Serotonin Reuptake Inhibitors for Dizziness With Psychiatric Symptoms

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Objective: To investigate the efficacy and tolerability of selective serotonin reuptake inhibitors (SSRIs) for the treatment of patients with dizziness and major or minor psychiatric symptoms, with or without neurologic illnesses.

Design: Review of 60 consecutive cases of patients with dizziness who were treated with an SSRI for at least 20 weeks during the 30-month period from July 1998 to December 2000.

Setting: Tertiary care, multidisciplinary referral center.

Patients: Sixty men and women, aged 13 to 81 years, with (1) psychogenic dizziness, (2) dizziness due to a neurologic condition, as well as significant psychiatric symptoms, or (3) idiopathic dizziness.

Interventions: Open-label treatment with an SSRI titrated to 1 of 3 end points: optimal clinical benefit, intolerable adverse effects, or no therapeutic response.

Main Outcome Measure: Change in dizziness and psychiatric symptoms measured by the 7-point, clinician-rated, Clinical Global Impressions-Improvement Scale.

Results: Thirty-eight (63%) of 60 patients in the intent-to-treat sample and 32 (84%) of 38 patients who completed treatment improved substantially. The response rates did not differ between patients with major psychiatric disorders and those with lesser psychiatric symptoms. Patients whose only diagnosis was a psychiatric disorder and those with coexisting peripheral vestibular conditions or migraine headaches fared better than patients with central nervous system deficits. Before being treated with an SSRI, two thirds of the study patients took meclizine hydrochloride and/or benzodiazepines, with minimal benefit.

Conclusions: Treatment with SSRIs relieved dizziness in patients with major or minor psychiatric symptoms, including those with peripheral vestibular conditions and migraine headaches. Patients fared far better with SSRI treatment than with treatment with vestibular suppressants or benzodiazepines.


Patients with dizziness often experience psychiatric symptoms, such as anxiety, panic attacks, phobic behaviors, and depression.1-11 Psychiatric disorders may coexist with neurologic illnesses, or they may be the sole cause of patients’ complaints.1,2 Several terms have been used to describe dizziness with psychiatric or behavioral symptoms, including psychogenic dizziness,1 phobic postural vertigo,4-5 space phobia,6 space-motion discomfort, and space-motion phobia.7 Most patients with dizziness and psychiatric symptoms suffer from anxiety or depressive disorders, whether or not they have coexisting neurologic conditions.3,5,7-11 However, only limited anecdotal data exist on the medical treatment of these patients,4 almost none of which incorporates the substantial advances from the last decade in the pharmacotherapy of anxiety and depression.12,13 Clinical experience suggests that the medications most often prescribed for these patients, including vestibular suppressants and benzodiazepines, provide only transient or incomplete relief of symptoms.1

Over the last 10 years, the group of antidepressants known as selective serotonin reuptake inhibitors (SSRIs) has supplanted tricyclic antidepressants, monoamine oxidase inhibitors, and benzodiazepines as first-line therapy for most anxiety and depressive disorders.12,13 Five SSRIs—fluoxetine hydrochloride (Prozac, Sarafem), sertraline hydrochloride (Zoloft), paroxetine hydrochloride (Paxil), fluvoxamine maleate (Luvox), and citalopram hydrobromide (Celexa)—have been approved by the Food and Drug Administration for the treatment of at least 1 anxiety or mood disorder. None of these agents is consistently superior to the others, but all have advantages over earlier antidepressants and benzodiazepines, including bet-
PATIENTS AND METHODS

Data for this report were abstracted from a research database containing anonymous information on 110 consecutive patients who underwent a formal psychiatric examination as part of a multidisciplinary, clinical evaluation for dizziness at an urban, university-based, tertiary care, neurology referral center from July 1998 through December 2000. The database includes patient demographics, presenting symptoms, duration of illness, medical and psychiatric diagnoses, treatment histories prior to referral, therapies prescribed by the authors, and ratings of clinical outcomes. The research database contains no unique identifying information on any patient and is maintained separately from all medical records. Therefore, the institutional review board at the University of Pennsylvania School of Medicine, Philadelphia, classified this study as exempt from human subjects review.

PATIENT SELECTION

All patients in this study underwent a thorough neurologic examination as well as balance function tests and neuroimaging, if clinically indicated. Patients were referred for psychiatric evaluation if their neurologic examination revealed 1 of the 3 following clinical conditions: (1) psychogenic dizziness, characterized by vague, persistent sensations of dizziness, subjective imbalance, lightheadedness, fullness in the head, or detachment from the environment that were worse in open spaces (eg, warehouses and churches) or active visual surroundings (eg, busy malls); (2) dizziness due to a neurologic condition, as well as significant psychiatric symptoms (eg, Meniere disease with depression or benign paroxysmal positional vertigo with anxiety); and (3) idiopathic dizziness, defined as atypical complaints not consistent with a central or peripheral vestibular deficit but not overt psychiatric symptoms.

