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BRIEF REPORT

Prospective Cohort of Fluvoxamine for Early Treatment of Coronavirus Disease 19

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We report a real-world experience using fluvoxamine for coronavirus disease 19 (COVID-19) in a prospective cohort in the setting of a mass outbreak. Overall, 65 persons opted to receive fluvoxamine (50 mg twice daily) and 48 declined. Incidence of hospitalization was 0% (0 of 65) with fluvoxamine and 12.5% (6 of 48) with observation alone. At 14 days, residual symptoms persisted in 0% (0 of 65) with fluvoxamine and 60% (29 of 48) with observation.

Keywords. cohort; coronavirus; COVID-19; fluvoxamine; SARS-COV-2.

We read with interest Lenze et al's [1] double-blind randomized clinical trial testing fluvoxamine for early treatment of coronavirus disease 2019 (COVID-19). In this 152 person outpatient trial, fluvoxamine decreased clinical progression, defined as hypoxia (<92% oxygen saturation) coupled with either shortness of breath or hospitalization, from 8% (6 of 72) with observation alone to 0% (0 of 80) with fluvoxamine at up to 300 mg daily ($P = .009$) [1]. Although fluvoxamine is a selective serotonin reuptake inhibitor, fluvoxamine also activates sigma-1 receptors present intracellularly in the endoplasmic reticulum, thereby decreasing cytokine production [2]. We wish to share our recent real-world experience using fluvoxamine inspired by this recent trial.

METHODS

In November–December 2020, a mass outbreak of COVID-19 occurred in an occupational setting with congregate living at a horse racing track in California. We instituted 3 successive rounds of mass testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with simultaneous BinaxNOW COVID-19 Antigen Cards (Abbott) coupled with polymerase chain reaction (PCR) confirmation of collected nasal swabs by the California Department of Public Health Viral and Rickettsial Disease Laboratory in Richmond, California. All PCR testing results were concordant with the Abbott BinaxNOW rapid diagnostic tests.

After receiving their rapid diagnostic test results, persons with COVID-19 were required to isolate as per local health protocols. On the same day as positive rapid testing, patients were offered fluvoxamine as an optional therapy. All patients were counseled by author D.S. regarding the limited nature of the data supporting fluvoxamine. After evaluation for any specific contraindications or deleterious drug-drug interactions (none excluded), the choice was at the patient's discretion. Fluvoxamine was prescribed with a 50- to 100-mg loading dose, then 50 mg twice daily for 14 days. The facility provided the fluvoxamine at no cost. All patients were followed up in-person at 7 and 14 days. No patients were lost to follow up.

Patient Consent Statement

Patients consented for their medical treatment. As a quality improvement initiative, we assessed 14-day outcomes, analyzing the existing collected, deidentified data (Institutional Review Board exempt by the University of Minnesota).

RESULTS

Of 113 SARS-COV-2 antigen positive persons, approximately half were asymptomatic when initially tested. The median age was 42 years (interquartile range, 33 to 56), and 75% were men; 84% were Latino, and 14% were white. In total, 65 persons opted for fluvoxamine, and 48 opted for observation alone with no therapy. Demographics were generally similar among those choosing fluvoxamine versus observation, with the exception that more nonwhite persons opted for fluvoxamine (Table 1). Fewer patients opting for fluvoxamine were asymptomatic (38%) at time of initial diagnostic testing than those opting for observation (58%). Overall, 30% had 1 or more chronic medical comorbidities. Those opting for fluvoxamine had slightly more frequent diabetes (17% vs 8%) and slightly less treated hypertension (17% vs 35%) than those receiving observation.

The incidence of subsequent hospitalization was 0% (0 of 65) with fluvoxamine and 12.5% (6 of 48) with observation ($P = .005$). Two persons required intensive care unit stay with mechanical ventilation, 1 of whom died. Respiratory rates were slightly elevated at diagnosis and improved faster by day 7 with fluvoxamine ($P = .001$).

Received 21 December 2020; editorial decision 26 January 2021; accepted 27 January 2021.

