Slovenian Medical Journal

Psychotropic medication challenges in patients with COVID-19

Izzivi pri predpisovanju psihofarmakoterapije bolnikom s covidom-19

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Abstract

The SARS-CoV-2 pandemic has brought a "new reality" into the management of patients with mental disorders. Due to the lack of COVID-19-specific psychopharmacology guidelines as well as the lack of clinical experience, prescribing psychotropic medications to COVID-19 patients may be associated with some challenges. Interactions between psychotropic drugs and drugs for the treatment of COVID-19 and the adverse effects of psychotropic drugs on the symptoms of infection occasionally require adjustment of psychopharmacotherapy in COVID-19 psychiatric patients. On the other hand, the potential drug-drug interactions and the effect of psychotropic drugs on the progression of the infection should be considered when treating psychopathological symptoms that may be caused by SARS-CoV-2 infection or drugs used to treat the infection. In the paper, several considerations in prescribing psychopharmacotherapy to patients with COVID-19 are discussed and, based on the literature published in recent months, recommendations for the choice of therapy for acute psychiatric conditions in these patients are summarized.

Izvleček

Pandemija koronavirusa SARS-CoV-2 je »novo realnost« prinesla tudi v vsakodnevno obravnavo bolnikov z duševno motnjo. Ob pomanjkanju specifičnih smernic in kliničnih izkušenj je predpisovanje psihofarmakoterapije bolnikom s covidom-19 povezano z različnimi izzivi. Zaradi možnih interakcij med psihofarmaki in zdravili, ki se uporabljajo za zdravljenje bolnikov s covidom-19, ter zaradi neugodnega vpliva psihiatričnih zdravil na simptome okužbe je občasno treba prilagoditi terapijo pri psihiatričnih bolnikih, obolelih s covidom-19. Po drugi strani pa je morebitne interakcije in vpliv psihofarmakov na potek okužbe potrebno upoštevati tudi ob zdravljenju psihopatoloških simptomov, ki jih lahko povzroči sama okužba s koronavirusom SARS-CoV-2, ali pa so posledica zdravil, ki se uporabljajo za zdravljenje okužbe. V prispevku so predstavljene dileme, s katerimi se srečujemo pri predpisovanju psihofarmakov bolnikom s covidom-19 in na podlagi literature, objavljene v zadnjih mesecih, povzete usmeritve glede izbire zdravil za akutna psihiatrična stanja pri teh bolnikih.

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Key words: coronavirus SARS-CoV-2; mental disorders; psychopathological symptoms; psychotropic drugs; drug-drug interactions

Ključne besede: koronavirus SARS-CoV-2; duševne motnje; psihopatološki simptomi; psihiatrična zdravila; interakcije med zdravili

Received / Prispelo: 29. 10. 2020 | **Accepted / Sprejeto:** 20. 3. 2021

Cite as / Citirajte kot: Čelofiga A, Smogavc Ž. Psychotropic medication challenges in patients with Covid-19. Zdrav Vestn. 2021;90(9–10):550–8. **DOI:** https://doi.org/10.6016/ZdravVestn.3186

1 Introduction

The SARS-CoV-2 coronavirus pandemic introduced new challenges in the management of psychiatric patients. Both the clinical and the hospital environment required numerous organizational adjustments in order to ensure relative safety for employees and patients. Psychiatrists who work in a hospital environment and are included in liaison psychiatry at least occasionally work with COVID-19 patients who also have mental disorder symptoms. There are mainly two situations in clinical practice: patients with a known mental disorder fall ill with COVID-19 or patients with COVID-19 who had no known psychiatric medical history develop psycho-pathological symptoms (1). In the first case such patients are generally managed with psychopharmacotherapy, while for the second case there is a need to prescribe drugs. It is important to know the potential impact of psychotropic drugs on the course and symptoms of the infection, while on the other hand changes in organ systems that can be the result of infection can lead to changes in serum concentrations of psychotropic drugs and affect their effectiveness and safety (1-5). If patients are receiving so-called experimental drugs for treating COVID-19, there may be interactions between these drugs and the psychotropic drugs, which occasionally requires adjustments to dosages or drug discontinuation (1,2,4). Due to the lack of specific guidelines as well as the lack of clinical experience, prescribing psychotropic medications to COVID-19 patients may frequently present a major challenge.

