (40)	85.7 (36)	81.8 (36)	88.1 (37)	0.95	0.85, 1.06	NS
PRN to Decrease Agitation											
Ever-recovered BPD	% (N) 69.8 (44)	67.5 (27)	54.3 (19)	32.6 (15)	48.4 (15)	57.5 (23)	62.9 (22)	53.9 (14)	0.84	0.74, 0.97	0.016
Never-recovered BPD	% (N) 79.8 (63)	74.1 (40)	72.1 (44)	37.3 (25)	61.1 (33)	81 (34)	59.1 (26)	76.2 (32)	0.80	0.68, 0.95	0.009

Abbreviations: FU= Follow-up RRR = Relative Risk Ratio, CI = Confidence Interval, NS = Non-significant.

^a : Comparison with the ever-recovered and never-recovered borderline patients over the 14 years of follow-up.

^b : Change from 2-year follow-up to 16-year follow-up in the two groups combined.