For Early COVID-19 Treatment Antidepressant Fluoxetine found Ineffective

Researchers characterized the antiviral activity of a selective serotonin reuptake inhibitor (SSRI), fluoxetine, in early coronavirus disease 2019 (COVID-19).

Study

In the present study, researchers assessed the antiviral efficacy of fluoxetine in early COVID-19. If they had early symptomatic COVID-19, individuals aged 18–50 were enrolled in an ongoing, phase 2, randomized, controlled adaptive platform trial (PLATCOV).

Pregnant individuals, subjects taking antivirals or other medicines, and those with morbidity, chronic illness, hematological abnormalities, or contraindications to study drugs were excluded.

The fluoxetine arm was added to the platform in April 2022 in Thailand, June 2022 in Brazil, December 2022 in Laos, and February 2023 in Pakistan and was removed in May 2023. Patients were randomized to one of the 11 treatment arms.

Intervention arms were fluoxetine, molnupiravir, nitazoxanide, favipiravir, casirivimab/imdevimab, remdesivir, tixagevimab/cilgavimab, ensitrelvir, ivermectin, ritonavir-boosted nirmatrelvir, or no-study drug.

The ritonavir-boosted nirmatrelvir arm served as the positive-control group. Fluoxetine (40 mg) was given for seven days from baseline. Oropharyngeal swabs were collected on days 0–7, 10, and 14.

Patients recorded their vital signs thrice daily, as well as symptoms and adverse effects. Viral loads were quantified using a polymerase chain reaction (PCR) assay, which detects viral spike, nucleocapsid, and human RNase P genes.

The primary outcome was the viral clearance rate from viral genome densities in swabs collected on days 0 to 7. Secondary outcomes were all-cause hospitalization and the time-to-resolution of fever and symptoms.

The viral clearance rate was estimated under a hierarchical linear model and fitted to log10 viral densities between days 0 and 7.

Results

In total, 675 patients were randomized to intervention arms. Of these, 120 were randomized to the fluoxetine arm, 151 to the no-study drug arm, and the remaining patients were randomized to other interventions.

Most patients (90%) were recruited in Thailand. The median interval since the onset of symptoms was two days. The mean SARS-CoV-2 eluate density was 350,000 genomes/ml. SARS-CoV-2 Omicron BA.5, BA.2, and BA.2.75 were the most common infecting variants.

Fluoxetine recipients reported higher somnolence than the no-study drug group. Two patients did not complete the fluoxetine course. No serious adverse events, hospitalizations, or deaths occurred. Moreover, the time to symptom or fever resolution was not significantly different between the fluoxetine and no-study drug arms.

Fluoxetine recipients had a 15% faster viral clearance, on average, than the no-study drug arm. The median viral clearance half-life was 14 hours in the fluoxetine arm and 14.9 hours in the no-study drug group.

A post hoc sensitivity analysis estimating fluoxetine's treatment effect using data from the first five days post-randomization showed a substantially larger treatment effect (at 26%).

In addition, a meta-analysis of all drugs and antibodies was performed using individual patient data. This revealed that fluoxetine increased clearance by 16% relative to the no-study drug arm. It also had a greater clearance rate relative to favipiravir and ivermectin.

However, fluoxetine's treatment effect was lower than that of remdesivir, ritonavir-boosted nirmatrelvir, casirivimab/imdevimab, and molnupiravir.

Conclusion

In sum, the findings illustrate fluoxetine's weak antiviral activity in adults with early symptomatic COVID-19. There were no significant differences in the time to symptom or fever resolution between fluoxetine and no study drug arms.

The acceleration in viral clearance with fluoxetine was substantially lower than contemporaneous antivirals. As such, fluoxetine is unlikely to be used in COVID-19 treatment, given that other more effective antivirals are available.

Source:

https://www.news-medical.net/news/20250122/Antidepressant-fluoxetine-found-ineffective-for-early-COVID-19-treatment.aspx