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Open Forum Infectious Diseases®2021

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DOI: 10.1093/ofid/ofab050

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Table 1. Demographics and Outcomes in Prospective COVID-19 Cohort

Group	Fluvoxamine N = 65	No Therapy N = 48	*P* Value[a]
Men	50 (59%)	35 (41%)	.66
Age, years	44 ± 15	43 ± 15	.74
Age >65 years	5 (7%)	2 (4%)	
Age 50–64 years	17 (26%)	15 (31%)	
Race/Ethnicity			.001
Latino	61 (94%)	34 (71%)	
White, non-Hispanic	3 (5%)	13 (27%)	
African American	1 (1.5%)	0 (0%)	
Asian	0 (0%)	1 (2%)	
Chronic comorbidity	16 (25%)	18 (38%)	.15
Diabetes	11 (17%)	4 (8%)	
Hypertension, treated	11 (17%)	17 (35%)	
Lung disease	2 (3%)	1 (2%)	
Days for PCR confirmation	3.7 ± 1.3	3.4 ± 1.4	.25
Disease Status at Time of Testing			.064
Asymptomatic	25 (38%)	28 (58%)	
Mild	24 (37%)	9 (19%)	
Moderate[b]	16 (25%)	11 (23%)	
Respiratory Rate			
Day 1	17.7 ± 2.9	17.7 ± 3.4	.95
Day 7[c]	12.9 ± 1.6	15.1 ± 4.1	.001
Hospitalized within 14 days	0	6	.005
ICU care and/or Death	0	2	–
Symptoms at Day 14[d]			<.001
None	65 (100%)	19 (40%)	
1–3	0 (0%)	15 (31%)	
4–6	0 (0%)	11 (23%)	
≥7	0 (0%)	3 (6%)	

Abbreviations: COVID-19, coronavirus disease 19; ICU, intensive care unit; PCR, polymerase chain reaction.

NOTE: Values are N (%) or mean (±standard deviation).

[a]*P* values are by Fisher's exact test for categorical variables and independent *t* test for continuous variables.

[b]Those with moderate symptoms had reduction in activities of daily living.

[c]Six persons hospitalized had their day 1 value carried forward.

[d]Symptoms assessed at day 14 included the following: persistent anxiety (n = 19); difficulty concentrating, or memory challenges, or brain fog (n = 18); fatigue (n = 16); insomnia (n = 12); persistent body aches, muscle or joint pain (n = 10); headache (n = 9); dizziness (n = 9); inability to exercise (n = 6); chills or sweats (n = 5); persistent, intermittent nonproductive cough (n = 5); episodic chest tightness; pressure, or pain (n = 3); intermittent heart palpitations or tachycardia (n = 3); shortness of breath or difficulty breathing (n = 3); diarrhea (n = 0); elevated temperature (n = 0).

At day 14, ongoing symptoms were present in 0% (0 of 65) with fluvoxamine compared with 60% (29 of 48) with observation alone ($P < 0.001$); 10 (21%) of whom had ≥5 persisting symptoms. The most common persisting symptoms were as follows: persistent anxiety (n = 19), difficulty concentrating/memory challenges (n = 18), fatigue (n = 16), insomnia (n = 12), myalgia/arthralgia (n = 10), and headache (n = 9). No serious adverse events occurred with fluvoxamine. No adverse events led to early discontinuation.

DISCUSSION

This prospective, open-label cohort is a real-world evidence study supporting the initial observations made by Lenze et al [1] in their 152 participant phase II double-blind randomized trial of fluvoxamine for early COVID-19 therapy as well as providing evidence of patient tolerability using a lower dose of 50 mg twice daily [3]. Limitations include the quasi-randomized nature of the comparison; however, if anything, one would expect confounding by indication whereby those with worse symptoms would opt for fluvoxamine over observation alone. Since the initial quality improvement review, 12 additional patients at the facility have been treated with 50 mg of fluvoxamine twice daily with similar outcomes of no hospitalizations and no ongoing symptoms at 14 days, bringing the total to 77 patients treated.

CONCLUSIONS

Overall, fluvoxamine seems to be promising as early treatment for COVID-19 to prevent clinical deterioration requiring hospitalization and to prevent possible long haul symptoms persisting beyond 2 weeks. Further randomized trial evidence is needed. On December 17, 2020, a new nationwide, internet-based phase III randomized trial began to confirm these initial results for

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those with ≤6 days of COVID-19 symptoms (StopCovidTrial.com; Email:stopcovidtrial@wustl.edu ClinicalTrials.gov: NCT04668950). For patients uninterested in participating in clinical trials, healthcare providers might consider shared decision-making with patients to discuss fluvoxamine as an option, after reviewing possible drug-drug interactions (eg, benzodiazepines). However, participation in clinical trials contributes to the world's medical knowledge of how best to treat COVID-19.

Acknowledgments

Potential conflicts of interest. D. R. B. is an unpaid coinvestigator on the phase III trial investigating fluvoxamine for coronavirus disease 19. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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