The Use of Prescription Opioid Medication by Patients With Borderline Personality Disorder and Axis II Comparison Subjects: A 10-Year Follow-Up Study

Frances R. Frankenburg, MD; Garrett M. Fitzmaurice, ScD; and Mary C. Zanarini, EdD

ABSTRACT

Objective: The first purpose was to determine the rate of use of prescription opioid medication reported by patients with borderline personality disorder and to compare that to the rate reported by Axis II comparison subjects during a 10-year period of prospective follow-up. The second purpose was to determine the most clinically relevant predictors of prescription opioid use among borderline patients.

Method: The medical conditions and Axis I disorders of 264 borderline patients and 63 Axis II comparison subjects were assessed at 6-year follow-up and 5 contiguous follow-up waves that were 2 years apart. These assessments were conducted between July 1998 and December 2010. Family history of psychiatric disorder was assessed at baseline by interviewers blind to the diagnostic status of the subjects. All 3 areas were assessed using semistructured interviews with proven psychometric properties: the Medical History and Services Utilization Interview (MHSUI), the Structured Clinical Interview for *DSM-III-R* Axis I Disorders (SCID-I), and the Revised Family History Questionnaire.

Results: Borderline patients were significantly more likely to report the use of prescription opioid medication over time than Axis II comparison subjects (OR = 1.79; 95% CI, 1.01–3.17). The best predictors of opioid use among borderline patients were the time-varying presence of back pain (OR = 1.95; 95% CI, 1.41–2.70), fibromyalgia (OR = 3.29; 95% CI, 1.70–6.36), and osteoarthritis (OR = 3.32; 95% CI, 2.08–5.29) as well as a baseline history of drug abuse (OR = 1.89; 95% CI, 1.27–2.81).

Conclusions: The sustained use of prescription opioids is common among and discriminating for patients with borderline personality disorder. The results also suggest that these borderline patients may be particularly sensitive to physical pain—mirroring their well-known heightened sensitivity to emotional pain.

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Corresponding author: *Frances R. Frankenburg, MD, McLean Hospital, 115 Mill St, Belmont, MA 02478 (Frances.Frankenburg@med.va.gov).*

Opioid medications are highly effective pain-relieving agents. Although these medications were usually used in the past for patients with pain caused by malignancies, Portenoy and Foley, in an influential 1986 article,[1] studied 38 patients with nonmalignancy-based pain and found that opioid maintenance was safe and effective. They reported difficulty in managing the opioids in only 2 patients, both with a history of prior drug abuse. Since 1986, the use of opioid medications to treat nonmalignant pain has increased in the United States.[2]

Opioid medications have risks, including lethality in overdose. In 2008, these medications were involved in 14,800 deaths in the United States, or nearly three-fourths of all prescription drug overdose deaths.[3] Because of their action at the mesolimbic dopaminergic reward pathway, they can cause dependency and addiction. Between 1999 and 2008, opioid medication–related sales, substance abuse admissions, and overdose death rates all roughly quadrupled.[3]

Other problems with opioid medications include side effects such as constipation, drowsiness, and decreased libido. Over time, the analgesic efficacy may diminish.[4] Chronic opioid use can also increase sensitivity to pain.[5,6]

Since the work of Portenoy and Foley, the rates of opioid addiction among pain patients have been thought to be very low. Fishbain et al[7] reviewed over 67 studies of opioid treatment of nonmalignant pain and found that, of 2,500 patients, just over 3% developed abuse or addiction. The rates were lower if subjects were ineligible for treatment when they had any current or previous history of abuse or addiction. Urine toxicology, however, revealed a higher number of problems. For example, some patients had no opioids in their urine, suggesting possible diversion of these medications. In general, the rates of addiction to prescription opioids are higher if the patient has a history of substance abuse, comorbid mental illness, or somatization or if the patient is young or female.[8]

Clinical experience suggests that patients with borderline personality disorder have a complex relationship to pain, often inflicting pain on themselves, while also often seeming intolerant of chronic pain.[9] About 30% of those with chronic pain may also have comorbid borderline personality disorder.[10]

Given the increasing rate of opioid prescriptions in the general population, the risk of diversion or abuse, the lethality of overdose, the possible exacerbation of pain sensitivity, and the complex relationship between pain and borderline personality disorder, it is surprising that, to our knowledge, little is known about opioid pain medication use over time in patients with borderline personality disorder. Opioid medications might be particularly difficult to use in borderline personality disorder because of the risks of overdose and addiction in this patient group with high rates of co-occurring depression, impulsivity, and suicidality.[11,12]

The current study describes the prevalence of prescription opioids in a large sample of well-defined borderline patients and Axis II comparison subjects over 10 years of prospective follow-up. It also assesses predictors of prescription opioid use in borderline patients.

