Fluoxetine in Family Practice Patients

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Background. Many patients with depression are seen only by family physicians, yet it is unknown how their physicians prescribe newer antidepressants.

Methods. Charts of family practice patients receiving fluoxetine were reviewed using a standardized format. Information reviewed included patient demographics, diagnosis, prescriptions, and course of treatment.

Results. Depression was documented in 92.5% of the 40 patients studied. There were significantly more female patients in the fluoxetine sample than in the base sample of depressed patients ($P<.04$). Fluoxetine patients weighed significantly more than the base sample, with a mean difference of 20.8 pounds ($P<.03$). Side effects were documented in the charts of 12 (30%) patients. Prescription practice was considered optimal in 43% of patients who were told to take fluoxetine in the morning. No differences in improvement or side effects were found based on optimal prescribing behavior. Improvement was documented in 68% of patients. Fluoxetine was discontinued in 6 (15%) cases because of adverse side effects.

Conclusions. An improvement rate of 68% among patients taking 20 to 40 mg of fluoxetine per day indicates that an adequate response can be achieved without the risk of side effects that typically accompany higher doses. In this study, fluoxetine was prescribed more often to obese patients. This prescribing pattern may indicate that primary care physicians perceive overweight patients as good candidates for fluoxetine regardless of inconclusive evidence about the effectiveness of this drug for weight loss.

Key words. Fluoxetine; serotonin uptake inhibitors; depression; prescriptions, drug; treatment outcome; primary health care; family medicine. (*J Fam Pract 1994; 39:45-49*)

Fluoxetine hydrochloride, a relatively new selective inhibitor of serotonin reuptake, has been shown to be effective in the treatment of depression.[1-11] Studies have proven fluoxetine to be more effective than placebo and equally as effective as tricyclics.[1-7,11] However, there are no published clinical trials on the use of fluoxetine to treat depression in primary care settings. Based on data from the US National Center for Health Statistics, Eisenberg[12] estimates that there were more than 75 million primary care physician visits for depression in 1989. While generalists underreport psychiatric disorders by between 45% and 90%, it would seem logical for trials of therapeutic effectiveness to take place in a primary care setting, where the majority of patients with depression are treated.[13,14] No data are available that show the frequency with which fluoxetine is prescribed in primary care settings. Numerous questions remain concerning the overall safety and efficacy of this agent in the treatment of depressed patients receiving their care from nonpsychiatrist physicians.

The purpose of this retrospective chart review was to document the circumstances leading to fluoxetine prescribing for family medicine patients.

Methods

All patients with a diagnosis of depression assigned by their primary care physician were identified from the com-

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puter database of the Family Medicine Center of the Medical College of Georgia (N=828). The decision to diagnose depression was based on the judgment of the individual physician and did not necessarily conform to standardized clinical assessment. A total of 524 charts were randomly selected and reviewed to identify 40 (7.6%) fluoxetine users. All charts were reviewed using a standardized review form developed by one of the authors. Review topics included data on demographics, diagnosis leading to the prescription, prescriptions, and course of treatment. All data were retrieved by a research pharmacist.

The descriptive data were analyzed using frequency and percentage tabulations. Comparisons between improved and not improved, presence or absence of side effects, and morning and nonmorning recommendations were made by chi-square. Comparisons across age, height, and weight were made using *t* tests.

Results

The sample consisted of 5 (12.5%) male and 35 (87.5%) female patients. Eight (20%) patients were black and 32 (80%) were white. Mean age was 49.5 years, with a range of 17 to 77 years. Race and age were similar to the base sample of 828 depressed patients. There were significantly more women in the fluoxetine treatment group than in the base population of depressed patients (51.7%; $\chi^2=4.21$; $P<.04$). Patients were an average of 64.8 inches in height, with a mean weight of 182.4 pounds. Patients received their care from 23 different primary care physicians.

A randomly selected sample of 40 depressed patients proportionately matched by sex to include 35 women and 5 men for whom fluoxetine had not been prescribed was compared for height and weight with the fluoxetine sample. There were no differences in height but patients in the fluoxetine sample weighed significantly more than did those in the comparison group (182.4 lb vs 161.6 lb; $t=2.16$; $P<.03$), with a mean difference of 20.8 pounds.

Thirty-seven (92.5%) patients had documentation of depression in their clinical chart. Symptoms used for documenting depression are listed in descending order of frequency in Table 1. One person was treated for seasonal affective disorder, one was treated for headache, and one patient had no stated diagnosis included in the chart.

Eight (20%) patients had a concurrent psychiatric diagnosis in addition to depression. A variety of coexisting medical diagnoses were also present. Twenty-six (65%) patients had previously received antidepressant therapy (Table 2).

