Retrospective Chart Review of Antidepressant Use in Patients with Carcinoid Tumors

Elie Isenberg-Grzeda MD CM FRCPC[1], Meredith MacGregor MD[2], Afton Bergel MD[2], Stacy Eagle MD[3], Fernando Espi Forcen MD[4], Reema Mehta MD[5], Konstantina Matsoukas MLIS[2], Jonathan Wills BA[2], Diane Reidy-Lagunes MD[2], Yesne Alici MD[2]

(1) University of Toronto/Sunnybrook Health Sciences Center (2) Memorial Sloan Kettering Cancer Center (3) Stony Brook Medicine
(4) Rush University Medical Center (5) Jacobi Medical Center

Background

Patients with carcinoid tumors have higher than expected rates of depression and therefore may require treatment with antidepressant medications.

However, these medications, particularly serotonergic antidepressants (SA), carry a theoretical risk in carcinoid patients.

Case reports of serotonergic antidepressants unmasking or worsening carcinoid syndrome have argued against the use of SAs in this population.

Limited data exist about the safety of antidepressants in patients with carcinoid tumors.

Methods

Retrospective chart review of patients (age 18-89) with carcinoid tumors at Memorial Sloan Kettering Cancer Center (MSKCC) who were also prescribed anti-depressants from January 1, 2008 through April 1, 2015. Patients were excluded if no evidence of disease at the time of initial presentation to MSKCC.

Outcomes measured included :

Duration of antidepressant use, dosage ranges, reason for starting / stopping.

Whether or not antidepressants were stopped during the study period.

Any instance of serotonin syndrome or carcinoid crisis during the study period.

Funding: This research was funded in part through the NIH/NCI Cancer Center Support Grant P30 CA008748

Results

92 patients (76 CS-, 16 CS+); 127 antidepressants prescribed.

No instances of serotonin syndrome or carcinoid crisis documented.

Of 76 CS- patients, none developed carcinoid syndrome during the study period.

The majority did not discontinue antidepressants at any point during the study.

Among CS+ patients who discontinued antidepressants, carcinoid syndrome was never the reported reason for stopping.

No instances of monoamine oxidase inhibitor usage were recorded.

Frequencies And Dosage Range of Antidepressants among 127 Instances of Use.

	Group			
	Carcinoid Syndrome Present (*n*=25)		Carcinoid Syndrome Absent (*n*=102)	
Antidepressant	*n* (%)	Dosage (mg)	*n* (%)	Dosage (mg)
SSRI	14 (56%)		55 (53.9%)	
Escitalopram	3 (12%)	10 – 30 mg	20 (19.6%)	5 – 30 mg
Sertraline	1 (4%)	50 – 100 mg	20 (19.6%)	25 – 200 mg
Paroxetine	4 (16%)	10 – 40 mg	5 (4.9%)	10 – 40 mg
Fluoxetine	3 (12%)	20 – 40 mg	6 (5.9%)	20 – 40 mg
Citalopram	2 (8%)	20 mg	4 (3.9%)	10 – 40 mg
Fluvoxamine	1 (4%)	150 mg		
NDRI	3 (12%)		20 (19.6%)	
Bupropion	3 (12%)	300 mg	20 (19.6%)	150 – 450 mg
SNRI	3 (12%)		9 (8.8%)	
Venlafaxine	1 (4%)	75 mg	7 (6.9%)	75 – 300 mg
Duloxetine	2 (8%)	20 – 60 mg	2 (2.0%)	20 – 60 mg
SARI	3 (12%)		7 (6.9%)	
Trazodone	3 (12%)	25 – 50 mg	7 (6.9%)	25 – 100 mg
TCA	2 (8%)		6 (5.9%)	
Amitriptyline	1 (4%)	25 mg	6 (5.9%)	10 – 150 mg
Doxepin	1 (4%)	25 mg		25 mg
NaSSA			5 (4.9%)	
Mirtazapine			5 (4.9%)	7.5 – 15 mg

