Once-Weekly Dosing of Fluoxetine in the Maintenance of Remission in Panic Disorder

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Background: Fluoxetine and its active metabolite norfluoxetine have long half-lives of 4–6 days and 4–16 days, respectively. We postulated that, owing to the long elimination half-life, patients diagnosed with panic disorder might be maintained on fluoxetine taken once a week, after being treated initially with daily doses of fluoxetine.

Method: Ten patients with DSM-III-R panic disorder were treated openly with fluoxetine, 20–40 mg daily. Once panic free, these patients were switched to once-weekly dosing of fluoxetine, and dosage was titrated as needed.

Results: All 10 patients successfully switched to once-weekly dosing. One patient reported recurrence of panic attacks 18 months after the switch. After a brief treatment for 4 weeks with benzodiazepines and daily fluoxetine, the patient was once again maintained on once-weekly dosing when rechallenged. Patients have been maintained in a panic-free state for up to 26 months with a single weekly dose of fluoxetine ranging from 10 to 60 mg. The medication was well tolerated.

Conclusion: Fluoxetine at doses ranging from 10 to 60 mg administered once weekly appears to be effective maintenance treatment for patients with panic disorder who were initially treated successfully with daily fluoxetine. A once-weekly regimen may allow for considerable cost savings and may serve as a convenient alternative method for treating panic disorder.

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Published clinical trials and cumulative clinical experience support the efficacy of fluoxetine in the treatment of panic disorder. Gorman and colleagues[1] treated 16 DSM-III panic disorder patients with fluoxetine in an open study with doses ranging from 10 to 70 mg/day. The author reports that 7 of 16 subjects had a complete cessation of their panic attacks with 4 of the 7 responding to a dose of 10 mg/day. Eight of the 9 nonresponders terminated secondary to adverse effects. Schneier and colleagues,[2] in a retrospective chart review, demonstrated that 19 of 25 patients with DSM-III-R panic disorder were moderately to markedly improved on doses ranging from 20 to 80 mg/day of fluoxetine for up to 12 months of treatment. Michelson et al.[3] found, in a double-blind sample of 243 patients diagnosed with DSM-III-R panic disorder, that fluoxetine, 10 or 20 mg/daily, was significantly more effective than placebo.

Since fluoxetine and its active metabolite norfluoxetine have elimination half lives of 4–6 days and 4–16 days, respectively,[4] it is reasonable to consider the efficacy of a once-a-week dosing regimen. Taking advantage of the drug's long half-life, patients may actually be maintained on once-weekly dosing. For example, Montgomery and colleagues,[5] in a double-blind trial of 20 patients per group, determined that once-weekly dosing of 80 mg was as effective as 60 mg/day in alleviating symptoms of major depression. Recently, Burke and colleagues[6] randomly assigned 32 patients with major depression who had responded to fluoxetine, 20 mg daily, to either weekly or daily doses of fluoxetine. Fluoxetine, 60 mg weekly, was as efficacious as 20 mg of fluoxetine daily, with both groups responding better than placebo in the maintenance therapy of major depression.

We report a preliminary follow-up study of panic patients who were treated daily with fluoxetine and then switched to once-weekly dosing after reaching a panic-free state. To our knowledge, this is the first report using once-weekly doses of fluoxetine to treat patients with panic disorder.

METHOD

Subjects were outpatients at our anxiety disorders clinics (Charleston and Columbia, S.C.). Patients were evaluated using a Structured Clinical Interview, patient version with psychotic screen (SCID)[7] and met DSM-III-R diagnosis for panic disorder, with or without agoraphobia, as the principal diagnosis. Informed consent was obtained after describing the procedure and possible side effects. Physical examination and laboratory test results were nor-

Table 1. Outcome of Patients Treated With Once Weekly Fluoxetine for Panic Disorder

Patient No.	Age (y)	Comorbid Agoraphobia?	Duration (y) of Panic Disorder	Weeks Until Panic Free (daily fluoxetine)	Final Daily Dose (mg/d)	Maintenance Dose (mg/wk)	CGI Score at Endpoint	Duration Panic Free (mo)
1	39	No	1	2	20	20	1	26[a]
2	42	Yes	4	4	20	40	1	5
3	41	No	21	8	20	40	2	24[a,b]
4	27	Yes	5	2	20	60	1	24[a]
5	29	Yes	4	3	20	40	1	4
6	48	Yes	19	14	40	60	2	1
7	44	Yes	3	3	20	20	1	2
8	37	Yes	19	6	20	40	1	4
9	30	None	23	2	20	20	1	2
10	30	None	20	3	10	10	1	3

