

# Risks Associated with the Use of Psychotropics in Patients Diagnosed with COVID-19<sup>†</sup>

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**Abstract:** In the context of the pandemic, negative implications for mental health have increased considerably, as well as the existing associations of psychotropics in this period to combat the new coronavirus. In view of this, the present integrative review aimed to verify the health impact of COVID-19 infection in patients with mental disorders who use psychotropics. As a result, the co-administration of these drugs represented a great risk at the systemic level, and can be lethal in certain cases. Thus, it is possible to conclude that patients with mental disorders taking psychotropic drugs are exposed to a greater risk of pharmacological interactions during COVID-19 treatment. That said, careful evaluations must be taken in order to implement an effective intervention that meets the needs of patients, always considering the risks of these drug associations.

**Keywords:** COVID-19; mental disorders; psychiatry; public health



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## 1. Introduction

The COVID-19 pandemic has disrupted essential mental health services in 93% of countries worldwide, while the demand for mental health is increasing, according to the WHO. Also referring to this situation, there was a 45% reduction in maintenance treatments with opioid agonists for cases of dependence, and more than a third (35%) reported interruptions in emergency interventions, including those for people who had prolonged seizures, severe substance use withdrawal syndromes and delirium, usually a sign of a serious pre-existing medical condition. Furthermore, 30% reported interruptions in access to drugs for mental, neurological and substance-use disorders [1].

In addition, in 80% of patients, psychotic symptoms appeared more than two weeks after the first somatic manifestation attributed to COVID-19 and disappeared in less than two weeks. Delusions of prejudice, persecutory and referential beliefs were the most frequent outcomes. Convulsive symptoms were not present in the patient whose onset of psychosis was not preceded by the treatment of the disease. Furthermore, the individual whose psychosis was not preceded by virus manifestation could be an example of a primary psychotic episode triggered by stress [2], with a worse prognosis because of the premorbid schizoid personality [3].

In this context, patients with COVID-19 with known psychiatric disorders should be monitored closely for neurological manifestations, including headache, dizziness and symptoms, changes in mental status, meningeal signs and dyskinesias. Patients with severe infection may be at a higher risk of developing neurological sequelae and increased mortality [4]. Aiming to contribute and join efforts to improve mental health and psychiatric events, the present investigation was proposed with the aim of evaluating the evidence available in the literature and understanding the main interactions between medications

often used in the treatment of COVID-19 and psychotropic drugs, as well as their systemic effects on patients' bodies.

## 2. Methodology

This work consists of a descriptive and exploratory retrospective study, with a qualitative–quantitative approach, using the methodological device of integrative review that employs bibliographic research as an indirect documentation process in order to verify the impact of COVID-19 infection in the health of patients with mental disorders who are undergoing chronic and non-chronic use of psychotropic drugs. We chose to carry out an integrative review, defined as an instrument for obtaining, identifying, analyzing and synthesizing the literature directed to a specific theme. It also allows for the construction of a broad analysis of the literature, including discussions about the results of publications covering the subject studied.

For the elaboration of this study, the following steps were taken: the establishment of the hypothesis and objectives of the integrative review, establishment of inclusion and exclusion criteria for articles (sample selection), definition of the information to be extracted from the selected articles, and analysis of the results and discussion of the results found in the research.

The following inclusion criteria were adopted: articles available in full, publication in Portuguese, English, or Spanish, with abstracts available in the selected database, in national and international journals and indexing in the database referred from December 2019 to July 2020 (first case of COVID-19 confirmed in Wuhan, China); published articles whose adopted methodology allowed to obtain strong evidence in the following types: research articles, case reports, correspondence, discussion, editorials, mini-criticisms, practical guidelines and short communications; patients who make chronic use of psychotropic drugs; hospitalized or non-hospitalized patients and patients with COVID-19. Care was taken to exclude duplicate articles and those that carried out research with animals.

For the analysis of the results found in the literature, the researchers carried out search on the platform Science Direct individually and compared the results found through the descriptors: COVID-19, sertraline, carbamazepine, quetiapine, pharmacological treatment, psychiatry and psychotic; using the Boolean operators “AND” and “OR”, in the following order: COVID-19 AND (sertraline OR carbamazepine OR quetiapine) and Pharmacological treatment AND COVID-19 AND (Psychiatry OR Psychotic).

The small number of psychotropic drugs used in the search was based on a previous search carried out on the topic, resulting in the most cited drugs: sertraline, carbamazepine, and quetiapine. To avoid restricting the results and encompassing other psychotropic drugs, the general term “Pharmacological treatment” was used, which resulted in the other drugs mentioned in the research.

The presentation of the results and the discussion of the data obtained took place in a descriptive–descriptive manner, taking into account the following point: co-administration of psychotropics and first-line drugs in the fight against COVID-19, enabling the reader to evaluate the applicability of the integrative review elaborated, in order to achieve the objective of this method, that is, positively impact the quality of decision making for the practice of the relationship of patients with COVID-19 and its relationship with psychotropic drugs.

