

THE TABLET: PALLIATIVE CARE PHARMACY TIPS



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If you have a topic you
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TODAY'S TOPIC:

Neuroendocrine Tumors and Antidepressants

Background:

Neuroendocrine tumors are cancers of neuroendocrine cells within the aerodigestive tract. NET incidence has increased over the past few decades. A subset of these tumors may secrete neurotransmitters and hormones, including serotonin which can lead to carcinoid syndrome (CS) which presents as diarrhea, abdominal cramping, wheezing, and flushing. Given the burden of physical symptoms related to their disease, patients with NET encounter psychological distress and depressive symptoms. Given that some of these tumors secrete serotonin, there has been concern regarding the treatment of the depression with Selective Serotonin Reuptake Inhibitor (SSRI) or Serotonin/Norepinephrine Reuptake Inhibitor (SNRI) in this population in fear of making these previously mentioned symptoms worse. There has been some mixed low-grade evidence regarding the safety surrounding the use of SSRIs/SNRIs in patients with NET. We intend to explore available evidence related to safety of antidepressant use in patients with NET.

Importance:

Given increase in NET incidence and our common utilization of antidepressants, it is important for palliative care clinicians to be aware of the safety considerations for the use of antidepressants in those with NET as this clinical question may arise more frequently in practice.

The Literature:

[Palliat Support Care. 2020 Oct;18\(5\):602-608.](#)

Must antidepressants be avoided in patients with neuroendocrine tumors? Results of a systematic review

Methods:

- Literature review through September 2018, included studies describing NET patients who were prescribed serotonergic antidepressants (SA)
- n=15 articles included, 12 of which were single case studies, 3 were larger case series

Objectives:

1. Do SAs precipitate CS in NET patients
2. Is CS exacerbated by SA use in NET patients with pre-existing CS
3. Do SA cause serious adverse outcomes (e.g., carcinoid crisis, death) when prescribed to NET patients ?

Results:

1. N = 89; Average of 14.3 month duration in one case series (76 cases) of antidepressant use without CS precipitation
2. N=72; 10 patients experienced exacerbation of CS, although did not lead to discontinuation of the antidepressant in all cases, suggesting mild/tolerable symptom burden related to CS exacerbation
3. N = 161; no instances of carcinoid crisis or death following antidepressant use; two cases of hospitalization related to dehydration

Conclusion: There is insufficient evidence to warrant a broad cautionary statement to avoid SSRIs in patients with NET

[Eur J Surg Oncol. 2018 Jun;44\(6\):744-749.](#)

Antidepressants appear safe in patients with carcinoid tumor: Results of a retrospective review

*this study was included in the literature review above, felt it warranted a more detailed exploration of findings, so including it separately

Methods: Retrospective chart review of patients with well differentiated NET prescribed antidepressants 1/2008-4/2015

Outcomes:

- Primary: duration of treatment of antidepressant therapy and frequency of treatment discontinuation
- Secondary: Reason for starting/stopping antidepressants, dosage ranges of antidepressants, whether or not patients developed serotonin syndrome or carcinoid crisis during treatment period

Results: n = 92; n = 16 with established CS (average age: 61.8 years) and n=76 without (average age: 60.1 years)

- Median antidepressant Rx duration 11.6 months (CS+ group) and 14.3 months in (CS- group)
- Antidepressants were stopped in 31 cases overall although reason was unspecified in 18 cases; described reasons were unrelated to serotonin syndrome or carcinoid crisis
- No CS- patient developed CS at any point during the study period
- Dosage ranges listed within normal ranges of prescribed antidepressants
- No patients developed carcinoid crisis

Conclusion:

- Several classes of antidepressants appear safe in NET patients, both with and without CS

Bottom Line:

- Precipitation of CS is very unlikely with use of antidepressants in NET, despite long durations of use of antidepressants (> 1 year)
- Symptom exacerbation may occur if patients have pre-existing CS, although potentially these exacerbations are mild...
- Antidepressants appear safe for use in patients with NET and would recommend careful monitoring for symptoms related to carcinoid syndrome like diarrhea, abdominal cramping, wheezing, and flushing
- GI disturbances are a side effect of many antidepressants, it may make sense to avoid SSRI with highest prevalence of GI side effects (ie. sertraline)