[a]Patient not referred out to other clinics.
[b]Patient 3 had a relapse of panic attacks during this time period, which resolved.

mal. Patients initially received either 10 or 20 mg of fluoxetine daily, which was increased to a maximum of 60 mg/day depending on response and adverse events. Patients initially were seen approximately every 2 weeks until panic free. Once panic free, patients were instructed to select a particular day of the week and switch the current daily dose to a once-weekly dose. Dosages were titrated by 10 or 20 mg if limited-symptom attacks were present or if the effects of the drug seemed to wear off in less than a week. Patients were seen approximately once a month following the switch. Assessment scales included the Clinical Global Impressions-Improvement scale (CGI-I),[8] a panic diary to record panic attacks, the Hamilton Rating Scale for Anxiety (HAM-A),[9] and the Hamilton Rating Scale for Depression (HAM-D).[10]

RESULTS

Patients were initially treated with daily fluoxetine. All patients responded to daily dosing ranging from 10 to 60 mg and were panic free prior to switching to weekly dosing. Study results and demographic data are presented in Table 1.

Patient 1 had comorbid specific phobia for closed spaces, patient 2 had generalized anxiety disorder, patients 6 and 7 had dysthymia, and patient 8 had comorbid social phobia and specific phobia for heights. Once panic free, the patients switched to weekly dosing without any incident. The dose was titrated up if the patient experienced anxiety between weekly doses.

Only 1 (patient 3) of the 10 patients experienced a recurrence of panic attacks, which occurred 18 months after switching to weekly dosing. Patient 4 had mild jitteriness, which began while she was on a daily dose of fluoxetine and continued after she had switched to weekly dosing. Clonazepam, 0.5 mg/day, was added and was followed by a resolution of symptoms. Patient 6 experienced some depressive symptoms after switching to weekly dosing. After 4 weeks of weekly dosing and despite being panic free, the patient returned to daily dosing to help with her depressive symptoms. Patients 1, 3, and 4 are currently being followed at this clinic. The remaining 7 patients, once stabilized, were referred to their physicians for follow-up.

Case 1

Patient 1, a 39-year-old white divorced woman, presented with panic disorder with agoraphobia. She received fluoxetine, 20 mg/day. Once panic free, she was asked to select a particular day for once-weekly dosing. The patient switched to 20 mg of fluoxetine once a week without any incident and was maintained panic free on the weekly dosing. In addition, patient 1 noticed a significant improvement in her agoraphobia and comorbid irritable bowel syndrome symptoms. As a result of reduction in her symptoms, she became more outgoing and began dating again.

Case 2

Patient 3, a 41-year-old white woman was diagnosed with panic disorder without agoraphobia. She received 20 mg/day of fluoxetine. Eight weeks later, when panic free, she was switched to fluoxetine, 20 mg weekly. She continued to be free of panic attacks, but experienced episodes of mild jitteriness, which resolved when the fluoxetine was increased to 40 mg/week.

Approximately 18 months later, patient 3 experienced a sudden recurrence of her panic disorder. There were no stressors or precipitating factors. She was switched to fluoxetine, 20 mg/day, and clonazepam, 0.5 mg b.i.d., was added. After 2 weeks of daily treatment, she was switched back to fluoxetine, 40 mg/week, and again became panic free 4 weeks later, at which time the clonazepam was tapered and discontinued. The patient did not have any full-blown attacks after this switch, but did have an occasional (once a month) mild limited-symptom attack, which did not cause her any distress.

DISCUSSION

We found that fluoxetine, 10–60 mg administered once a week, was effective in maintaining a panic-free state. This may be due to the long half-life of fluoxetine and its metabolites. Weekly dosing may reduce the cost of treatment. Thus, it appears that because of its unique pharmacokinetic profile, fluoxetine may provide an advantage over shorter acting selective serotonin reuptake inhibitors by allowing weekly maintenance dosing for some patients.

An interesting observation was that fluoxetine at 10 to 60 mg weekly was selective in alleviating symptoms of panic disorder but not symptoms of reported concurrent depressed mood in some patients. This selectivity may suggest that panic attacks may respond to a lower dose of fluoxetine than what is indicated for symptoms of depression. Our experience suggests that a controlled trial is warranted to test once-weekly dosing of fluoxetine in maintenance therapy of panic disorder.

Drug names: clonazepam (Klonopin), fluoxetine (Prozac).

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