SSRI = Serotonin Specific Reuptake Inhibitor, NDRI = Norepinephrine-Dopamine Reuptake Inhibitor, SNRI = Serotonin-Norepinephrine Reuptake Inhibitor, SARI = Serotonin Antagonist and Reuptake Inhibitor (SARI), TCA = Tricyclic Antidepressant, NaSSA = Noradrenergic and Specific Serotonergic Antidepressant

Patient Demographics And Antidepressant Variables

	Group		
	CS Present *n* (%)	CS Absent *n* (%)	p-value
Total	16 (17.4%)	76 (82.6%)	
Age (years), *M*(SD)	61.8 yr (14.9)	60.1 yr (10.9)	
Gender			
Male	9 (56.3%)	26 (34.2%)	p=.087 [a]
Female	7 (43.8%)	50 (65.8%)	
Tumor Location			
Lung		41 (53.9%)	
Pancreas		9 (11.8%)	
Ileum	10 (62.5%)	8 (10.5%)	
Duodenum	1 (6.3%)	5 (6.6%)	
Appendix		5 (6.6%)	
Unknown Primary	4 (25%)	2 (2.6%)	
Jejunum	1 (6.3%)	1 (1.3%)	
Other		5 (6.6%)	
Illness Features			
Metastases	16 (100%)	34 (44.7%)	
Somatostatin Analog	14 (87.5%)	4 (5.3%)	
Biomarker Positive	12 (75%)	0 (0%)	
Duration of Antidepressant Use (months), *Md* (range)	11.6 mo. (0-121)	14.3 mo. (0-172)	p=.641 [b]
Reason for starting			
Depression/Anxiety	13 (81.3%)	53 (69.7%)	
Sleep	3 (18.8%)	6 (7.9%)	
Other psych symptom		4 (5.3%)	
Somatic Symptoms		3 (3.9%)	
Smoking Cessation		2 (2.6%)	
Unspecified		8 (10.5%)	
Reason for stopping			
Unspecified	1 (25%)	17 (63.0%)	
Remission	2 (50%)	5 (18.5%)	
Ineffective		2 (7.4%)	
Delirium		2 (7.4%)	
Side-effects	1 (25%)	1 (3.7%)	
Antidepressant Variables			
Stopped for Any Reason	4 (25%)	27 (35.5%)	p=.308 [c]
Monotherapy	12 (75%)	64 (84.2%)	p=.289 [d]
Serotonergic Antidepressant	15 (93.8%)	68 (89.5%)	p=.511 [e]

[a] Fisher's exact test $X^2(1)=2.724$; [b]Mann-Whitney U Test (normal distribution was not assumed); [c]Fisher's exact test $X^2(1)=.656$; [d]Fisher's exact test $X^2(1)=.780$; [e]Fisher's exact test $X^2(1)=.274$. *M* = Mean, *Md* = Median

Discussion

Modest number of patients prescribed antidepressants for long durations.

Majority did not stop antidepressants at any point during the study. Among those that did stop, CS was never the reason for stopping.

No patient without a history of carcinoid syndrome (CS-) developed CS following administration of antidepressants.

Few were prescribed non-SAs (eg bupropion).

Findings do not support the conclusion of previous authors that SSRIs should be avoided in this population.

Limitations

Nomenclature of carcinoid and neuroendocrine tumor (NET) changed over the sampling period.

Retrospective design / potential reporting bias.

Sample limited to charts from 2008 onwards.

References

Furse RM, Green CJ, Mee AS. Carcinoid syndrome unmasked by fluoxetine, a selective serotonin reuptake inhibitor. *Clinical Gastroenterology and Hepatology.* 2008; 6(8):e27-8.

Noyer CM, Schwartz BM. Sertraline, a selective serotonin reuptake inhibitor, unmasking carcinoid syndrome. *American Journal of Gastroenterology.* 1997;92(8):1387-8.

Soliday E GJ, Smith SR. Depression and antidepressant use in gastrointestinal carcinoid cancer patients. *Journal of Applied Biobehavioral Research.* 2004;9(2):80-90.

Contact Information

Elie Isenberg-Grzeda MD CM FRCPC
Department of Psychiatry, University of Toronto,
Odette Cancer Center, Sunnybrook Health Sciences Center
eisenberggrzeda@sunnybrook.ca