Clinical Points

- Patients with borderline personality disorder are prescribed opioid pain medications at increasing rates.
- Back pain, fibromyalgia, osteoarthritis, and a baseline history of drug abuse were the best predictors for prescription of opiod pain medications.
- Opiod medications carry with them potential risks, such as dependence, diversion, or overdose.

METHOD

Subjects

The current study is part of a multifaceted longitudinal study of the course of borderline personality disorder: the McLean Study of Adult Development (MSAD).[13] The methodology of this study, which was reviewed and approved by the McLean Hospital Institutional Review Board, has been described in detail elsewhere.[13] Briefly, our subjects had initially been inpatients at McLean Hospital in Belmont, Massachusetts. Each patient was screened to determine that he or she (1) was between the ages of 18 and 35 years; (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 a serious organic condition that could cause psychiatric symptoms; and (4) was fluent in English.

Procedures

After the study procedures were explained at baseline, written informed consent was obtained. Each patient then met with a masters-level interviewer blind to the patient's clinical diagnoses. Three semistructured diagnostic interviews were administered: (1) the Structured Clinical Interview for *DSM-III-R* Axis I Disorders (SCID-I),[14] (2) the Revised Diagnostic Interview for Borderlines (DIB-R),[15] and (3) the Diagnostic Interview for Personality Disorders (DIPD-R).[16] Good to excellent levels of interrater and test-retest reliability were achieved at baseline for both Axis I and II disorders.[17,18] Family history of psychiatric disorder was assessed at baseline by another interviewer blind to patient diagnoses using a semistructured interview with proven psychometric properties: the Revised Family History Questionnaire.[19]

At each 24-month follow-up wave, diagnostic information was assessed via interview methods similar to the baseline procedures by staff members blind to baseline diagnoses. After informed consent was obtained, the MSAD diagnostic battery was readministered (a change version of the SCID-I, the DIB-R, and the DIPD-R). Good to excellent interrater reliability was maintained throughout the course of the study for both Axis I and II diagnoses.[17,18]

Beginning at the time of the 6-year follow-up and at each subsequent follow-up wave, the Medical History and Services Utilization Interview (MHSUI)[20] was administered to all patients. These assessments were conducted between July 1998 and December 2010. The MHSUI, developed by the authors of this article, assesses the health of the patients (and their first-degree relatives), lifestyle issues related to physical health, and health care utilization. All medical diagnoses were made by physicians. In a sample of 14 patients, good convergent validity was found between self-report answers on the MHSUI and information contained in medical records.

We defined prescription opioid use as a period of at least 3 months during a 2-year follow-up period in which the patients used opioid medications prescribed by physicians. We further required that a subject not meet criteria for opioid abuse or dependence or abuse/dependence of any other drug during this 2-year period.

We selected 7 predictors for a number of reasons. Three of them represent painful conditions we have previously found to be common among borderline patients (back pain, fibromyalgia, osteoarthritis)[20] and a fourth medical condition (cancer) for which opioids are often used. The other 3 variables pertain to conditions that could predict opioid use: either a family history of substance abuse[21] or a personal history of alcohol or drug abuse/dependence[11] at the time of study entry.

Statistical Analyses

Between-group comparisons involving categorical demographic data (gender and race) were computed by using the χ^2 statistic corrected for continuity; the between-group comparisons involving the continuous demographic variables of age, socioeconomic status,[22] and Global Assessment of Functioning (GAF)[23] score were computed using the Student *t* test.

Data obtained from the MHSUI were assembled in panel format (ie, multiple records per patient, with 1 record for each follow-up period for which data were available). Generalized estimating equations, appropriately accounting for repeated measures on the same patients, were used to fit longitudinal logistic regression models assessing the role of diagnostic group (borderline vs other personality disorder), time, and their interaction, and controlling for gender (as a significantly higher percentage of borderline patients than Axis II comparison subjects were female) in the analysis of the prevalence of prescription opioid data over time.

Generalized estimating equations were also used in analyses of predictors of prescription opioid use among borderline patients. As noted above, 7 clinically meaningful variables were assessed for significance in a bivariate manner. Those that were significant were then assessed in a multivariate model. Probability was set at an α level of $< .05$.

