



COVID AND ANTIDEPRESSANTS

Ongoing Use of SSRIs and the Hospital Course of
COVID-19 Patients: A Retrospective Outcome
Analysis

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Background

SARS-CoV2 continues to have devastating consequences worldwide.

Though vaccinations have helped reduce spread, new strains still pose a threat.

Therefore, it is imperative to identify treatments that prevent severe COVID-19 infection.

Recently, acute use of SSRI antidepressants in COVID+ patients was shown to reduce symptom severity.

Literature Review

The potential value of selective serotonin reuptake inhibitors (SSRIs), typically prescribed for anxiety, depression and obsessive-compulsive disorder (OCD), has been discussed significantly in the scientific literature and lay press

Numerous in vitro studies have carefully delineated multiple inflammatory pathways in which SSRIs might be beneficial in reducing inflammation. The key role of inflammation in the progression, morbidity, and mortality of COVID has been well documented in the medical literature and anti-inflammatory effects of SSRIs may underlie their possible protective role in COVID-19

Literature Review

Early in the pandemic a large French multi-center retrospective study suggested the beneficial role of SSRIs in preventing intubation and death in hospitalized COVID-19 patients.

The SSRIs needed to be continued within the first 48 hours of hospital admission. Prior use of these drugs in individuals as outpatients before contracting COVID-19 is not clearly described. There was also a noteworthy exclusion of many patients because of incomplete medical records.

A key limitation of this ambitious and important review is the sudden inundation of the French health care system with large numbers of very sick COVID-19 patients. The retrospective nature of the study was intended to encourage more rigorous prospective investigations.

Literature Review

There have since been multiple publications on SSRIs and COVID-19, and these have garnered attention from the lay press. Stories have appeared in the Los Angeles Times and CBS News and the subject was featured on the national television news magazine program “60 Minutes”.

The importance of exploring the role of SSRIs in COVID was noted in Nature by a co-author of this paper, Steven Rauchman.

With the presence of effective vaccines, conducting a large prospective clinical trial of therapeutics in the US, Europe, and other nations with large vaccination programs loses feasibility. Simply stated, those fortunate populations cease being a control or treatment group available for potential therapeutic drugs, yet the need for effective therapeutics to prevent suffering and death among a significant part of the world population remains. Vaccines will not reach many less advantaged nations in time and, with new strains, breakthrough cases may emerge in vaccinated populations.

Purpose/Aim

Recently, acute use of SSRI antidepressants in COVID+ patients was shown to reduce symptom severity. The aim of this retrospective observational study was to determine whether COVID+ patients already on SSRIs upon hospital admission had reduced chance of admission to ICU or mortality compared to COVID+ patients not on chronic SSRI treatment.

Methods/Approach

Providence IRB approved research study; approval from CMOs; data sharing agreement obtained

- The target population included adult patients admitted with a diagnosis of Covid-19 on SSRI/SNRIs
- Retrospective chart review of adult patients admitted with Covid-19 from 6 Providence Southern California ministries
- Time frame: 03/2020 to 03/2021
- Data: SSRI/SNRI; age; gender; race; mortality

Methods/Approach

- Analysis: Using R 3.6.2 (R Core Team, 2021), a logistic regression model was run with mortality as the outcome and SSRI status as the exposure.
- An adjusted logistic regression model was run to account for age category, gender, and race.
- Logistic Regression in R Programming
 - Classification algorithm to find the probability of event success and event failure
 - Used when the dependent variable (outcome variable is binary-in this case yes or no)

VARIABLES

Age	18-30	31-40	41-50	51-60	61-70	71-80	≥81
Gender	M	F	Other				
Ethnicity	African/American	Hispanic	Caucasian	Asian	Other		
Admission Date to Hospital							
Discharge Date from Hospital							
Admission date to ICU							
Discharge/Transfer date from ICU							
Discharge disposition	Alive	Deceased					
LOS							
Admission diagnoses	1.	2.	3.	4.			
Medications on admission	1.	2.	3.	4.	5.	6.	7.
Ventilator Use	Yes/Number of days	No					
Chest X-Ray findings	Diagnosis	Date					
Supplemental O2	Yes/Number of Days	No					
O2 Saturation	Admission	Admission to ICU	Upon Transfer From ICU	Discharge			
Discontinuation of SNRIs or SSRIs upon admission or admission to ICU	Discontinued on admission Yes	Discontinued on admission No	Discontinued on admission to ICU Yes	Discontinued on admission to ICU No			
SNRIs on admission	venlafaxine	duloxetine	desvenlafaxine				
SSRIs on admission	citalopram	escitalopram	sertraline	fluoxetine	paroxetine		

