Effect of serotonin reuptake inhibiting agents on risk of bleeding in patients with cirrhosis

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Background

- Selective serotonin reuptake inhibitors (SSRI) and serotonin-norepinephrine reuptake inhibitors (SNRI) are used to treat depression in patients with cirrhosis[1,2]
- SSRI and SNRI therapy and cirrhosis are independent risk factors for bleeding[4,5]
- SSRIs inhibit serotonin uptake in platelets which limits platelet-mediated hemostasis, and bleeding risk is further increased due to thrombocytopenia, low fibrinogen, and formation of varices in cirrhosis[4-7]
- Risk of bleeding related to SSRI and SNRI use in patients with cirrhosis has not been evaluated

Objective

Compare the risk of major and minor bleeding in patients with cirrhosis with or without SSRI or SNRI therapy

Outcomes

- Primary outcome: Relative risk of composite major and minor bleeding over 18 months in patients with cirrhosis prescribed SSRIs or SNRIs versus those prescribed neither
- Secondary outcomes: Major bleeding, minor bleeding, composite gastrointestinal bleeding, and variceal bleeding

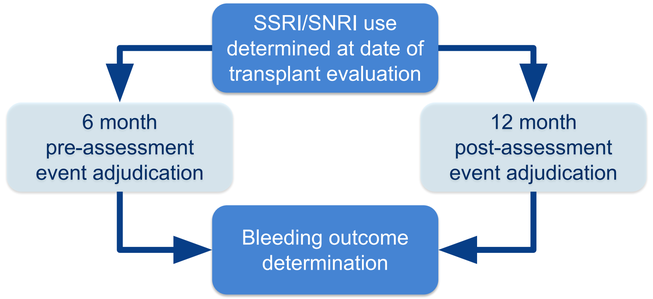
Outcome	Definition
Major bleeding	Clinically overt or symptomatic bleeding requiring intervention, or a ≥ 2 unit blood transfusion following a decrease in hemoglobin of more than 2 g/dL[7]
Minor bleeding	Any overt bleeding not determined to be major bleeding
Gastrointestinal (GI) bleeding	Any variceal, peptic ulcer-associated, or documented GI bleeding of unknown source marked by at least one episode of hematemesis, melena, or hematochezia
Variceal bleeding	Any acute variceal bleeding event including rebleeding

Statistical Analysis

- Baseline characteristics between groups assessed using Wilcoxon Rank Sum and Chi-Square testing
- All primary and secondary outcomes are reported as chi-squared odds ratios of bleeding events

Methods

- IRB-approved, single-center, retrospective analysis including all patients receiving liver transplant evaluation from January 2017 to June 2018
- Patients are excluded if they were candidates for multi-organ transplant or had truncated evaluations due to clinical decompensation



Baseline Characteristics

Characteristic	SSRI/SNRI Use (n=42)	No SSRI/SNRI Use (n=208)
Age, mean (*σ*)	55 (9.8)	57 (7.6)
Gender, male (%)	52.4	66.3
Caucasian (%)	97.6	83.7
Comorbidities (%)		
Depression*	61.2	31.7
Hypertension	52.4	49.0
Diabetes	35.7	28.8
Malignancy	26.2	26.5
History of Bleeding (%)	47.6	44.2
Hemoglobin < 10 mg/dL (%)	30.9	36.2
Platelets < 100,000 (%)	61.9	63.3
MELD Score, median (IQR)	16.9 (10.3, 21.5)	14.9 (10.1, 20.3)
SCr, median	1.0 (0.9, 1.5)	1.0 (0.8, 1.3)
Total bilirubin, median	2.6 (1.3, 6.2)	2.5 (1.5, 5.9)
INR, median	1.4 (1.3, 1.8)	1.5 (1.3, 1.8)
Albumin, median	2.9 (2.4, 3.4)	3.0 (2.5, 3.6)

*$p < 0.05$; IQR = interquartile range; *σ* = standard deviation

Results

Medication Use	SSRI/SNRI Use (n=42)	No SSRI/SNRI Use (n=208)
Aspirin (%)	7.1	8.2
NSAID (%)	0	6.3
P2Y12 inhibitor (%)	0	0.5
Anticoagulant (%)	2.4	1.0
PPI (%)*	71.4	53.8
H2RA (%)	4.8	4.3

*$p < 0.05$

Outcome	SSRI/SNRI Use (n=42)	No SSRI/SNRI Use (n=208)	Odds Ratio
Average duration of follow-up (mo.)	8.2	7.5	N/A
Composite Primary Endpoint, n (%)	26 (61.9)	58 (27.8)	2.22 (1.61-.3.12)*
Major Bleeding, n (%)	17 (40.5)	38 (18.3)	2.22 (1.38-3.57)*
Minor Bleeding, n (%)	9 (21.4)	20 (9.6)	2.22 (1.10-4.54)*
GI Bleeding, n (%)	16 (38.1)	40 (19.2)	2 (1.23-3.22)*
Variceal Bleeding, n (%)	9 (21.4)	19 (9.1)	2.38 (1.15-5)*

*$p < 0.05$

Conclusions

- SSRI/SNRI therapy is associated with an increased risk of bleeding in patients with cirrhosis despite a higher proportion of PPI use
- SSRI/SNRI therapy is associated with increased risk of both GI and variceal bleeding in patients with cirrhosis
- Limitations include a retrospective design and modest sample size
- Future directions include multivariate analysis to explore bleeding risk factors

References

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Disclosures

Authors of this presentation have nothing to disclose concerning possible financial conflicts of interest related to the content of this presentation

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