## 3. Results and Discussion

In the current pandemic scenario, the study of interactions between psychotropic drugs and those recommended for the treatment of COVID-19 is extremely important to prevent harmful prognosis for psychiatric patients. In the context of this association, the prolongation of the QTc heart rate interval (measured from the beginning of the QRS complex to the end of the T wave) was demonstrated as a significant result. This interval represents the total duration of ventricular electrical activity [5] and the inhibition of cytochrome CYP3A, which increases liver toxicity in patients [6,7]. In addition, the damage

caused by COVID-19 to the cardiovascular system is multifactorial and can result both from an imbalance between high metabolic demand and low cardiac reserve, as well as systemic inflammation and thrombogenesis, which can also occur through direct cardiac injury by the virus [8]. Notably, doctors, in order to properly treat patients with COVID-19 who use psychiatric medication, need a thorough understanding of these possible consequences.

#### *Psychotropic Drugs*

There is evidence that the gradual discontinuation of benzodiazepines is feasible, safe and can be completed in primary care, as well as in mental health treatment settings [9]. However, instructing these patients to discontinue certain medications, such as benzodiazepines and antipsychotics, can cause them to experience withdrawal symptoms. In addition, patients who have these severe symptoms are often admitted to hospitals, but this circumstance provides a greater risk of acquiring COVID-19 and negatively impacting their health [10]. It should be noted that the virus generally causes lymphopenia, so the leukopenic effect caused by carbamazepine (a medication often used to treat affective and bipolar disorders) [11] can further increase this adverse condition that would already be present in diagnosed individuals with COVID-19.

Still referring to the verification of the leukocyte count, it appears that in patients treated with clozapine, infection by COVID-19 can cause leukopenia [12]. In this sense, reducing the dosage of clozapine or replacing it would be a recommended alternative. In addition, for patients who make chronic use of carbamazepine, it is necessary to monitor the serum levels of leukocytes. This recommendation should also be extended individually to the sodium channel blockers used in the therapy of trigeminal neuralgia: eslicarbazepine acetate, oxcarbazepine (level of evidence IV, level of recommendation C), and lamotrigine (level of evidence II, level B recommendation) since these drugs have therapeutic class and interactions with the organism similar to those of carbamazepine [13]. carbamazepine also reduces the levels of atazanavir, remdesivir, chloroquine, and hydroxychloroquine [14]. Therefore, if adequate precautions and care are not taken, the combinations of these drugs mentioned above can be lethal for psychiatric patients who depend on this psychotropic to control their underlying diseases.

Within the scope of selective serotonin reuptake inhibitors (SSRIs), a drug class used as antidepressants and anxiolytics by modulating serotonin in the brain, they act as inhibitors that increase serotonin by controlling its reuptake in the presynaptic cell and then increasing the level of serotonin within the synaptic cleft so that coupling to the postsynaptic receptor occurs [15]. Sertraline, a member of the (SSRIs), is suggested as a favorable drug for patients with COVID-19 because it has a broad therapeutic index and minimal anticholinergic activity, making it a safe option for elderly patients or patients with underlying cardiovascular disorders [16].

Antipsychotics can help control the symptoms of delirium, specifically in this patient population; this drug class should be carefully monitored as its use together with the drugs used for COVID-19 (e.g., hydroxychloroquine, azithromycin) can prolong the QTc interval, causing a risk of arrhythmias. This increases the risk of worsening of the condition in these patients, since the Brazilian Society of Cardiac Arrhythmias states that patients with cardiac arrhythmias have a higher risk of serious infection with the new coronavirus [17], as well as other cardiac manifestations [18]. Therefore, if the usual doses of psychotropic drugs taken by the patient are at low levels compared to the recommended medians, it is worth noting that, during the co-administration of these drugs, clinical monitoring of adverse effects (that is, extrapyramidal effects with antipsychotics, sedation with benzodiazepines, adrenergic or serotonergic reactions with antidepressants) and the monitoring of drug levels (if possible and/or necessary) in addition to the ECG test should be carried out to guarantee the patient's homeostasis [19].

Among the safest antipsychotic drugs, mainly because they do not prolong the QTc interval (if the QTc is greater than 440 mSec in men or 470 mSec in women, there is a risk of developing cardiac arrhythmia), olanzapine and aripiprazole can be considered, if

necessary, in cases of COVID-19 infection, with no need to discontinue them in psychiatric patients [20]. In general, there is an association between the administration of antipsychotics and an increased risk of pneumonia (not demonstrated in the specific case of COVID-19 infection), but the balance between the risk–benefit of using or not using the antipsychotic is generally favorable for psychopharmacological treatment [21].

It is important to note that the results presented by the research have some limitations: it is not a systematic review, and it addresses a reduced number of psychotropic drugs, which leaves room for other important clinical correlations in the group of patients studied.

#### 4. Conclusions

It is possible to conclude that patients with mental disorders taking psychotropic drugs are exposed to a greater risk of pharmacological interactions during COVID-19 treatment. Therefore, it is concluded that the decision making of physicians who carry out psychiatric follow-up on the use of pharmacological treatment mechanisms should be based on a careful and individualized assessment of each patient, always considering the risks of the associations between the drugs frequently used for the treatment of COVID-19 and those administered to control mental disorders.

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