RESULTS

In total, we studied 264 patients meeting DIB-R and *DSM-III-R* criteria for borderline personality disorder and 63 subjects meeting *DSM-III-R* criteria for another *DSM-III-R* personality disorder (and neither criteria set for borderline personality disorder). Of these 63 comparison subjects, 4.8% met *DSM-III-R* criteria for an odd cluster personality disorder, 33.3% met *DSM-III-R* criteria for an anxious cluster personality disorder, 15.9% met *DSM-III-R* criteria for a nonborderline dramatic cluster personality disorder, and 54% met *DSM-III-R* criteria for personality disorder not otherwise specified (which was operationally defined in the DIPD-R as meeting

Table 1. Demographic Characteristics of Study Groups at 6-Year Follow-Up

Characteristic	Borderline Personality Disorder (n = 264)	Axis II Comparison Subjects (n = 63)	χ^2/t Test	*P* Value
Female gender, % (n)	80.7 (213)	66.7 (42)	5.82	.016
White, % (n)	87.5 (231)	88.9 (56)	0.09	NS
Age, mean (SD), y	33.0 (5.8)	33.5 (8.0)	0.59	NS
Hollingshead-Redlich Socioeconomic Scale score, mean (SD)[a]	3.4 (1.4)	2.9 (1.3)	−2.73	.0067
Global Assessment of Functioning score, mean (SD)[b]	54.2 (13.2)	65.1 (12.7)	5.90	< .0001

[a]Score of 1 = highest and 5 = lowest.
[b]Score of 0 = lowest and 100 = highest.
Abbreviation: NS = nonsignificant.

all but 1 of the required number of criteria for at least 2 of the 13 Axis II disorders described in *DSM-III-R*).

Table 1 shows the demographic characteristics of the subjects at the time of the 6-year follow-up. As can be seen, both study groups were predominantly white and about 33 years old, on average. However, a significantly higher percentage of borderline patients were female. Borderline patients also came from a significantly lower socioeconomic status and had a significantly lower GAF score than Axis II comparison subjects.

Over the decade of prospective follow-up, 46.6% (n = 123) of borderline patients and 31.8% (n = 20) of Axis II comparison subjects used prescription opioid medication ($\chi^2 = 4.56$, $P = .033$). Table 2 shows the rates of use of prescription opioid medication reported by the subjects over time. At 6-year follow-up, 27 of the 264 patients with borderline personality disorder (10%) were using opioid pain medications. A decade later, 60 of the 231 borderline patients (26%) were using opioid pain medications. At 6-year follow-up, 4 of the 63 Axis II comparison subjects (6%) were receiving opioid pain medications. A decade later, 9 of the 58 Axis II comparison subjects (16%) were receiving opioid pain medications.

Looking at the odds ratio for diagnostic group in Table 2, borderline patients were 79% more likely to report the use of prescription opioids than Axis II comparison subjects. In addition, the rate of use increased 3-fold for those in both study groups over the decade of prospective follow-up.

It should be noted that all of these subjects denied doctor shopping to attain this type of medication. Rather, they reported that, in most cases, their primary care physician prescribed it on a regular basis because it allowed them to function more effectively as well as experience a lower degree of pain.

Table 3 shows the bivariate predictors of prescription opioid use among borderline patients. As noted above, we studied 7 variables: 3 were assessed at baseline, and 4 were assessed over the 10 years of prospective follow-up described above. The prevalences of the 3 baseline variables were history of alcohol abuse or dependence (n = 135, 51.1%), history of drug abuse or dependence (n = 123, 46.6%) (20 of whom or 16.3% had a history of abusing or being dependent on an opioid), and family history of substance abuse (n = 182, 68.9%). The prevalences of the 4 medical conditions, when aggregated over time, were cancer (n = 23, 8.7%), back pain (n = 185, 70.1%), osteoarthritis (n = 73, 27.7%), and fibromyalgia (n = 33, 12.5%). In terms of the baseline predictors, a personal history of alcohol abuse or dependence at baseline was not significant. However, a personal history of drug abuse or dependence at study entry and a family history of substance abuse assessed at study entrance were significant predictors of prescription opioid use among borderline patients over the decade of prospective follow-up. They both increased the odds of prescription opioid use by a factor of 2. Four medical conditions that were assessed at 5 follow-up periods were also studied: cancer, back pain, osteoarthritis, and fibromyalgia. All 4 were found to increase the odds of borderline patients reporting the use of prescription opioids: cancer and back pain by a factor of about 2, osteoarthritis by a factor of 4, and fibromyalgia by a factor of about 5.