2 COVID-19 and psychopathological symptoms

2.1 Patients with mental disorder and COVID-19

High prevalence of smoking and homelessness, cognitive disorders, neglecting risk of infection, abuse of psychoactive substances and general poor health during the epidemic contribute to an increased risk for infection of psychiatric patients with the SARS-CoV-2 virus (2,6). An additional risk factor are the limitations in regular clinical treatment and pharmacological therapy, along with poorer access to health care due to the limitations related to epidemiological interventions. This results in more frequent relapses and exacerbations of existing mental disorders (2,7). When a patient with a mental disorder becomes infected with COVID-19, they occasionally require therapy with antiviral drugs alongside psychotropic drugs. Potential discontinuation of psychotropic drugs could result in an exacerbation of the mental illness, and bring on related abnormal behaviour (e.g. restlessness, uncooperative, impulsive behaviour), which can significantly hinder the management of such a patient (1). This naturally raises the question of which psychiatric drugs are safe to use after infection with the SARS-CoV-2 virus and when should we begin monitoring the patient for potential complications.

2.2 Psychopathological symptoms in COVID-19 patients who had not previously been treated by a psychiatrist

The psychopathological symptoms that occur with COVID-19 patients can be reactively conditioned by external factors. In such cases there are mainly the symptoms of anxiety and stress disorders and insomnia, which are the consequence of facing a new and unknown disease with unpredictable progression (8). These psychopathological symptoms, apart from being reactively conditioned, may also occur because of the infection with this virus (3,9). Acute psychopathological symptoms that emerge with a SARS-CoV-2 infection are similar to infections with other viruses that affect the central nervous system (CNS), especially with symptoms that have been documented during the epidemic of the SARS-CoV-1 virus. Considering the relatively short time since the emergence of SARS-CoV-2 virus, the mechanism of the onset of acute psychiatric complications is not yet fully clear, nor are any potential subacute and especially late neuropsychiatric consequences of the infection (9). Due to major similarities between the SARS-CoV-1 and 2 viruses, and the fact that their genomes are nearly 80% identical, any forecasts of such complications and consequences are mostly based on experience with the SARS-CoV-1 virus (10-13). Studies show that four years after an infection with the SARS-CoV-1 virus nearly half of survivors reported having at least one mental disorder, most frequently depression, panic disorder, obsessive-compulsive and post-traumatic stress disorder (14). It is not clear whether this is the result of the viral infection or the immune system response of those who became ill. Studies also show that after a severe form of sepsis more than a half of survivors

list cognitive disorders. There is also higher prevalence of depressive and post-traumatic stress disorder, anxiety and tendency to self-harm (15-17).

The infection with the SARS-CoV-2 virus can cause the onset of psychopathological symptoms through direct action on the CNS (9,18). Neuropsychiatric symptoms were observed in more than a third of those who fell ill and half of those with a severe illness, including acute cerebrovascular events, encephalopathy, and muscle injury (18). Approximately a fifth of those who succumb to the illness have experienced encephalopathy with disorders of consciousness, which has been linked to the so-called cytokine storm (10). The term cytokine storm refers to an excessive activation of the immune system due to an infection or other triggers that cause a high increase of cytokines in the blood (19). Three cytokines (IP-10, MCP-3 and IL-1ra) were especially significant predictors for the progression of the SARS-CoV-2 infection, with their serially high values linked to a severe progression of the disease and higher mortality (20). Proinflammatory cytokines activate endothelial cells, increasing their permeability which results in an expression of proteins that permit the transfer of activated immune cells through the damaged blood-brain barrier in the CNS and in neurotransmission disorders (21,22). Coronaviruses can infect macrophages, microglial cells and astrocytes in the CNS, and by activation trigger or sustain the inflammatory condition. Hypoxia has an additional negative effect on the brain function (23). Acute encephalopathy, i.e. delirium, is a frequent complication, especially with older patients in intensive care units, as they may suffer from the prolonged type, and with possible late neurocognitive impairment that can occur even up to 18 months after discharge (24). Mild cognitive impairment is another consequence described in the later stages after surviving sepsis (25).