The psychiatric evaluation closely followed the Structured Clinical Interview for Axis I DSM-IV Disorders, Research Version, Patient Edition (SCID-I/P), an instrument that is widely accepted as the diagnostic standard in psychiatric clinical research.

We treated 60 of the 110 patients with an SSRI because of their multidisciplinary evaluation. The remaining 50 patients were seen for 1-time consultations (n=20), had diagnoses that required other therapies (n=18), declined treatment with an SSRI (n=6), or were unavailable for follow-up (n=6). To be included in this study, patients must have remained in treatment until they reached 1 of 3 clinical endpoints: (1) optimal clinical benefit, (2) intolerable adverse effects (defined as persistent adverse effects that prevented patients from continuing to take their medications), or (3) lack of clinical response (defined as the absence of any noticeable improvement [see rating scale in the “Outcome Measure” section] in patients who had taken an SSRI for at least 20 weeks and had reached a dose equivalent to 150 mg/d of sertraline hydrochloride).

MEDICATION DOSING

The SSRIs were prescribed in open-label fashion after patients were informed of the clinical indications, common adverse effects, and anticipated course of treatment. The regimens were started at the lowest available doses because of the concern that adverse effects would lead to premature discontinuation. In 1998, sertraline was available in the lowest-strength tablets relative to other SSRIs, so it was used most frequently (n=40). Later, the other SSRIs were marketed in equivalent low-dose tablets or elixirs, but they were prescribed less often (fluoxetine [n=11], paroxetine [n=13], and citalopram [n=5]). Fluvoxamine, the most sedating SSRI, was not used. Patients followed 1 of the 2 dosing schedules shown in Figure 1, depending on their tolerance for the starting dose (equivalent to 12.5 mg/d of sertraline hydrochloride). In 2 cases, the final dose was an intermediate titration step (37.5 mg of sertraline hydrochloride in one case and 125 mg in the other). Five patients were taking an SSRI at the time of referral. The dosage of their medication was adjusted to the optimal clinical benefit. The dosages of all other psychotropic medications were tapered gradually. The use of vestibular suppressants and other otologic agents was minimized for patients with active neurologic conditions and discontinued for all others. No other treatments (eg, psychological or behavioral therapies) were used during the first 20 weeks of SSRI therapy.

OUTCOME MEASURE

Treatment outcomes were measured with the Clinical Global Impressions-Improvement (CGI-I) Scale, a clinician-rated instrument that is used widely in psychiatric research to score overall changes in patients’ symptoms:

Continued on next page

ter tolerability, ease of prescribing, far greater safety in overdose, no need for monitoring of serum levels, and fewer complications in the medically ill.12,13 For patients with anxiety disorders, treatment with SSRIs can be discontinued more successfully than treatment with benzodiazepines, and SSRIs have no addiction liability.

Despite these advantages, there were several concerns about prescribing SSRIs for patients with dizziness. Nausea is one of the most common adverse effects of all 5 SSRIs. It occurs at least transiently in about 20% of patients and is a leading cause of medication discontinuation. Dizziness is reported in up to 8% of patients taking an SSRI.14 Other adverse effects, such as physical fatigue and mental sluggishness, might mimic symptoms that accompany chronic dizziness. An SSRI discontinuation syndrome has been reported after abrupt withdrawal from the use of these medications, with dizziness a prominent symptom.15 Nevertheless, SSRIs offered the same potential advantages for neurologic patients with dizziness and psychiatric symptoms as they did for patients with psychiatric disorders alone. In July 1998, we began to prescribe SSRIs regularly for patients with dizziness and psychiatric symptoms, including those with and without comorbid neurologic illnesses. The goals of this effort were to achieve better clinical outcomes than those of existing treatments and to evaluate the efficacy and tolerability of SSRI therapy for this challenging patient population.
1, very much improved; 2, much improved; 3, minimally improved; 4, no change; 5, minimally worse; 6, much worse; and 7, very much worse. In clinical trials, the CGI-I scale often is used as a dichotomous measure to separate patients with a positive treatment response (score of 1 or 2) from those with no clear benefit (score ≧3). This approach sets a more rigorous standard for a positive outcome (definite improvement) and presents the results in a clinically relevant manner (percentage of individuals who benefit, rather than group means). The CGI-I scale was used dichotomously in this study. Scores were based on the change in severity of both dizziness and psychiatric symptoms from the initial evaluation to 20 weeks after the initiation of an SSRI therapy. We treated 28 patients for at least 1 year and rated them a second time, comparing their clinical status at 12 months with that at 20 weeks.