All patients received an initial daily dose of 20 mg of fluoxetine. Thirty-two patients remained on the 20-mg regimen throughout their therapy. Although not statistically evaluated in this study because of its small sample size, there was no apparent increase in side effects among the eight patients whose daily dosage was increased to 40 mg. Seventeen (42.5%) were instructed to take fluoxetine in the morning; 18 (45%) were to take it once per day with no time specified; four (10%) were to take it at bedtime; and one (2.5%) was to take it every other day with no time

Table 1. Symptoms of Depression Listed in Descending Order of Frequency for a Group of Family Practice Patients Treated with Fluoxetine (N=40)

Symptom	% of Patients
Depression	42.5
Insomnia	30.0
Anxiety/nervousness	27.5
Fatigue	25.0
Lethargy	20.0
Loss of enjoyment	17.5
Stress	12.5
Anorexia	10.0
Poor self-image	10.0
Irritability	7.5
Suicidal ideation	7.5
Cognitive dysfunction	7.5
Loneliness	7.5
Hypersomnia	5.0

Table 2. Previous Antidepressant Therapy Among a Group of 40 Patients Using Fluoxetine

Antidepressant*	% of Patients
Amitriptyline	32.5
Trazodone	22.5
Desipramine	17.5
Nortriptyline	17.5
Imipramine	12.5
Doxepin	12.5
Other	5.0
None	35.0

Some patients received more than one antidepressant prior to fluoxetine therapy.

Table 3. Trends in Symptomatic Improvement Among a Group of 40 Patients Using Fluoxetine

No. of Symptoms of Depression	No. of Patients	Improvement Rate, %
0	3	33.3
1	9	55.6
2	8	75.0
3	7	100.0
≥4	8	61.5

specified. Length of fluoxetine therapy in 32 patients ranged from 1 month to at least 2½ years, with an average duration of 9 months. Duration could not be determined for eight patients because of inadequate documentation of follow-up.

Patients were classified as improved if there was any documentation of improvement in the chart. Improvement was documented for 27 (67.5%) patients. Notations of improvement included such dimensions as depression reduced (n=18, 45%); feeling better (n=19, 47.5%); better mood (n=8, 20%); anxiety or nervousness reduced (n=7, 17.5%); and insomnia reduced (n=4, 10%). Improvement was noted on one of the above dimensions for 6 (15%) patients, two dimensions for 11 (27.5%) patients, three dimensions for 7 (17.5%) patients, and four dimensions for 3 (7.5%) patients.

The rates of improvement for each of the symptoms reported by at least 8 patients were compared. Overall, the improvement rate was about 70%. Symptom-specific improvement rates were 72.7% for anxiety or nervousness, 75% for insomnia, 62.5% for lethargy, 80% for fatigue, and 64.7% for depression. There was an interesting linear trend: improvement rates increased with increasing numbers of symptoms up to three; patients with four or more symptoms showed less improvement (Table 3).

Side effects were documented in 12 (30%) patients. Insomnia was the most frequently reported symptom (four patients, 10%). There were no differences in the self-report of insomnia between patients receiving the morning recommendation and those receiving the anytime-of-day recommendation. Although a greater percentage of patients in the bedtime group (50% vs 6%) reported insomnia, the actual numbers of patients in each group were so small that the validity of that conclusion is limited. Patients were classified as either having side effects or not. Prescribing behavior was considered optimal among patients who were instructed to take their medication in the morning. Chi-square comparisons indicated no differences in improvement or side effects based on optimal prescribing behavior.

Fluoxetine was discontinued in 17 (42.5%) patients. In nine (22.5%), it was discontinued at patient request because of the cost of the medication (n=2), bad publicity by the media (n=2), patient preference for another antidepressant (n=2), resolution of depression (n=1), patient complaint that the medication "didn't do any good" (n=1), and no reason stated (n=1). In only six (15%) patients was fluoxetine discontinued because of side effects. It was discontinued in two additional cases: one at the request of a consulting neurologist and one for which no reason was stated.

Discussion

Which patients are selected for fluoxetine therapy in primary care? Comparison of fluoxetine patients with the base population of depressed patients in our practice setting showed no difference in race and age but a greater percentage of women. Although there were no differences in height between the two groups, there was a significant difference in weight. Patients in the fluoxetine sample weighed more, by a mean weight difference of 20.8 pounds. This finding suggests that primary care physicians view overweight female patients as good candidates for fluoxetine therapy, even though the use of this medication to achieve weight loss at the dosage used in this study has not been demonstrated in clinical trials.