Table 4 shows the significant multivariate predictors of prescription opioid use among borderline patients. These 4 predictors were the time-varying presence of back pain, osteoarthritis, and fibromyalgia as well as a baseline history of drug abuse or dependence. Borderline patients reporting a personal history of drug abuse or dependence at baseline or back pain were twice as likely to report prescription opioid use over time as borderline patients who did not report these predictors. Borderline patients reporting osteoarthritis or fibromyalgia were 3 times as likely to report prescription opioid use over time as borderline patients who did not report these conditions.

DISCUSSION

Three important findings have emerged from this study. The first finding is that the prevalence of opioid medications prescribed to borderline patients is almost twice as great as that of Axis II comparison subjects.

The second finding is that the rate of opioid prescription use among borderline patients increased significantly over time, from about 10% to 26%. The rate of increase was similar in borderline personality disorder and Axis II comparison subjects. This increase may be due to a combination of several factors, including the aging of our subjects and their increasing physical illnesses. As well, some of the increase may be due to patterns of prescription by physicians, since prevalence of prescription of opioid medications is increasing dramatically in the United States.[2]

The third finding is that the best multivariate predictors of opioid use among borderline patients were the time-varying presence of back pain, osteoarthritis, and fibromyalgia as well as a baseline history of drug abuse/dependence. The finding that back pain and osteoarthritis are associated with opioid medications is not surprising. In 1 study[24] of community patients, opioids were the most frequently prescribed medication for these conditions. The finding that fibromyalgia was associated with opioid prescription may be explained in part by the complex nature of this syndrome. Fibromyalgia is comorbid with a number of medical and psychiatric disorders,

Table 2. Rates of Prescription Opioid Medication Use Reported by Patients With Borderline Personality Disorder and Axis II Comparison Subjects

Variable	6-y Follow-Up	8-y Follow-Up	10-y Follow-Up	12-y Follow-Up	14-y Follow-Up	16-y Follow-Up	Odds Ratio	95% CI	*P* Value
Borderline personality disorder									
n	264	255	249	244	238	231	1.79[a]	1.01–3.17[a]	.045
% (n)	10.2 (27)	10.2 (26)	18.1 (45)	11.5 (28)	22.3 (53)	26.0 (60)			
Axis II comparison subjects									
n	63	62	61	60	59	58	3.03[b]	2.17–4.22[b]	< .001
% (n)	6.4 (4)	9.7 (6)	11.5 (7)	10.0 (6)	8.5 (5)	15.5 (9)			

[a]Borderline personality disorder compared to Axis II comparison subjects.
[b]Over time.

Table 3. Bivariate Predictors of Prescription Opioid Medication Use Among Borderline Patients

Predictor	Odds Ratio	95% CI	*Z* Score	*P* Value
Baseline history of alcohol abuse/dependence	1.43	0.94–2.17	1.66	.098
Baseline history of drug abuse/dependence	1.95	1.28–2.97	3.09	.002
Family history of substance abuse	1.96	1.18–3.27	2.58	.010
Cancer	1.73	1.05–2.83	2.17	.030
Back pain	2.35	1.74–3.18	5.54	< .001
Osteoarthritis	4.07	2.63–6.29	6.31	< .001
Fibromyalgia	4.83	2.63–8.87	5.08	< .001

Table 4. Multivariate Predictors of Prescription Opioid Medication Use Among Borderline Patients

Predictor	Odds Ratio	95% CI	*Z* Score	*P* Value
Baseline history of drug abuse/dependence	1.89	1.27–2.81	3.16	.002
Back pain	1.95	1.41–2.70	4.03	< .001
Fibromyalgia	3.29	1.70–6.36	3.53	< .001
Osteoarthritis	3.32	2.08–5.29	5.04	< .001
Time	2.73	1.86–4.01	5.14	< .001

including major depression.[25] Depression and dysthymia are common in borderline personality disorder,[11,26,27] and there is an overlap between depression and physical pain.[28] Older antidepressants, such as the tricyclic antidepressants, and newer antidepressants, such as venlafaxine or duloxetine, are used to treat poorly understood pain syndromes such as fibromyalgia and migraine.[29] It is understandable, then, that patients and their physicians might turn to opioids for relief from the distress of fibromyalgia.