**DIAGNOSTIC CATEGORIES**

Patients were divided into 2 groups by psychiatric diagnoses: major psychiatric disorders and minor psychiatric conditions (Table 1). The major disorders are well-known anxiety and depressive disorders, such as panic disorder and major depression. The minor conditions are less familiar to those outside the mental health professions. Undifferentiated somatoform disorder is a condition in which patients have a persistent physical symptom out of proportion to objective medical findings. This diagnosis was given in cases involving chronic dizziness but no active neurologic illness and no other psychological symptoms (eg, no significant worry, dysphORIA, changes in daily routines, or avoidance of situations associated with dizziness). The patient with specific phobia had dizziness and phobic avoidance limited to driving situations only. Individuals with anxiety disorder, not tolerant outcomes. The completer analyses excluded patients who could not tolerate SSRIs and compared those with a positive outcome (CGI-I ≤2) with those who received no benefit from a full medication trial (CGI-I >2).

The second hypothesis was examined using the same statistical approaches. Patient demographics and treatment outcomes were compared between patients with and without medical illnesses, and then outcomes were analyzed within the medically ill cohort. Medical diagnoses were grouped into 4 categories for statistical analysis: peripheral vestibular deficits, central nervous system illnesses, cardiovascular conditions, and other diagnoses. There was insufficient power for a 2 × 2 × 2 analysis (psychiatric diagnosis by medical condition by outcome).

This report covers 30 months of experience with SSRIs. We hypothesized that patients with major psychiatric disorders would have a more favorable outcome than those with lesser psychiatric symptoms, because their established psychiatric illnesses would be targeted specifically by the SSRIs. Preliminary findings showed substantial clinical benefit across a wide range of psychiatric symptom severity. We also hypothesized that patients with coexisting neurologic and psychiatric conditions would benefit from treatment with SSRIs.

Demographic characteristics of the study patients are shown in Table 2. The groups with and without major psychiatric disorders did not differ significantly in age, sex, race, presence of medical comorbidity, or duration of dizziness, which exceeded 4 years on average. The clinical outcomes of the 2 groups are compared in Table 3. Mean and modal medication doses and dose ranges are listed in Table 4 for patients with a positive treatment response. There were no differences between the psychiatric groups in SSRI efficacy, tolerability, mean or modal medication doses, or dose ranges. In the intent-to-treat analysis, 38 (63%) of 60 patients tolerated their medication well and were rated much or very much improved on the CGI-I scale at 20 weeks. Among those who completed treatment, 38 (84%) of 45 responded well (CGI-I ≤2).

Twenty-eight patients with a positive outcome at 20 weeks were followed up for 12 months or more (23 with...
major psychiatric disorders and 5 with minor conditions). Twenty-six (93%) enjoyed continued success throughout the year. One patient with a long history of major depression, panic disorder, and bilateral Meniere disease was hospitalized with an acute exacerbation of her psychiatric symptoms. The other patient experienced worsening depressive symptoms while taking cyclophosphamide for a rheumatologic condition.

The length of time that patients were ill affected the extent of their response to SSRI therapy. When the population was divided at the median duration of illness (33.5 months), the positive response rate did not differ significantly between patients who had been ill for 3 to 31 months (16/30, 53%) and those who had been ill for 36 to 336 months (22/30, 73%) ($\chi^2 = 4.45; P < .10$). However, positive responders who had been dizzy for the shorter period of time were more likely to achieve a CGI-I score of 1 (very much improved) rather than 2 (much improved) after 20 weeks. Thirteen (81%) of 16 positive responders with a short duration of illness had a score of 1, compared with 8 (36%) of 22 who had been ill for 36 months or more ($\chi^2 = 10.2; P < .001$).