Experimental drugs used to treat COVID-19 may also have an effect on the onset of psychopathological symptoms (1,2). In the first wave of the epidemic numerous drugs were used, such as chloroquine, hydroxychloroquine, azithromycin, a combination of lopinavir/ritonavir, remdesivir, favipiravir, atazanavir, interferon beta, ribavirin, tocilizumab and dexamethasone (2,5). Different neuropsychiatric symptoms may occur when using chloroquine and hydroxychloroquine, ranging from agitation to psychosis (2,3). These are present with only 1–2% of the patients who were treated with chloroquine, and even rarer in patients who were receiving hydroxychloroquine (26). When treating COVID-19 patients, high doses of corticosteroids are often used, especially dexamethasone (27). Undesired psychiatric side effects of corticosteroid therapy are well known. They include particularly mood swings, manic behaviour, depression and psychotic symptoms. These mostly occur in the first weeks of corticosteroid therapy, and are dose dependent (28). High doses of corticosteroids have already been used for treating acute infection with SARS-CoV-1, and were related to the onset of manic symptoms and hallucinations (29,30). Undesired psychiatric side effects are also described when using interferon, with the most common ones being mood and anxiety disorders, delirium, irritability, emotional instability, apathy, suicidal behaviour, sleep disorders and cognitive disorders, and rarely also manic behaviour or psychosis (5,31). Neuropsychiatric symptoms can also occur when using lopinavir/ritonavir, with researchers noting the onset of agitation, anxiety, confusion and emotional instability, and anxiety, aggressive outbursts, delirium, depression and catatonic reactions when using azithromycin (5).

3 COVID-19 and psychotropic medication

3.1 The effect of COVID-19 on the safety and effectiveness of psychotropic medication

COVID-19 can affect many organ systems. Besides the lungs, it can affect the cardiovascular system, the digestive system, kidneys, liver, immune system and the haematopoietic system (32). This can lead to changes in pharmacokinetics, and to an increased risk of undesired side effects of psychotropic medication. The SARS-CoV-2 virus can have an arrhythmogenic effect resulting in QT interval prolongation, which has to be taken into account when prescribing the psychotropic medication that can also affect the QT interval (2,5,33). A COVID-19 infection is often accompanied by leukopenia and lymphopenia; therefore, it is reasonable to pay more attention to those patients receiving psychotropic medication with known hematologic side effects, such as clozapine and carbamazepine (4,5,13). Because of the potential impact on the liver and kidneys it is reasonable to avoid psychotropic medication that is hepatotoxic or those medicines that are fully metabolized by the liver (valproate, carbamazepine, some antipsychotics and antidepressants), as well as those with excretion mainly through the urinary tract or those with nephrotoxic effects, such as lithium (5). An increased risk for thromboembolic complications in COVID-19 and potentially prescribed anticoagulative prophylactic therapy have to be taken into account when prescribing psychotropic medications that increase the risk for haemorrhaging (for example, selective serotonin reuptake inhibitor

(SSRI) type antidepressants) (5,34). It is also reasonable to exercise caution with patients receiving drugs with a narrow therapeutic window, for example lithium (2,5,35). Because of the high prevalence of delirium with COVID-19, it is recommended to pay special attention to prescribing benzodiazepines, opioids and drugs with a strong anticholinergic effect (5).

3.2 The effect of psychotropic medication on the progression of COVID-19 and the symptoms of the infection

Some psychotropic medications have undesired side effects (for example, sedation) and affect certain organ systems, both of which can exacerbate the infection (1,2). Neutropenia occurs in approximately one fifth of COVID-19 patients (13). This can become an issue if the patient is regularly receiving clozapine, as it can be related to the onset of neutropenia and agranulocytosis, especially during the first 18 weeks of therapy (36). COVID-19 patients who are receiving clozapine most likely have an increased risk for neutropenia compared to those who do not have COVID-19 and also compared to those with COVID-19 who are not receiving clozapine. With a COVID-19-related inflammation the plasma concentration of clozapine can increase. Consequently, some recommend reducing clozapine dosage and monitoring the blood levels more frequently, even if patients are not running a fever (2). Lymphopenia is especially linked to a severe progression of the disease, and therefore it is reasonable to avoid other psychotropic medications that can affect the number of leukocytes and especially lymphocytes (10,13,18). Caution is also advised when using benzodiazepines and other drugs with a sedative effect that in high doses can pose a danger for patients with respiratory distress. In cases where use of these drugs is necessary, the lowest possible dosage is recommended (2).

4 Interactions between psychotropic medications and medications used for treating COVID-19

There can be serious interactions between psychiatric therapy and COVID-19 experimental drugs (1-5). Clinically significant consequences of interactions between COVID-19 drugs and psychotropic medication can be roughly divided into two groups:

a) effects on changes in plasma concentration of drugs,

b) effects on changes in ECG – QT and PR interval prolongation (2).

