

INPLASY PROTOCOL

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None declared.

INTRODUCTION

Review question / Objective: Recently, several randomized controlled trials (RCTs) of fluvoxamine have been successfully conducted for the treatment of patients with coronavirus disease 2019 (COVID-19). This systematic review and meta-analysis was to evaluate the efficacy and safety of fluvoxamine in patients with COVID-19.

The efficacy and safety of fluvoxamine in patients with COVID-19: a systematic review and meta-analysis

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Review question / Objective: Recently, several randomized controlled trials (RCTs) of fluvoxamine have been successfully conducted for the treatment of patients with coronavirus disease 2019 (COVID-19). This systematic review and meta-analysis was to evaluate the efficacy and safety of fluvoxamine in patients with COVID-19.

Condition being studied: MEDLINE, EMBASE, Cochrane Library and the ClinicalTrials.gov.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 March 2023 and was last updated on 21 March 2023 (registration number INPLASY202330078).

Condition being studied: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection that led to the coronavirus disease 2019 (COVID-19) has had a significant negative impact on the world economy and posed several health risks. The COVID-19 outbreak has been going on for more than three years, and as of March 2023, there has been more than 758 million confirmed instances of the virus, including more than 6.9 million fatalities, according to the World Health Organization's (WHO)

incomplete records. Along with irritating the respiratory system, the SARS-CoV-2 virus also has negative effects on the heart, gastrointestinal tract, liver, kidney, and central nervous system, which can finally result in multiorgan failure. Thus, finding COVID-19 treatments that work is urgently needed and of the utmost importance for clinical researchers in light of this global epidemic.

Currently, COVID-19 is managed supportively because there is no specific medication with a definite effect, and respiratory failure from acute respiratory distress syndrome (ARDS) is the main cause of death. A subgroup of individuals with severe COVID-19 may have cytokine storm syndrome, according to mounting data. Hence, controlling cellular immunity and the inflammatory response is crucial in the management of COVID-19. Sigma-1 receptor (S1R) agonism is one possible method of immunological control. One of the many biological tasks of the S1R, an endoplasmic reticulum chaperone protein, is the control of cytokine production. Additionally, as the development of novel therapies often requires years of concerted work, the majority of research into the therapy of COVID-19 has therefore been centered on drug repositioning, or examining the efficacy of medications licensed for use in treating other diseases on COVID-19 patients.

METHODS

Participant or population: Patients ≥ 18 years of age confirmed with SARS-CoV-2 infection.

Intervention: Fluvoxamine.

Comparator: Placebo.

Study designs to be included: RCT.

Eligibility criteria: We set the inclusion criteria as follows: (1) study type: RCT; (2) language restriction: only available in English; (3) participants: patients ≥ 18 years of age confirmed with SARS-CoV-2 infection; (4) intervention: fluvoxamine and corresponding placebo; (5) outcomes:

efficacy outcomes including the number of patients with clinical deterioration, the number of patients with hospitalization, the number of patients with mechanical ventilation and the time to clinical deterioration. Clinical deterioration was a composite outcome including hypoxemia, urgent care visit, emergency department visit, hospitalization or death. As long as the patient's condition has further deteriorated, it can be classified as clinical deterioration regardless of whether they receive medical assistance. Our safety outcomes including adverse events (AEs) and serious adverse events (SAEs). We also defined mortality as an exploratory outcome. Included RCTs were not requested to supply all the outcomes mentioned above. We set the exclusion criteria as follows: (1) study type: retrospective studies, cohort studies, case reviews and case reports; (2) control: active control (i.e. that a known, effective treatment as opposed to a placebo is compared to an experimental treatment).

Information sources: MEDLINE, EMBASE, Cochrane Library and the ClinicalTrials.gov

Main outcome(s): Efficacy outcomes including the number of patients with clinical deterioration, the number of patients with hospitalization, the number of patients with mechanical ventilation and the time to clinical deterioration. Our safety outcomes including adverse events (AEs) and serious adverse events (SAEs).

Quality assessment / Risk of bias analysis: The risk of bias plot was evaluated with the Review Manager 5.3 software. The uniform criteria of the Cochrane Collaboration was used to assess the risk of bias for RCTs, which included selection bias, performance bias, detection bias, attrition bias, reporting bias, and other potential biases. Each bias criterion was classified as "low", "high", or "unclear".

Strategy of data synthesis: Review Manager 5.3 software was used to perform pair-wise meta-analysis of direct evidence. The relative risk (RR) with 95% confidence interval (95% CI) was analyzed and

calculated for the dichotomous outcomes. The mean difference (MD) was used only for the continuous outcome “the time to clinical deterioration”. We estimated heterogeneity through the I² statistic, which was as follows: I² < 30% suggests “low heterogeneity”; I² between 30% and 50% means “moderate heterogeneity”; I² > 50% denotes “substantial heterogeneity”. The data were analyzed with a fixed effects model for those with less than 50% heterogeneity, and for those with greater than 50% heterogeneity, we used the random effects model. For all the analyses, two tailed tests were performed and a P value < 0.05 was considered to be statistical significant.

Subgroup analysis: Not applicable.

Sensitivity analysis: Sensitivity analysis was also used to explore the stability of the consolidated results.

Country(ies) involved: China.

Keywords: clinical deterioration, fluvoxamine, COVID-19, meta-analysis, systematic review.

Contributions of each author:

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