However, there is anecdotal evidence that opioids are not effective in fibromyalgia, perhaps because of reduced μ-opioid receptor availability within regions of the brain that normally process and dampen pain signals—specifically, the nucleus accumbens, the anterior cingulate, and the amygdala.[30] In a Canadian study,[31] about a third of over 400 patients referred to a multidisciplinary fibromyalgia clinic were prescribed opioids. The use of opioids was associated with unemployment, disability payments, lower education, current unstable psychiatric disorder, previous suicide attempts, and a history of substance abuse.

The finding that a history of drug abuse/dependence but not alcohol abuse/dependence predicts prescription opioid use suggests a specific relationship between earlier drug abuse and later prescription opioid use in some subjects with borderline personality disorder. They may have a higher rate of opioid prescriptions, in part, because of their greater experience of pain. Emotional and physical pain often coexist and can exacerbate each other. For example, researchers have suggested that "psychological distress" more than doubles the later risk of reporting low back pain.[32] Patients with borderline personality disorder often report dysphoria, and the amplitude of this symptom may be a good marker for this diagnosis.[33] More than 40 years ago, Martin and Inglis[34] noted that some patients addicted to opioids might take opioid drugs because of "an abnormally low tolerance for painful stimuli." It seems possible that a subset of people with borderline personality have low tolerance for pain and that their emotional distress further lowers their tolerance.

One key to understanding the convergence of these types of pain and the appeal of opioid medications lies within the anatomy of the brain. The pain of rejection and physical harm is processed in the anterior cingulate cortex.[35] The body's own opioid system modulates responses to physical and also emotional pain connected with separation and rejection. Animal work suggests that opioids mediate pleasurable and soothing feelings early in life and later reinforce relief after separation from meaningful objects.[36] In other words, the actual neurocircuitry and neurochemistry of somatic pain overlap with that underlying the pain involving interpersonal injuries.

Perhaps some patients with borderline personality disorder who have complaints of somatic pain find that the opioid pain medications also alleviate other types of pain that they experience. Or, it may be that their psychological distress exacerbates their sense of physical pain, making them more likely to seek relief from opioids. A complicating factor is that psychophysiological pain studies suggest that some patients with borderline personality disorder actually have higher pain perception thresholds than comparison patients without a diagnosis of borderline personality disorder.[37] Perhaps this seeming contradiction reflects that borderline patients can tolerate pain that they either inflict upon themselves or that they have agreed to in an experimental situation quite well. However, they may be more sensitive to pain from chronic physical ailments, particularly as they grow older. In any case, most of the borderline patients who are being prescribed opioids for chronic pain do not have a history of abusing this class of medication upon study entry.

Whatever the reason(s) for these high rates of opioid prescriptions, it is striking that a quarter of this relatively young

population is being treated with opioid pain medications 16 years after study entry. Patients with borderline personality disorder and their clinicians are left in a difficult situation. Opioid medications are effective analgesics, yet they need to be used with caution because of the risks associated with them.[38] Patients with borderline personality disorder may be particularly vulnerable to these risks due to their general impulsivity and reactivity to interpersonal disappointments.

Limitations and Directions for Future Research

Our data on prescription opioid use were obtained by self-report. It is possible that some of our patients were abusing this type of medication and/or were going from doctor to doctor to obtain it but denied these practices to our raters. Our patients might have been mistaken about, exaggerated, or denied use of opioid medications. In future research, urine toxicology and/or review of prescriptions would be a way of verifying opioid use. Also, all subjects in this study were inpatients with borderline personality disorder at baseline, and never-hospitalized subjects may differ from this group.

CONCLUSIONS

This is the first long-term study of opioid medication use in borderline patients. Our findings suggest that opioid medications are often prescribed for borderline patients and that this practice is increasing over time. The long-term implications of the prescription of opioid medications in this group of patients are serious and include possible dependency, addiction, loss of efficacy, or accidental overdose. This finding of the common use of opioids in borderline personality disorder also suggests that there might be a role for interventions with opioid-like agents without addicting properties to address the emotional and physical dysphoria associated with borderline personality disorder.

Drug names: duloxetine (Cymbalta), venlafaxine (Effexor and others).

Author affiliations: Laboratory for the Study of Adult Development, McLean Hospital (all authors), Belmont; Boston University School of Medicine and the Edith Nourse Rogers Memorial Veterans Hospital (Dr Frankenburg); and Harvard Medical School, Boston (Drs Fitzmaurice and Zanarini), Massachusetts.

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