Undertreatment of Panic Disorder in Primary Care: Role of Patient and Physician Characteristics

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Background: **In contrast with many studies describing the usual care for major depression in the primary care setting, there are few data on treatment received by primary care patients with panic disorder.**

Methods: **This prospective cohort study describes the self-reported medication use, at 3-month intervals for 1 year, of 58 patients with panic disorder and predictors of the use of appropriate (type, dose, and duration) medication.**

Results: **Approximately one half the patients received some type of antipanic medication at each interval, with selective serotonin reuptake inhibitors (SSRIs) the most common. Pharmacy records indicate that about 40% of patients not taking medication had received an initial physician prescription. Adequacy of dose and duration was achieved in only two thirds of the medication trials, usually with an SSRI. Patient characteristics (agoraphobia and low neuroticism) but not physician characteristics (eg, specialty, level of training, or years in practice) predicted those patients who had an adequate trial during at least one time interval. The relation between adequacy of medication and outcome was minimal.**

Conclusion: **These findings highlight the continued undertreatment of panic disorder in primary care but suggest that focused efforts at physician education about diagnosis and treatment are less likely to increase rates of treatment compared with efforts to educate patients and improve the care process with more frequent visits and monitoring. (J Am Board Fam Pract 2002;15:443–50.)**

As is major depression, panic disorder is commonly treated in the primary care setting, with more than 80% of patients with panic disorder complaining of such physical symptoms as chest pain, tachycardia, or dyspnea.[1] Of patients receiving care for mental and emotional problems, a greater proportion of patients with panic disorder receive their care in medical settings (46%) than do depressed patients (32%).[2] In contrast with a growing literature describing the characteristics of usual care for major depression in the primary care setting,[3–7] there are few data on treatment received by patients with panic disorder in the primary care setting.

Only two published studies describe treatment received by patients in this setting,[8,9] and in one of these studies, patients with panic disorder were not distinguished from patients with generalized anxiety or phobic disorder. These two reports only describe the type and the adequacy of treatment using patient self-report. Neither study determined how much the lack of recognition of panic disorder might have contributed to the absence of treatment, neither was able to describe treatment over time, neither examined how patient and clinician characteristics related to the adequacy of treatment, and neither systematically examined the outcome of treatment and its relation to quality of care.

In this article, we use patient self-reports to document the type and adequacy of pharmacotherapy and the use of specialty mental health services (a likely proxy for psychotherapy) for patients with panic disorder treated by primary care physicians. We also report associations between physician and patient variables and the adequacy of medication received, as well as between adequacy of medication and clinical and functional outcomes at 3-month intervals for the 1-year study period.

Methods

Setting

We recruited patients in roughly equal proportions from three primary care clinics in the Seattle area.[10]

Two were university-associated internal medicine clinics caring for 8,000 and 6,000 patients, respectively. At these clinics, 50% to 60% of the patients had private health insurance. Thirty faculty physicians provided 70% of the care, and rotating medical residents provided the rest. The third clinic was a community family medicine clinic that is part of a multisite health care system. Eight family physicians cared for 10,000 patients, 80% to 90% of whom had private health insurance.

Subjects

Patients (n = 58) were all English speaking, between 18 and 65 years old, had a telephone, and met *Diagnostic and Statistical Manual of Mental Disorders (Fourth edition)* (DSM-IV) criteria for panic disorder (see Assessments) with at least one panic attack in the month before recruitment into the study. Patient exclusions were limited to those that were potentially life-threatening (eg, active suicidal ideation or terminal medical illness) or those that would limit patient participation or adherence to the protocol (psychosis, current substance abuse, dementia, and pregnancy).