Numerous antipsychotics and antiviral drugs are metabolized by the cytochrome P450 hepatic microsomal enzyme system (1). Most interactions happen at the level of isoenzyme CYP3A4, and to a smaller degree also at the level of CYP2D6 and 1A2 (1-3,5). The most important interactions are those between psychotropic medication and the lopinavir/ritonavir combination. Serum concentrations of psychotropic medications that are metabolized by CYP3A4 (Table 1) may increase with concurrent use of lopinavir/ritonavir and atazanavir because of the inhibition of CYP3A4 (2,5). Most interactions are clinically insignificant. With quetiapine, methadone, lamotrigine or bupropion therapy the combination can result in a 50% increase in plasma concentrations. If the psychotropic medication is prescribed in a low or a medium dosage, the dosage of most

Table 1: Psychotropic medications that are predominantly metabolized by CYP3A4. Summarized from Taylor, 2017 (38), English, 2012 (39) and Ayano, 2016 (40).

Substrates	Inhibitors	Inductors
Benzodiazepines – diazepam, alprazolam, midazolam, clonazepam, nitrazepam Tricyclic AD – amitriptyline, imipramine, clomipramine SSRI antidepressants – citalopram, escitalopram, paroxetine, fluoxetine, fluvoxamine* SNRI antidepressants – venlafaxine, mirtazapine Other AD – trazodone, nefazodone*, reboxetine Antipsychotics – risperidone, quetiapine, aripiprazole, ziprasidone, haloperidol, cariprazine, perphenazine*, lurasidone Hypnotics – zolpidem, zopiclone*, zaleplon* Other psychotropic medications – carbamazepine, methadone, buprenorphine, bupropion*	paroxetine fluoxetine reboxetine fluvoxamine* perphenazine	carbamazepine modafinil asenapine topiramate hypericum perforatum

Legend: AD – antidepressants, SSRI – selective serotonin reuptake inhibitor, SNRI – serotonin–norepinephrine reuptake inhibitors; *Drug is not registered in Slovenia.

psychotropic medications does not need to be changed during COVID-19 therapy with the lopinavir/ritonavir combination. It is recommended to take an ECG, and to monitor for potential undesired side effects and plasma concentrations of drugs, when possible (4). When patients are receiving high doses of psychotropic medications or doses higher than the recommended maximum, it is reasonable to adjust the dosage and monitor the condition (2,4). It is recommended to look for interactions between COVID-19 drugs and psychotropic medications with one of the online tools. Some (e.g. the website of Liverpool University) have set up special interaction checker for COVID-19 medications and other drugs (37).

Because some COVID-19 medications (chloroquine, hydroxychloroquine, lopinavir/ritonavir) prolong the QT and PR interval, special care must be taken when using psychotropic medication that also prolongs the QT interval (Table 2), and especially monitoring ECG of these patients (2). Usually, we monitor the values of QTc (corrected QT interval for heart rate), which is generally below 440 ms for men and below 470 ms for women (41). QTc values above 500 ms are related to an increased risk for abnormal heart rhythm, such as for example torsades de pointes (42).

5 Prescribing psychotropic medication for COVID-19 patients in practice

Psychiatric and non-psychiatric factors affect the selection of psychotropic medication for COVID-19 patients. Among the former, the most important are the type of their mental disorder or the set of psychopathological symptoms, their intensity and any potentially already introduced psychiatric drugs. Factors that are not directly related to psychopathological symptoms but are important for selecting the therapy are in particular the general somatic condition, the severity of infection, i.e. its effect on ventilation, any COVID-19 drugs prescribed and concomitant physical diseases (4).

Most pharmacological interactions between individual psychotropic medications and COVID-19 drugs are

Table 2: Impact of psychotropic medications on the QTc interval. Summarized from Taylor, 2003 (43), Taylor, 2017 (41), Ozeki, 2010 (44), and Cordes, 2012 (33).