Results

- The odds of dying do not differ significantly in hospitalized COVID+ patients based on whether or not they are taking SSRIs.
- There is no significant difference in the odds of dying between COVID+ patients on SSRIs vs COVID+ patients not taking SSRIs. The odds of COVID+ patients on SSRIs dying is 1.09 (95% CI: 0.91, 1.31) compared to COVID+ patients not on SSRIs ($p=0.35$).
- There is no significant difference in the odds of dying between COVID+ patients on SSRIs vs COVID+ patients not taking SSRIs, after controlling for age category, gender, and race. The odds of COVID+ patients on SSRIs dying is 0.98 (95%CI: 0.81, 1.18) compared to COVID+ patients not on SSRIs ($p=0.83$).

Table 2. Odds of death in COVID+ patients on continuation of SSRIs during hospitalization

Variables	Crude ORs (95% CI)	p-value	Adjusted ORs (95% CI)	p-value
SSRI on admission:				
No	1		1	
Yes	1.09 (0.91, 1.30)	0.353	0.98 (0.81, 1.18)	0.828
Sex:				
Female	1		1	
Male	1.34 (1.20, 1.49)	<0.001	1.54 (1.37, 1.72)	<0.001
Age category (years)^a:	1.04 (1.03, 1.04)	<0.001	1.04 (1.04, 1.05)	<0.001
Primary race:				
White or Caucasian	1		1	
American Indian or Alaska Native	1.09 (0.06, 7.42)	0.936	2.83 (0.14, 19.91)	0.359
Asian	1.27 (1.00, 1.59)	0.047	1.52 (1.19, 1.92)	<0.001
Black or African American	0.86 (0.67, 1.10)	0.236	1.18 (0.91, 1.52)	0.215
Hispanic or Latino	0.86 (0.76, 0.98)	0.018	1.44 (1.25, 1.66)	<0.001
Native Hawaiian or Other Pacific Islander	0.56 (0.23, 1.15)	0.148	0.92 (0.38, 1.95)	0.849
Other	1.12 (0.91, 1.38)	0.261	1.28 (1.03, 1.58)	0.023
Unknown	1.52 (1.04, 2.18)	0.026	2.13 (1.44, 3.12)	<0.001

CI = confidence interval, OR = odds ratio, SSRI = selective serotonin reuptake inhibitor

a = referent age category is <18 years

Conclusion

In this retrospective study of 9,043 patients hospitalized for COVID-19 in 6 California hospitals of a large hospital system in the Western US, prior use of SSRIs or SNRIs did not reduce mortality.

This study shows the utility of large clinical databases in addressing the urgent issue of determining what commonly prescribed drugs might be useful in treating COVID-19. The ongoing nature of the pandemic despite the vaccine rollout signals a pressing need to mitigate COVID-19 sequelae and the repurposing of readily available and inexpensive medications has the potential to save lives, particularly because rapid implementation could occur.

Implications For Practice

As a result of this study, the use of the SSRI /SNRI drug class does not hold a particular advantage, but a specific member of this class, such as fluvoxamine may be effective as found in other studies. Further, drug combinations that include SSRIs or SNRIs may exhibit synergy in mitigating COVID-19 severity and the data to make these determinations is likely available within health system electronic records.

Recent recommendation is to continue SSRIs/SNRIs upon ICU admission. Although this practice change has not been consistently implemented, it was found to be consistently implemented among all patients in this study.

Roles of an Interprofessional Team in a Clinical Research Study

Initial idea for the study: Dr. Steven Rauchman

Conceptualization: Dr. Steven Rauchman, Dr. Allison Reis;

Methodology: Dr. Sherri Mendelson; Dr. Lora Kasselmann

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Design of the Figures: Courtney Rauchman; Dr. Lora Kasselmann

IT TAKES A TEAM



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Questions?