Studies involving obese patients have shown that higher doses of fluoxetine may result in greater weight loss than placebo.[15–17] The study by Pijl and associates[16] demonstrated a significant reduction in food and calorie intake among all patients taking fluoxetine at a dose of 60 mg per day, resulting in a mean weight loss of 3.6±0.5 kg in 6 weeks. Weight loss was not examined in the present study; however, slightly greater improvement in depression symptoms was observed in patients labeled as obese (75% vs 64.3%) in their medical records. These results appear to support the evidence that fluoxetine is a legitimate choice of treatment in obese depressed patients but not solely for the purpose of achieving weight loss. In investigations of weight loss in the absence of depression, physicians have utilized higher doses than those prescribed by family physicians in this study.[15–17]

According to product literature provided by the manufacturer, fluoxetine should be prescribed initially at 20 mg per day in the morning. If higher doses are required, the medication should be administered on a twice-daily schedule (in the morning and at noon).[18] Bedtime dosing is not considered optimal because of the increased possibility of insomnia. All the patients in this study received the optimal dose initially (20 mg per day). However 10% of patients were told to take their dose at bedtime. Of these four patients, two complained of insomnia (50% as compared with only 6% of the non–bedtime group). This sample was too small to justify a valid

conclusion. The study by Usher and associates[4] suggests that there is no difference between the morning and evening doses in terms of activation and sedation. If this is true, fluoxetine could be administered at any time of day that suits an individual patient's needs.

Improvement was documented in 68% of the cases in our study, including some patients who later discontinued therapy. Although this rate was based on individual physician assessment and retrospective review of patient medical records, it corresponds well with studies using the Hamilton Rating Scale for Depression (HRSD) as a measure of clinical improvement. In these studies, improvement rates among patients taking similar or higher doses ranged from 50% to 80%.[2,3,7] Studies using higher doses, for example, that of Beasley and associates,[3] showed response rates ranging from 60% to 80%, with an average improvement rate of 68%. In actual clinical practice, the use of standardized depression assessments as a measure of depression and improvement is probably not as feasible as in controlled clinical trials. Our results indicate that physician assessment of improvement as reported by patients may be an acceptable alternative measure in clinical practice.

Our findings showed that improvement rates increased with increasing numbers of depression symptoms up to three. In patients with four or more symptoms, the improvement rate decreased to 61.5%. Severity of depression may be a factor that should be taken into account. Future research with standardized measures should examine this potential outcome difference.

Side effects of fluoxetine have been found to be dose-related. In general, the higher the dose, the greater the incidence and frequency of adverse events.[1–5,7,9,11] Insomnia was the most frequent side effect observed in our study, with a 10% incidence. Other side effects included anxiety, anorexia, headache, and nervousness, occurring in two patients each. One patient each reported nausea, palpitations, blurred vision, drowsiness, dry mouth, hyperactivity, and a dystonic reaction. Six (15%) patients discontinued fluoxetine because of side effects. This percentage corresponds exactly with the results of US premarketing clinical trials.[18] In addition, nine (22.5%) patients requested that fluoxetine be discontinued. That one fifth of all patients asked to be withdrawn from fluoxetine is certainly clinically important; however, only 3 of these 9 patients were withdrawn from therapy because of an inadequate therapeutic result. Cost and bad publicity, which were cited as other reasons for discontinuing therapy, certainly do not reflect on the efficacy of the medication itself.

The controversial nature of fluoxetine prescribing with regard to the potential for increased suicidal ideation has been recognized.[19–22] No indication of this result was found in the review of these charts, although some patients requested termination of medication because of publicity-based fears.

Conclusions

Fluoxetine appears to be an effective and safe treatment for depression among family practice patients. Its generally favorable side-effect profile and potential once-daily dosage increase the probability of compliance. Our study revealed an improvement rate of 68% among patients using a 20- to 40-mg per day dose, indicating that lower doses may provide adequate response without increasing the risk of side effects. Also, since there were significantly more women and more obese patients in the fluoxetine sample, primary care physicians apparently take into consideration sex and obesity when prescribing fluoxetine. It should be noted, however, that fluoxetine cannot be recommended solely for the treatment of obesity, particularly at lower daily doses.

Because bedtime dosing of fluoxetine occurred in only 4 (10%) of our patients, the relationship between the incidence of side effects and bedtime dosing could not be adequately determined. Since some family physicians may prescribe fluoxetine to be taken at bedtime, further studies should assess the possibility of increased insomnia with this dosage regimen.

Because the patients in this sample were not diagnosed by standardized criteria, future research should explore the relationship between severity of depression and efficacy of fluoxetine therapy. Fluoxetine may be useful in patients who fit a broader definition of depression than the traditionally accepted criteria for major depression set forth in the *Diagnostic and Statistical Manual of Mental Disorders,* Third Edition.

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