Effect on QTc	Antipsychotics	Antidepressants	Other psychotropic medications
No effect	aripiprazole	sertraline paroxetine reboxetine	lamotrigine valproate carbamazepine gabapentin benzodiazepine
Mild (5–9 ms)	olanzapine fluphenazine flupentixol	citalopram, escitalopram* mirtazapine* trazodone venlafaxine duloxetine* bupropion moclobemide* fluoxetine*	
Mild (9–16 ms)	risperidone* clozapine* ziprasidone sulpiride* amisulpride*	clomipramine	
High (≥ 17 ms)	chlorpromazine levomepromazine quetiapine* haloperidol*	maprotiline amitriptyline nortriptyline doxepin	methadone lithium*
Unknown	zuclopenthixol loxapine		

Legend: *Inconsistent data in some sources, the highest defined risk selected – impact on QTc.

not absolute and should be assessed individually for each patient. It is also reasonable to continue regular chronic therapy for known psychiatric patients if they become infected with COVID-19 (2,4). When patients who are receiving high doses of psychotropic medications also receive experimental COVID-19 drugs, it is recommended to lower the dosage of most psychiatric drugs by 25–50%, especially when using chloroquine, hydroxychloroquine and lopinavir/ritonavir (4). The exception is quetiapine, for which the recommendations in the summary of main product characteristics differ for the US and Europe. According to the US instructions, it is recommended to reduce the quetiapine dosage by 85% when using it concomitantly with lopinavir/ritonavir (4,45), while according to European instructions, this combination is not recommended (46). Concomitant use of lopinavir/ritonavir with lurasidone, pimosidone and midazolam in oral solution is also not recommended (45,46).

When concomitantly using lopinavir/ritonavir and asenapine, olanzapine or sertraline, it is recommended to increase the doses of these psychotropic medications, as well as when concomitantly using lamotrigine, bupropion or methadone – it is suggested that the latter are increased by 50% (4). When introducing psychotropic medication with potential cardiotoxic effects, it is recommended to gradually titrate dosages and monitor ECG (2,4).

In the event of delirium with agitation olanzapine is a relatively safe choice because of its sedative effects, high effectiveness and low risk of interactions with COVID-19 experimental drugs (4). Special attention should be paid to patients with a severe breathing disorder, where additional sedation is not desirable. In such cases the most suitable choice are antipsychotics with low sedative effects, such as aripiprazole, risperidone and haloperidol (47). These are recommended in dosages lower than usual and with gradual titration. Both olanzapine and aripiprazole are also available for intramuscular injection. For haloperidol therapy, regular ECG monitoring is recommended (4,35). Extra attention should also be paid to patients in delirium when using benzodiazepines, as they can affect respiratory disorders (48). For treating agitation, loxapine can be used in inhalation form, but only when the respiratory function is not affected. Concomitant use of lopinavir/ritonavir with cariprazine can result in increased serum concentration of cariprazine. From the perspective of interactions, another safe choice for treating psychosis is amisulpride (4). In patients receiving clozapine, it is not recommended to stop therapy upon a COVID-19 infection, but to regularly monitor ECG and complete blood count, especially with concomitant immunosuppressive therapy (2,4). In combination with lopinavir/ritonavir, the serum concentration of clozapine can increase; therefore, it is reasonable to adjust the dosage (4).

Some benzodiazepines, such as oxazepam and lorazepam, are not mainly metabolized by cytochrome P450, and are therefore relatively safe from the perspective of interaction in concomitant use with antiviral drugs (2,4). In case of insomnia, the use of low doses of trazodone or mirtazapine can be considered (4).

Most antidepressants, especially SSRIs, are also included among safe medications. It is especially sensible to select those with fewer interactions and with no effect on the QT interval (2). Vortioxetine and duloxetine are safe choices because of their relatively few interactions, while the use of tricyclic antidepressants is not recommended (4,5).

Caution is also needed with patients who are receiving mood stabilizers. Lithium has arrhytmogenic potential, and consequently ECG and serum concentration of the drug must be monitored. The latter may be affected by the somatic impact of the infection itself (e.g. dehydration) (2,4,5,35). When using valproate, the serum concentration of COVID-19 drugs, especially lopinavir/ritonavir, can increase up to 40%, while carbamazepine and oxcarbazepine may reduce the serum concentration of these drugs through the induction of cytochrome P450 enzymes (4). Remdesivir may increase value of transaminases, which means extra attention should be paid when administering psychotropic medications that are linked to hepatotoxicity or are mostly metabolized by the liver (valproate, carbamazepine, some antipsychotics and antidepressants) (5,49). The concentration of lamotrigine is reduced by half with concomitant use of lopinavir/ritonavir (4).