Patients with medical illnesses were older than those without ($45.1 \pm 16.5$ vs $36.8 \pm 12.9$ years; $P < .03$), but there were no other differences in demographic variables or duration of illness. Furthermore, there were no significant differences in SSRI efficacy, tolerability, or average daily medication dose between the 32 patients with medical illnesses and the 28 patients without medical illnesses. However, Table 5 shows that response rates and tolerability were not uniform across all medical conditions. The intent-to-treat analysis demonstrated that patients with peripheral vestibular deficits, migraine headaches, and autonomic symptoms responded well to treatment with SSRIs, while those with central nervous system illnesses fared quite poorly. The

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**Table 1. Psychiatric and Medical Diagnoses of 60 Patients Treated With SSRIs**

<table>
<thead>
<tr>
<th>Principal Psychiatric Diagnosis</th>
<th>Medical Condition Absent/Present</th>
<th>Medical Diagnoses (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major psychiatric disorders (n = 41)</td>
<td>BPPV (1), migraine (3), Meniere disease (1), vestibular neuritis (2), postoperative CVA (1)</td>
<td>23 (56%) with a medical diagnosis</td>
</tr>
<tr>
<td>Panic disorder with agoraphobia</td>
<td>Migraine (1), Wolff-Parkinson-White syndrome (1)</td>
<td></td>
</tr>
<tr>
<td>Panic disorder without agoraphobia</td>
<td>0/1</td>
<td></td>
</tr>
<tr>
<td>Agoraphobia without panic</td>
<td>0/1</td>
<td></td>
</tr>
<tr>
<td>Obsessive-compulsive disorder</td>
<td>Autoimmune ear disease (1)</td>
<td></td>
</tr>
<tr>
<td>Major depressive disorder</td>
<td>BPPV (2), migraine (1), Meniere disease (1), peripheral neuropathy (1), basilar TIA (1), ocular vergence abnormality (1), bradyarrhythmia (1)</td>
<td></td>
</tr>
<tr>
<td>Mood disorder due to head trauma</td>
<td>Closed head injury (3)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>18/23</td>
<td></td>
</tr>
<tr>
<td>Minor psychiatric conditions (n = 19)</td>
<td>Migraine (1), cerebellar CVA (1), autonomic dysregulation (3), unspecified childhood tumor AD (1)</td>
<td></td>
</tr>
<tr>
<td>Anxiety disorder, not otherwise specified</td>
<td>4/6</td>
<td></td>
</tr>
<tr>
<td>Specific phobia (driving)</td>
<td>Vestibular neuritis (1)</td>
<td></td>
</tr>
<tr>
<td>Undifferentiated somatoform disorder</td>
<td>6/0</td>
<td></td>
</tr>
<tr>
<td>No psychiatric diagnosis</td>
<td>Mal de debarquement (2)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>10/9</td>
<td>9 (47%) with a medical diagnosis</td>
</tr>
</tbody>
</table>

*SSRI indicates selective serotonin reuptake inhibitor; BPPV, benign paroxysmal positional vertigo; migraine, migraine headaches with dizziness; CVA, cerebrovascular accident; and TIA, transient ischemic attacks.

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**Table 2. Demographic Characteristics of Dizzy Patients With and Without Major Psychiatric Illnesses**

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Major Psychiatric Disorder (n = 41)</th>
<th>Minor Psychiatric Condition (n = 19)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD, y</td>
<td>42.4 ± 16.1</td>
<td>38.6 ± 13.7</td>
<td>&lt;.35</td>
</tr>
<tr>
<td>Sex, F/M</td>
<td>32/9</td>
<td>12/7</td>
<td>&lt;.25</td>
</tr>
<tr>
<td>Race, % white</td>
<td>98</td>
<td>100</td>
<td>&lt;.50</td>
</tr>
<tr>
<td>Medical illness, No. (%)</td>
<td>23 (56)</td>
<td>9 (47)</td>
<td>&lt;.40</td>
</tr>
<tr>
<td>Duration of dizziness, mean ± SD, (range), mo</td>
<td>51.0 ± 58.8 (4-274)</td>
<td>57.0 ± 78.7 (3-336)</td>
<td>&lt;.40</td>
</tr>
</tbody>
</table>

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Figure 1. The selective serotonin reuptake inhibitor (SSRI) dose titration schedule, showing sertraline hydrochloride as an example, emphasizes a “start low, go slow” approach for patients with dizziness. Fifty milligrams was the modal daily dose of sertraline hydrochloride (range, 25-150 mg/d). Equivalent doses are listed for other SSRIs.
small groups of patients with cardiac dysrhythmias and mal de debarquement also had negative outcomes.

The dosages of all other psychotropic medications were tapered in each case in which the patient responded to treatment with an SSRI, with the exception of 5 cases involving individuals with severe anxiety disorders who responded best when a benzodiazepine was used in conjunction with an SSRI. Patients without active neurotologic conditions successfully discontinued all otologic therapy. Patients with histories of benign paroxysmal positional vertigo and vestibular neuritis were treated with SSRIs alone, while those with Meniere disease, autoimmune ear disease, and migraine headaches were maintained on a regimen of medications typically used for those disorders.