Design

This prospective cohort study focused on 58 patients in the usual care arm of a randomized effectiveness study of pharmacotherapy with disease management for panic disorder. All physicians in the study clinics were informed about the study, and referrals from physicians were encouraged. In addition, patients were recruited by using a waiting room screening procedure with a two-question test that is highly sensitive to panic disorder.[11] All patients with a positive screening test and all referred patients received a telephone diagnostic interview to determine final eligibility. Four hundred twenty-nine of 2,925 (15%) screened patients and 50 of 110 (45%) referred patients had positive screening tests, and 408 (14%) and 50 (45%) were interviewed. All eligible interviewed patients agreed to enroll. The study procedure was approved by the Institutional Review Board of the University of Washington School of Medicine. Eligible patients were asked for informed consent to participate in a randomized trial of an "intervention designed to improve the care for panic disorder." Patients were randomized, after stratifying for screened (n = 71) vs referred (n = 44) source, using a random number table, either to the intervention group (n = 57) or to usual primary care treatment (n = 58).

Usual Care Protocol

Patients randomized to usual care received treatment as usual from their primary care physician. This usual care was augmented in several ways, however. The primary care physician received the results of the initial diagnostic telephone assessment to eliminate nonrecognition of panic and associated disorders as a factor in outcome. In addition, before the initiation of the study, all physicians received a 1-hour didactic session on recognition and antidepressant treatment of panic disorder, as well as a previously published medication algorithm outlining appropriate types of medications and dosing strategies for panic disorder patients.[12] Finally, medications for panic disorder were provided free of charge to all patients participating in the study and were obtained through either hospital pharmacies (for the university-associated clinics) or at the family medicine clinic itself. Hence, this sample represents augmented usual care, perhaps a ceiling effect for the best usual care primary care physicians can be expected to render under the most ideal circumstances.

Assessments

Patients were assessed at 3-month intervals during the course of 1 year by college-graduate telephone interviewers who were blind to the patient's randomization status. The 60- to 75-minute interview included the following assessments:

1. Portions of the Composite International Diagnostic Interview (CIDI) modified for DSM-IV.[13] The portions used assess panic disorder, generalized anxiety disorder, social phobia, obsessive-compulsive disorder, post-traumatic stress disorder, major depressive disorder, and dysthymia.
2. The Panic Disorder Severity Scale, which rates a spectrum of panic disorder symptoms, including attack frequency and intensity and phobia. It is sensitive to treatment effects[14] and has good reliability, validity, and internal consistency.[15]
3. The Anxiety Sensitivity Index, which measures apprehension and discomfort about psychological and physical symptoms of anxiety.[16] These factors have been shown to be approximately

40% heritable in twin studies[17] and are thought to form a temperamental trait that predisposes to the development of panic disorder.

4. The Fear Questionnaire,[18] which measures agoraphobia, social phobia, and blood-injury phobia symptoms.
5. The Center for Epidemiologic Studies Depression Scale (CES-D),[19] which is a reliable and valid measure of depression symptom severity.
6. The SF-36 (Medical Outcome Survey 36-item Short-Form Health Survey), which is a widely used health status inventory that measures mental health symptoms and social and occupational functioning.[20]
7. A single Likert scale item, derived from a previous study,[21] that measures patient satisfaction with health care for personal and emotional problems in the previous several months.
8. The Cumulative Illness Rating Scale (CIRS),[22] which uses medical chart review to record types and severities of medical problems and measure the degree of medical comorbidity. The CIRS ratings were completed independently and then jointly to resolve disagreements by a board-certified internist and a psychiatrist.
9. The NEO Neuroticism Scale,[23] which measures a neurotic trait that has been shown to predict poor outcome in primary care patients with major depression.[24]

The nature of usual care was determined by patient self-report. Patients were asked to report any medication they were taking, its dose, and the duration of time they had been taking it. During the interview, they were encouraged to bring their pill bottles to enhance reporting accuracy. This self-report measure has a high concordance with automated pharmacy refill data.[23] Adequacy of antipanic treatment (ie, use of an effective antidepressant or benzodiazepine at an adequate dose for at least 6 weeks) was rated using a previously published algorithm,[14] which is based on published efficacy studies in panic disorder. Medications must have been shown to be more efficacious than placebo for panic (appropriate type) at specific doses (appropriate dose). Adherence was assessed by patient self-report of the number of days they took their medications. Patients also reported receipt of any psychotherapy or other specialty mental health service.