Numerous psychotropic medications can prolong the QT interval. These are in particular antipsychotics, tricyclic antidepressants, and the SSRI antidepressants citalopram and escitalopram. Among traditional antipsychotics, thioridazine and haloperidol present the highest risk, while among atypical ones, ziprasidone and iloperidone. The safest choices are aripiprazole and lurasidone (5). It is recommended to avoid psychotropic medications with a significant impact on the QT interval due to increased risk for arrhythmia that may be the result of COVID-19 and the additional impact of some antiviral drugs (chloroquine, hydroxychloroquine, lopinavir/ritonavir) (2,3,5).

The risks related to using individual psychotropic medications in COVID-19 patients are presented in Table 3. This takes into account the risk of interactions

Table 3: Selection of psychotropic medication for COVID-19 patients. Summarized from Luykx, 2020 (2), Anmella, 2020 (4), Bilbul, 2020 (5), Orsini, 2020 (35) and Kahl, 2020 (47).

Risk Psychotropic medications	Safe or low risk	Moderate risk	Moderate to high risk
Antidepressants	fluoxetine sertraline duloxetine[1] vortioxetine	escitalopram citalopram venlafaxine mirtazapine trazodone reboxetine bupropion[2] paroxetine agomelatine[3]	tricyclic AD[4]
Antipsychotics	aripiprazole paliperidone olanzapine[5] cariprazine[6] amisulpride[7] brexpiprazole	risperidone haloperidol loxapine[8] sulpiride clozapine fluphenazine zuclopenthixol lurasidone[9]	quetiapine[10] ziprasidone pimozide
Benzodiazepines/hypnotics	lorazepam oxazepam	alprazolam bromazepam clonazepam diazepam zolpidem flunitrazepam flurazepam	midazolam[11]
Mood stabilizers	gabapentin pregabalin topiramate	oxcarbamazepine lamotrigine lithium[12] valproate[13]	carbamazepine[14]

Legend:
[1] Caution with liver function failure (5).
[2] Caution with risk for epileptic seizures (5).
[3] Caution with liver function failure (4).
[4] Danger of prolonged QT interval, especially in combination with hydroxychloroquine or chloroquine (4,35).
[5] Caution with respiratory disorder (47).
[6] Concomitant use of lopinavir/ritonavir can result in increased serum concentration (4).
[7] Affects the QTc interval, caution with concomitant use with medication that prolongs the QTc interval (47).
[8] Use with respiratory disorder prohibited (47).
[9] Opposing opinions: Concomitant use with lopinavir/ritonavir not permitted (45,46), otherwise moderate (4) or low risk (2).
[10] Affects the QTc interval, concomitant use with lopinavir/ritonavir not permitted (45,46).
[11] Not recommended because of potential interactions at the CYP3A4 level, and because it affects hypoventilation (4), midazolam in oral solution is not permitted with concomitant use of lopinavir/ritonavir (45,46).
[12] Caution for arrhythmogenic potential and potential fluctuations in lithium plasma concentration, regular laboratory controls needed (2,5,35).
[13] Caution with liver function failure, regular laboratory controls needed (4,5).
[14] Use is not recommended because of interactions at the CYP3A4 level (4,5).

with COVID-19 experimental drugs, the effect on the QTc interval, the potential detrimental impact of psychotropic medications on COVID-19 symptoms and undesired side effects that could have a detrimental impact on the progression of the disease. It should be emphasized that the data has been collected based on recommendations that different authors have published over the past year. Such recommendations are based in particular on existing clinical trials, as potential studies that would clearly define the safety of individual psychotropic medications in COVID-19 patients have not yet been conducted. Before selecting the drug, the physician must first inquire about any potential comorbidities, assess the severity of the clinical presentation, and look out for any additional drugs that the patient is receiving (especially COVID-19 experimental medication). For example, psychotropic medications that might be contraindicated with patients receiving COVID-19 experimental drugs (especially lopinavir/ritonavir) or those with a high potential for interactions can be completely safe if patients are not receiving any additional drugs. On the other hand, using some psychotropic medications can only pose a risk with comorbidities or damage to organ systems resulting from the SARS-CoV-2 infection (cardiovascular diseases, liver or renal failure). These exceptions are listed in notes below Table 3.

6 Conclusion

The COVID-19 epidemic has brought new challenges to the use of psychotropic medication. With the growing number of infections both in Slovenia and across the globe, COVID-19 has become a factor with an important impact on the onset and expression of psychopathological symptoms and treatment with psychotropic medication. When facing challenges that the epidemic brings it is important to focus on personalized psychotropic medication treatment that will allow for a safe and successful management of psychopathological symptoms with COVID-19 patients.

Conlfict of interest

None declared.

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