Four Cases of Tardive Dyskinesia Associated with Ziprasidone

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Abstract

Introduction: Ziprasidone is a second-generation antipsychotic (SGA) used to treat psychotic disorders. SGAs are thought to carry reduced risks of tardive dyskinesia (TD) compared to first generation agents. However, there are several reports of TD or tardive dystonia associated with ziprasidone. We report herein four additional cases of TD associated with ziprasidone.

Methods: The patients were four males aged between 53-57 years, who were being treated in the outpatient mental health clinic at an urban Veterans Administration Medical Center. None of the patients had any history of antipsychotic medication exposure prior to starting ziprasidone. The Abnormal Involuntary Movement Scale (AIMS) was administered in a non-blind manner by E.D. at baseline before starting ziprasidone and after the emergence of TD (range, 9-15 months after baseline).

Results: All patients had AIMS score totals on items 1-7 of zero at baseline. The mean time on ziprasidone was 12.75 months. At the end of ziprasidone treatment the AIMS scores on items 1-7 had increased by a mean of 9.75 (range, 4-14).

Conclusion: The timeline of these cases strongly suggest that ziprasidone was the cause of their TD. The suddenness with which TD emerged and rapidly escalated to quite severe levels in cases 2-4 was particularly striking. Regarding TD risk, all patients were over 50 years old, putting them in a relatively high-risk category. They all had affective disorders, which may have rendered them more vulnerable to TD than persons with schizophrenia. These new cases and prior published reports suggest that TD risk with ziprasidone may warrant particular vigilance by clinicians.

Case Series

Introduction

Ziprasidone is a second-generation antipsychotic (SGA) used to treat psychotic disorders. SGAs are thought to carry reduced risks of tardive dyskinesia (TD) compared to first generation agents [1-3]. In a comprehensive review, Taras and Baldessarini cite an annual incidence of TD associated with first generation agents of 4-8%, although higher in the elderly [3,4]. In contrast, the annual incidence associated with SGA exposure has been estimated at an average of 2.1% [3]. There are a number of published reports of TD or tardive dystonia associated with ziprasidone (OVID search: ziprasidone+tardive) [2,5-12]. We report herein four additional cases of TD associated with ziprasidone (see Table 1 for summary).

Case 1

A 53 year old Caucasian male diagnosed with bipolar disorder and generalized anxiety disorder was taking temazepam, venlafaxine and valproate. Ziprasidone 40 mg twice daily was added, at which time his Abnormal Involuntary Movement Scale (AIMS) [11] score total on items 1-7 was 0. One month later, the dose was increased to 60 mg twice daily with AIMS total remaining at 0. Thirteen months after starting ziprasidone he reported involuntary leg movements as well as mild hand tremor. His AIMS total was 4. Ziprasidone was switched to quetiapine. Four weeks afterwards his AIMS total returned to 0.

Case 2

A 56 year old Caucasian male carrying clinical diagnoses of posttraumatic stress disorder, bipolar disorder, and restless legs syndrome was taking bupropion and venlafaxine. Ziprasidone 40 mg twice daily was added, at which time his AIMS total was 0. Two months later, AIMS total remained 0 and ziprasidone was increased to 60 mg twice daily. Nine months after starting ziprasidone he complained of lip smacking and tongue movements; his total AIMS score was 14. Ziprasidone was discontinued and carbamazepine started. Ten days later, total AIMS remained at 14. One month thereafter he reported some improvement, although his total AIMS declined only to 13.
and there is some evidence that these agents may increase risk of TD [14, 20]. Finally, cases 1-3 were receiving antidepressants, schizophrenia, since the presence of an affective disorder carries a relatively high-risk category [3,13-15]. They all had affective disorders, which may have rendered them more vulnerable to TD than persons with other disorders, including schizophrenia, since the presence of an affective disorder carries a heightened risk of TD [3,13-17]. Case 3 had a history of stroke, which may have heightened his risk for TD. There are reports of heightened vulnerability to TD in patients with multi-infarct dementia [4] and brain damage [3,18,19], although there is evidence to the contrary on this point [14, 20]. Finally, cases 1-3 were receiving antidepressants, and there is some evidence that these agents may increase risk of TD [21-23], although other studies failed to detect increased risk with these medications [24, 25]. In summary, these new cases and prior published reports suggest that TD risk with ziprasidone may warrant particular vigilance by clinicians, especially in patients that have risk factors that may confer added vulnerability to TD.

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**References**


**Table 1:** Change scores in AIMS from baseline to last rating on ziprasidone.

<table>
<thead>
<tr>
<th>Group</th>
<th>Muscles of Facial Expression</th>
<th>Lips and Perioral Area</th>
<th>Jaw</th>
<th>Tongue</th>
<th>Upper (arms, wrists, hands, fingers)</th>
<th>Lower (legs, knees, ankles, toes)</th>
<th>Neck, shoulders, hips</th>
<th>AIMS totala</th>
<th>Time on druga</th>
<th>Changes in AIMS total (item 8)b</th>
<th>Time off druga</th>
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<tbody>
<tr>
<td>Case 1</td>
<td>0</td>
<td>0</td>
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<td>2</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>4</td>
<td>13</td>
<td>-4</td>
<td>1</td>
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<tr>
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<td>4</td>
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<td>0</td>
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<td>9</td>
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<tr>
<td>Case 3</td>
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<td>3</td>
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<td>0</td>
<td>10</td>
<td>14</td>
<td>-7</td>
<td>3</td>
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<td>2</td>
<td>3</td>
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<td>3</td>
<td>0</td>
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<td>15</td>
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<td>9.75</td>
<td>12.75</td>
<td>-4.25</td>
<td>1.83</td>
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</table>

aAIMS change scores = Treated - Baseline. Positive number indicates worsened score on ziprasidone. All cases had 0 on all AIMS items at baseline.
bMonths from baseline to last rating on ziprasidone.

cAIMS change scores = Off ziprasidone - on ziprasidone. Negative number indicates improved score after stopping ziprasidone.