Table 1. Patient Demographic and Clinical Characteristics.

Variable	Care as Usual (n = 58)	
	Mean	*SD*
Age	41.9	10.4
	No	*%*
Female	37	63.8
White	35	62.5
Employed	37	63.8
Agoraphobia	24	42.1
Major depression	28	49.1
Dysthymia	7	12.3
Generalized anxiety disorder	24	42.1
Obsessive-compulsive disorder	11	19.3
Post-traumatic stress disorder	12	21.1
Social phobia	23	40.4
Cumulative Illness Rating Scale (CIRS)—total score	5.3	3.4
NEO Neuroticism Scale	2.7	0.9
Center for Epidemiologic Studies Depression Scale (CES-D)	27.2	10.9
Panic Disorder Severity Scale	12.4	5.7
Anxiety Sensitivity Index	28.2	12.3
SF-36 (The Medical Outcome Survey 36-item Short-Form Health Survey)		
	Mean	*SD*
General health	52.2	24.6
Physical functioning	73.7	27.4
Mental health	51.0	21.5
Bodily pain	36.6	21.3
Vitality	36.1	20.5
Social functioning	58.3	28.9
Role dysfunction—emotional problems	34.5	39.5
Role dysfunction—physical problems	45.7	44.2

Results

Patients' Characteristics

Table 1 lists demographic, diagnostic, and clinical information of the patient sample. The sample was ethnically and socioeconomically diverse, with substantial psychiatric and moderate medical comorbidity. The mean CIRS score of 5.3 translates to an average of two chronic medical problems requiring modest first-line intervention. The Panic Disorder Severity Scale showed patients had a mean panic attack frequency of 1 to 2 in the past week with minimal (occasional, mild, nondisabling) phobic avoidance but considerable attack intensity (loses concentration and must cease activity) and moder-

Table 2. Number of Patients with Medication Received During 1 Year.

Medication	Baseline	3 Months	6 Months	9 Months	12 Months
Correct medication*	28 (48%)	30 (52%)	28 (48%)	27 (47%)	28 (48%)
Selective serotonin reuptake inhibitor (SSRI)[†]	13 [2 BZ] [3 TCA]	21 [2 BZ] [3 TCA]	18 [2 BZ] [3 TCA]	19 [1 BZ] [3 TCA]	21 [2 BZ] [3 TCA]
Tricyclic antidepressant (TCA)	7	5 [1 BZ]	5 [1 BZ]	3 [1 BZ]	2
Benzodiazepine (BZ)	8	4	5	5	5
Wrong type medication[‡]	3	1	1	2	2

*For patients on an SSRI, the SSRI is listed as the primary medication. For patients on a TCA only or TCA and BZ, the TCA is listed as the primary medication. Those taking a BZ only were on no antidepressants.
[†]Coadministered medication is listed in brackets.
[‡]Medications with no acute panic efficacy (eg, buspirone, trazodone).

ately severe anticipatory anxiety. The Anxiety Sensitivity Index mean and the SF-36 subscale scores were similar to those seen in other clinical samples of panic disorder patients. Of the 58 study patients, 48 (83%), 47 (82%), 43 (74%), and 46 (70%) completed the 3-, 6-, 9-, and 12-month interviews. Patients completing all interviews did not differ from those missing at least one interview on any demographic or clinical variable.

Treatment Received

Table 2 lists the types of medications patients reported taking during the course of the year-long study. In accordance with a previous review,[12] we list the order of preference for a primary antipanic agent as selective serotonin reuptake inhibitor (SSRI) (based on its greater tolerability), tricyclic antidepressant, (based on its lower risk for dependence) and benzodiazepine. Co-prescribed agents are listed in brackets. Because the number of patients assessed at each point varied, usage is described as a proportion of the total (ie, intent to treat) sample. Using this method, the proportion of patients receiving a correct type of antipanic medication remained fairly constant with time, at between 46% and 52%. Because the use of medications varied for each 3-month rating period, descriptive data are also organized by trial (medication use in the 3-month period before each assessment). In roughly two thirds of medication trials (92 of 141 trials in five time points), patients received various SSRIs, 27% (25 of 92 trials) of the time in combination with low-dose tricyclic antidepressants or benzodiazepines. There was a slight trend for more SSRIs to be used after the start of the study, perhaps reflecting physician awareness of the use of an SSRI in the intervention arm.