Fifteen patients (25%) could not tolerate treatment with an SSRI, including 4 who tried taking 2 different SSRIs, without success. Intolerable adverse effects were sedation or fatigue (n = 3), sexual adverse effects (n = 4), dulled mentation (n = 3), insomnia (n = 2), or nausea (n = 1). Another 5 patients did not tolerate their first SSRI treatment but were able to take a second medication successfully. A few patients experienced mild symptoms of the SSRI discontinuation syndrome during brief periods of medication noncompliance.

At least 1 medication for dizziness was prescribed to 56 (93%) of the 60 patients before they were referred to us (Figure 2). Fifty (83%) of the 60 patients had taken meclizine hydrochloride and/or benzodiazepines. Three patients, all with active vestibular illnesses, reported that meclizine temporarily reduced their symptoms during periods of acute vertigo. The others reported no benefit or worsening of symptoms due to sedation. No patient achieved sustained improvement in either dizziness or psychiatric symptoms with the use of benzodiazepines. The most common response was a partial symptom reduction for several days to weeks. Sedation or cognitive impairment limited attempts to increase the doses. One of the 2 patients with Meniere disease reported moderate improvement with the use of diuretics, including acetazolamide sodium. Treatment with corticosteroids, antihistamines, and buspirone hydrochloride provided no relief for any patient. Fourteen patients had taken an SSRI before they were evaluated by us, but their courses of treatment were too short to obtain clinical benefit. Ten (71%) of the 14 patients had excellent therapeutic outcomes in the present study. Tricyclic antidepressants were prescribed at migraine or insomnia doses, which were too low to be effective for psychiatric symptoms.

The results of the present study indicate that SSRI therapy can alleviate symptoms of dizziness in patients with ma-
or minor anxiety disorders and major depression, whether these psychiatric conditions are the sole causes of patients’ complaints or coexist with certain medical illnesses. Treatment with SSRIs also may be helpful for patients who experience chronic sensations of disequilibrium alone (ie, undifferentiated somatoform dizziness). Approximately two thirds of all patients who took an SSRI had a positive response, but those with psychiatric disorders alone, as well as those with psychiatric symptoms accompanied by peripheral vestibular deficits or migraine headaches, had the best outcomes. Patients with central nervous system illnesses, such as traumatic brain injury or stroke, fared poorly. Treatment with SSRIs was effective in patients with many years of disability, although individuals with a shorter duration of illness (<3 years) had a more robust response than those who had been ill for a longer time. The initial data on long-term outcomes were encouraging. Nearly all patients who were followed up for 12 months or more enjoyed sustained benefits. Finally, the patient population in this study was similar to those described in investigations of psychogenic dizziness, phobic postural vertigo, and space-motion phobia, suggesting that SSRI therapy may benefit patients with those syndromes.

The study was not designed to compare treatment with SSRIs directly with any other treatment for dizziness, but the high percentage of patients who obtained little benefit from the use of meclizine, benzodiazepines, and other medications indicates that SRI therapy may offer significant advantages over these treatments for patients with dizziness and major or minor psychiatric symptoms.

The positive results of this investigation are tempered somewhat by the fact that 1 in 4 patients could not take an SSRI, mostly because of somnolence, physical fatigue, and mental sluggishness. These adverse effects occurred at higher rates than in double-blind, placebo-controlled trials of SSRI therapy for uncomplicated anxiety and depressive disorders, suggesting that patients with dizziness may be particularly intolerant of adverse reactions that mimic the nagging symptoms that often accompany chronic disequilibrium. In contrast, gastrointestinal adverse effects were managed successfully with the slow titration schedules shown in Figure 1, and sexual adverse effects occurred at rates similar to those observed in other patient populations.

To our knowledge, this is the first investigation of the efficacy and tolerability of SSRI therapy for patients with dizziness accompanied by major or minor psychiatric symptoms. It introduces an encouraging new therapeutic approach for this difficult clinical problem. However, the study has several limitations, including an unblinded design and lack of a control group. Furthermore, the small amount of long-term data does not provide adequate information about the optimal length of treatment. These shortcomings are partially mitigated by the fact that our study comprised a consecutive case series and that the number of subjects was fairly large for an uncontrolled pharmacological study. A standardized clinical protocol was used for the neurotologic evaluations, and widely accepted clinical research tools were used for the psychiatric examinations and outcome measures. Retrospective bias was minimized by encoding clinical data into the research database in a prospective manner. Nevertheless, controlled trials are needed to confirm our findings. Future pharmacological research should include a broader selection of neurotologic and psychiatric outcome measures and investigate long-term treatment responses.

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REFERENCES


