Antidepressant Use in Patients with Carcinoid / Neuroendocrine Tumors: Results of A Systematic Review

Elie Isenberg-Grzedza MD CM FRCP(C)
Meredith MacGregor MD
Konstantina Matsoukas MLLIS
Diane Reidy-Lagunes MD
Yesne Ali MD

(1) University of Toronto / Sunnybrook Health Sciences Center
(2) Memorial Sloan Kettering Cancer Center

Introduction

- Patients with neuroendocrine tumors (NET) have high rates of depression.
- NETs may secrete vasoactive substances, including serotonin.
- Tryptophan is a precursor of serotonin, which may also contribute to carcinoid syndrome (CS).
- Antidepressants may theoretically worsen CS via their serotonergic properties.
- Few case reports have cautioned against prescribing antidepressants to patients with CS.
- No large studies have examined the safety of antidepressant use in NET with or without CS.

Methods

- 120 cases selected for full-text review
- 13 additional records identified through snowballing
- 100 records excluded

Results

<table>
<thead>
<tr>
<th>Article</th>
<th>Year</th>
<th>Age Gender</th>
<th>Antidepressant, dose, mg if reported</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bariani et al.</td>
<td>2013</td>
<td>64 M</td>
<td>Sertraline 12-month progression-free survival on octreotide and mTOR inhibitor</td>
<td>Only took 1 dose due to nausea/vomiting</td>
</tr>
<tr>
<td>Bajwah et al.</td>
<td>2005</td>
<td>67 F</td>
<td>Venlafaxine</td>
<td></td>
</tr>
<tr>
<td>Furse et al.</td>
<td>2008</td>
<td>55 M</td>
<td>Fluoxetine 10 mg</td>
<td>&quot;sudden deterioration in symptoms&quot; following fluoxetine. Symptoms rapidly improved after discontinuation.</td>
</tr>
<tr>
<td>Larsson et al.</td>
<td>2001</td>
<td>&quot;several&quot;</td>
<td>Unspecified</td>
<td>only a few patients suffered from depression, and those who developed symptoms of depression were successfully treated with antidepressants.</td>
</tr>
<tr>
<td>Noyer et al.</td>
<td>1997</td>
<td>56 F</td>
<td>Sertraline</td>
<td>Carcinoid tumor &quot;unmasked&quot; following overdose of sertraline (500 mg) in suicide attempt. Previously tolerated sertraline for 3 months.</td>
</tr>
<tr>
<td>Oberg et al.</td>
<td>1986</td>
<td>Unspec.</td>
<td>Tricyclics</td>
<td>Patient developed &quot;mental depression after 3 months of interferon which resolved on treatment with tricyclic antidepressants&quot;.</td>
</tr>
<tr>
<td>Patel et al.</td>
<td>2009</td>
<td>51 F</td>
<td>Unspecified</td>
<td>&quot;he was placed on antidepressants and remains stable at this time.&quot;</td>
</tr>
<tr>
<td>Philip et al.</td>
<td>2011</td>
<td>47 M</td>
<td>Unspecified</td>
<td></td>
</tr>
<tr>
<td>Russo et al.</td>
<td>2004</td>
<td>Unspec.</td>
<td>Amitriptyline</td>
<td></td>
</tr>
<tr>
<td>Seshamani et al.</td>
<td>2009</td>
<td>47 M</td>
<td>Citalopram</td>
<td>5-HIAA normal. &quot;No flushing, diarrhea, or fainting&quot;</td>
</tr>
<tr>
<td>Simbera et al.</td>
<td>2005</td>
<td>75 F</td>
<td>Citalopram 20 mg</td>
<td>Worsening of diarrhea (from twice daily to 14 times daily) with citalopram, leading to dehydration and hospitalization. Normalization when citalopram switched to mirtazapine.</td>
</tr>
<tr>
<td>Soliday et al.</td>
<td>2004</td>
<td>25 cases</td>
<td>Unspecified</td>
<td>13 patients taking SSRIs, 12 patients taking other antidepressants.</td>
</tr>
<tr>
<td>Vollmayr et al.</td>
<td>2005</td>
<td>67 F</td>
<td>Unspecified</td>
<td>Abdominal pain worsened. Upon diagnosis of NET (which followed antidepressant) and surgical resection, symptoms abated.</td>
</tr>
<tr>
<td>Williams et al.</td>
<td>2005</td>
<td>61M</td>
<td>Sertraline 50 mg</td>
<td>One of the patients (64F) had carcinoid syndrome. Two of the patients (64F and 68M) were treated with somatostatin analogs. None of the patients developed worsening carcinoid syndrome.</td>
</tr>
<tr>
<td>Wyatt et al.</td>
<td>1968</td>
<td>2 cases</td>
<td>MAOI</td>
<td>NET of the lung. No symptoms of carcinoid syndrome. Patient well 10 months post-resection.</td>
</tr>
</tbody>
</table>

Conclusion

- Over 42 cases reported
- Nearly all did not report adverse reactions
- One patient hospitalized due to dehydration
- One patient with worsening CS symptoms following overdose
- Based on the available evidence, it appears premature to eliminate antidepressants in patients with carcinoid / NET
- Future studies should examine whether somatostatin analogs protect against antidepressant-related side-effects in patients with carcinoid / NET
- Future studies should examine the role of non- serotoninergic antidepressants in NET

Learning Objectives

1. Define the core theoretical problem that may make antidepressant use unsafe in patients with carcinoid tumors
2. List the studies that have been published to date arguing for and against the safe use of antidepressants in carcinoid tumor patients.
3. Weigh the risks and benefits of antidepressant use in patients with carcinoid tumor.

References


Funding: This research was funded in part through the NIH/NCI Cancer Center Support Grant P30 CA08748.