Considering treatment adequacy in the aggregate, without reference to specific medication classes (Table 3), physicians who selected a correct type of antipanic medication achieved adequacy of dose and duration in about one half of medication trials (73 of 141 trials) for the five time points, with underdosing being far more common (45 of 68

Table 3. Numbers of Patients Receiving Adequate Pharmacotherapy and Any Psychotherapy.

	Baseline	3 Months	6 Months	9 Months	12 Months	Totals
Patients with correct medications* of adequate dose and duration[†]						
Selective serotonin reuptake inhibitor (SSRI)	6	16	14	16	18	70
Tricyclic antidepressant (TCA)	1	1	1	0	0	3
Benzodiazepine (BZ)	7	17	15	16	18	73
Patients receiving psychotherapy	9	16	18	14	11	
Patients receiving psychotherapy and adequate medication	4	6	6	8	6	

*Total trials: 141 (92 SSRI + 49 BZ-TCA).
[†]Dose and duration criteria:
  SSRI—paroxetine (Paxil) 20 mg/d, sertraline (Zoloft) 50 mg/d, fluoxetine (Prozac) 20 mg/d, citalopram (Celexa) 20 mg/d.
  TCA—150 mg/d, except 75 mg/d for nortriptyline.
  BZ—alprazolam 2 mg/d, clonazepam 1 mg/d, lorazepam 4 mg/d, diazepam 20 mg/d.

trials) than failure of the patient to continue medication for at least 6 weeks (13 of 68 trials). Only in 10 of 68 trials did patients fail to receive both correct dose and duration. Of 73 medication trials during the year that were adequate in type of medication, dose, and duration of trial, all but 4 were with SSRIs. Of 22 inadequate SSRI trials, inadequate dosing was almost as common (n = 8) as inadequate duration (n = 11), with only 3 trials being inadequate in both dose and duration. Of all 25 benzodiazepine trials, dose and often duration were inadequately low (ie, as-needed schedules). Of 20 trials of tricyclic antidepressants, all but 4 used inadequate dosing. The remaining three medications (trazodone, buspirone, and mirtazapine) have no established efficacy in panic disorder.

Of the 27 patients receiving adequate medication (type, dose, and duration) at some point during the year (n = 27, 47%), only 1 received the medication consistently across the year (at all time points where data were available). Finally, the proportion of patients receiving at least one trial of the correct type of medication after initiation of the study (47%) was similar to the proportion at baseline (48%). Only a small proportion of patients (between 15% and 30%) received specialty mental health services (last entry in Table 3). All the practitioners seen were nonphysician psychotherapists.

Predictors of Treatment Received

Bivariate relations between patients having (n = 27) and not having (n = 31) at least one assessment period with an adequate medication trial were examined using both patient variables (demographics, assessments 1 to 9, and use of psychotherapy) and physician variables (family vs internal medicine, clinic site, faculty vs trainee, years of experience). Chi-squares with corrections for continuity were used for categorical variables, and t tests were used for continuous variables to detect significance at $P < .10$ for use in logistic regression.

Adequately medicated patients were more likely to have comorbid agoraphobia ($\chi^2 = 60.1$, $df = 1$, $P < .001$), or post-traumatic stress disorder ($\chi^2 = 3.9$, $df = 1$, $P < .01$), were more likely to be in psychotherapy ($\chi^2 = 3.42$, $df = 1$, $P < .10$), and were more likely to be receiving care from faculty as opposed to resident physicians ($\chi^2 = 2.15$, $df = 1$, $P < .10$). These patients with at least one adequate medication trial also had more panic-related disability ($t = 2.12$, $df = 56$, $P < .05$), poorer SF-36 social function ($t = 2.05$, $df = 1$, $P < .05$) and overall SF-36 mental health ($t = 2.42$, $df = 56$, $P < 2.42$), more severe agoraphobia ($t = 2.06$, $df = 56$, $P < .05$), but less neuroticism ($t = 2.03$, $df = 56$, $P < .05$).

A stepwise logistic regression analysis using these variables was used to determine which physician and patient variables were independently related to receiving adequate medication at some point during the year. Two predictors were significant: having agoraphobia ($t = 5.96$, $P = .015$, odds ratio [OR] = 4.57; 95% CI = 1.3 to 15.5) and NEO neuroticism score (t = 3.97, $P = .046$, OR = 0.47, 95% CI = 0.22 - 0.98). Patients who received at least one adequate trial of antipanic medication within the year-long study period were therefore more likely to have agoraphobic panic disorder and to be less neurotic than patients who did not receive adequate antipanic medication. Similar results were found when adequate medication trial on at least 2 time points was used as the criterion.

Our total physician sample was 37. Of this group, 8 physicians cared for a total of 28 of the 58 patients. For 7 of the 8 physicians, one half their patients received adequate medication while the other half did not, suggesting that factors beyond physician knowledge or customary practice, such as patient-related factors and system-related factors (eg, brief, infrequent visits), were more likely to contribute to inadequate prescription.

Relation Between Treatment Received and Outcome

In accordance with a previous analysis, we used two distinct measures of outcome. At each 3-month point we compared the proportion of patients reaching predetermined levels of recovery on the Anxiety Sensitivity Index (a score of 20 or lower) and the larger proportion reaching partial responder criteria (40% reduction) on the Panic Disorder Severity Scale in the subgroup of patients with and without adequate type, dose, and duration of treatment at that time point. On the Anxiety Sensitivity Index, the quantitatively greater proportion of adequately treated patients who had recovered was significant only at 6 months ($\chi^2 = 5.3$, $df = 1$, $P = .01$) and 12 months ($\chi^2 = 3.8$, $df = 1$, $P = .03$). There was no relation between adequate treatment and partial response on the Panic Disorder Severity Scale.

Discussion

About one half of patients with panic disorder treated in primary care clinics took antipanic medication, with SSRIs the most commonly used medication. This rate is higher than that reported in two previous studies,[8,9] one of which surveyed two of the same clinics 4 years earlier.[9] This rate is also higher than reported in a recent national survey of anxious patients, 75% to 80% of whom received care for their anxiety in a primary care setting.[25] At the two clinics in this study that had been previously surveyed,[9] the use of SSRIs for this indication also seems to have increased. The higher use of SSRIs in this study could reflect either a spillover effect, because primary care physicians also cared for patients in the intervention arm of the study, or more likely the recently documented increased use of SSRIs in primary care practice, in large part as a result of their greater ease of use.[26]

Patients taking SSRIs also had a higher rate of correct dosing, consistent with the recent national survey noted above.[25] The ease of titration with SSRIs might partly account for the higher rate of correct dosing. Even though use of inadequately low doses of tricyclic antidepressants and benzodiazepines continues to occur, we do not know that these agents were being prescribed specifically for panic. Because low-dose tricyclic antidepressants are often prescribed for nonspecific symptoms of insomnia, pain, or headache, the low doses might represent appropriate treatment for these other conditions. The lack of any relation between comorbid conditions, such as depression and adequate treatment, however, suggest that the care rendered here was not simply targeted toward other diagnoses besides panic.

The greater apparent effect of patient rather than physician characteristics on adequacy of treatment is noteworthy. Although this finding might partly reflect the availability, in this analysis, of more information about patients and a lack of information about clinician knowledge and practice patterns, the variability in treatment for patients seeing the same physician suggests that patient-related factors might be more influential. Similarly, a recent study of depression treatment by primary care physicians[27] also showed little physician variability in quality of treatment (based on number of visits and antidepressant prescriptions) and little difference in clinical outcomes after controlling for patient-level demographic and clinical factors (ie, case mix variability).

Consistent with this notion, we examined the electronic medical records for 26 patients at two clinics who reported no medication at different time points and found that the physician had actually prescribed medication in 10 of these 26 patients, but the prescription was either not filled or not taken. This finding suggests that physicians factors might be less important, although a more complete description of variations in physician knowledge, practice habits, and treatment attitudes, and how they interacted with the educational interventions offered (information quite difficult to obtain) would be required to determine the importance of physician factors more definitively. Furthermore, nonpatient system-of-care factors, such as brief, infrequent visits and lack of close follow-up and monitoring, might be quite important in facilitating patient adherence to physician recommendations.

Participation of this sample in an effectiveness trial might limit the generalizability of results. Similarly, provision of the panic disorder diagnosis to patients could have increased the rate of treatment, although improved recognition of depression has only increased rates of treatment modestly and seldom affects outcome.[28,29] In addition, treatment of more than one half the patients by 8 physicians can also bias our results. It is interesting, however, that patients of these clinicians, who were overrepresented in this sample because they referred more patients to the study and were likely more interested in panic disorder, still were not more likely to receive adequate treatment.

The two significant measures in the logistic regression equation that predicted receiving adequate medication were having agoraphobia and being less neurotic. Because the former has been shown to be a severity marker for panic,[30,31] this finding would be consistent with physicians more often or more persistently prescribing for and perhaps more regularly monitoring more severely and obviously ill patients. This hypothetical mechanism might have overridden any tendency for these patients to be more fearful and avoid treatment. Because neuroticism is known to be associated with increased somatization,[23] it might make patients more prone to side effects, more sensitive to bodily sensations, or more resistant to accepting a diagnosis of panic disorder (ie, in lieu of a more medical explanation

for their somatic symptoms). Patients with less neuroticism might therefore have been able to accept treatment more easily in terms of dose adjustments and trial duration.

Additional information about patients' perceived need for or willingness to accept care, their preferences for or beliefs about medication vs psychotherapy,[32] and their view of the relative effectiveness of different treatments should be considered in future studies to better clarify determinants of adequate treatment. In addition, recruitment of a broader group of patients (ie, further narrowing the exclusion criteria) would limit the bias inherent in the recruitment methods used here.

Finally, that only a minimal relation was found between treatment adequacy and outcome (significance at only two of the eight available time points) could have been due to the small sample size and even smaller proportion of adequately treated patients. In most naturalistic, observational studies with uncontrolled treatment, however, patients with more severe and persistent symptoms tend to get more vigorous treatment, resulting in a paradoxical association between better quality of care and poorer outcome. Hence, the failure to find significant results between quality of care and outcome might be less surprising and is also consistent with recent studies in primary care depression.[33] Only a study in which patients were randomized to adequate and inadequate treatment (obviously an unethical design) could definitely test such a relation, although data from a much larger, naturalistically followed sample, in which risk of poor outcome could be determined before the start of treatment and controlled for in the analysis, might also shed light on this question.

Conclusion

These findings indirectly suggest that provision of a diagnosis of panic disorder to physicians is not associated with subsequent increases in antidepressant medication use by their patients. Only about one half of their patients with panic disorder reported taking effective antipanic medication, and of these patients, only one half to two thirds actually took a sufficiently high dose for a long enough time to have an adequate trial of medication. The substantial psychiatric comorbidity in this population of patients might have partly contributed by making it more complicated to discern which problem

to attempt to treat (although SSRI medications are generally effective for the entire range of mood and anxiety disorders). Comorbid agoraphobia (a proxy for panic severity) and low neuroticism were associated with receiving adequate treatment. The results of usual care, coupled with the robust effect of a brief, collaborative intervention in improving patient outcomes, suggest that more accurate physician recognition and enhanced physician screening and education about treatment are not enough to improve the process and outcome of care for patients with panic disorder. Future studies should instead focus on recognizing and minimizing patient- and health-system-related barriers that prevent adequate treatment in this patient population.

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