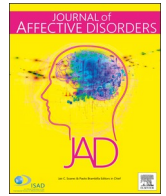




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Review article

Recommendations for the care of patients with bipolar disorder during the COVID-19 pandemic



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ABSTRACT

In recent months, there has been a rapid spread of coronavirus disease (COVID-19), being now regarded as a global pandemic. In this context, the governments of different countries have established strict containment measures, and subsequent deconfinement measures, with consequential alterations in the rhythms and living habits of the population, including patients with bipolar disorder (BD), who are in an extremely vulnerable situation. The present paper aims to propose a number of recommendations, based on scientific evidence, for mental health professionals who may be in charge of BD patients during this health crisis in the coming months. Among these recommendations, careful monitoring of pharmacological treatment, reinforcing medication adherence, and surveillance of drug-drug interaction risk in cases where the patient is being treated for COVID-19 are of utmost importance.

1. Introduction

In recent months, the coronavirus SARS-CoV-2 causing coronavirus disease (COVID-19) has spread throughout more than 100 countries in a matter of weeks and has been classified as a pandemic by the World Health Organization (WHO). In the current context characterized by the lack of effective treatments for this disease, each country has put in place strict containment measures, such as confining the population for weeks. Scientific evidence from previous pandemics (e.g., SARS in 2003) highlights the harmful psychological effects of lockdown and social isolation on the general population, along with the worsening of symptoms and the risk of relapse in individuals with a previous mental disorder (Chatterjee et al., 2020; Mahase, 2020; Pacchiarotti et al., 2020).

Nowadays, governments of different countries are implementing precautionary deconfinement measures with the hopeful aim of returning to pre-pandemic normality; this inevitably leads us to more uncertainty arising from the return to normal life after months of

lockdown, the adoption of new social distancing measures, and the fear of a possible resurgence (Vieta et al., 2020). In these circumstances, the changes in daily rhythms and living habits make BD patients an at-risk population, especially vulnerable to episode recurrence. Although there are recommendations for dealing with schizophrenia patients during the COVID-19 outbreak (Fonseca et al., 2020; Kozloff et al., 2020), to the best of our knowledge no recommendations have been developed for professionals who work with BD patients. Only a few articles deal with the nuances of bipolar disorder in the context of COVID-19 (Gil-Badenes et al., 2020; Stefana et al., 2020; Youngstrom et al., 2020) without developing specific recommendations. Therefore, it is necessary to provide clear and consistent advice for mental health professionals on how to manage the risks generated by COVID-19 and the subsequent deconfinement for BD patients. Consequently, the main goal of this work is to provide several recommendations to clinicians who have to treat BD adult patients during this period and in the coming months.

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Table 1
Evidence-based recommendations for mental health professionals treating BD patients.

Sections	Objectives	Clinical recommendations
Start of the interview section	To debrief and validate the emotional experience associated with the confinement experience	<ol style="list-style-type: none"> 1 Assess the patient's psychosocial functioning before the COVID-19 pandemic outbreak. 2 Assess and discuss the patient's experience and emotional reactions (e.g., fear, anxiety, sadness) during confinement. 3 Validate and normalize the emotional experience associated with confinement and the return to normality (e.g., fear, uncertainty, anxiety) (Omell et al., 2020). 4 Assess the presence of stressors during quarantine experience and subsequent deconfinement of the patient (e.g., family and/or partner conflict, grief over the death of a loved one, dismissal from work) (Brooks et al., 2020).
Physical health section	To reduce emotional distress	<ol style="list-style-type: none"> 1 Anticipate stress reactions that may arise when returning to normal activity after quarantine. 2 Encourage the patient to limit overexposure to the media, which is related to negative psychological effects such as anxiety (Fullana et al., 2020; O'Brien et al., 2020). 1 Inform the patient of the benefits of adopting the preventive and social distancing measures recommended by the health authorities (e.g., handwashing, use of masks, social distancing) (Güner et al., 2020).
	To promote adherence to hand-hygiene practices and both social distancing and respiratory measures	<ol style="list-style-type: none"> 1 Determine systolic and diastolic blood pressure, weight, height, body mass index (BMI = weight/height in m²), and waist circumference, and perform blood tests for glucose, total cholesterol, high-density lipoprotein cholesterol, and low-density lipoprotein cholesterol, triglycerides, and thyroid-stimulating hormone (Bobes et al., 2008). 2 Recommend the patient to monitor himself/herself at home during restrictions measures as weight, blood pressure, or blood glucose. Encourage the patient to attend a consultation when possible to take measures such as lithium levels or blood tests.
Pharmacological treatment section	To monitor physical health problems arising from confinement	<ol style="list-style-type: none"> 1 Recommend a healthy and low-salt diet, exercise appropriate to the patient's physical conditions, and weight reduction if there is overweight/obesity (Bobes et al., 2008). If the patient must be quarantined, we recommend keeping him/her physically active at home (e.g., doing a task at home, caring for the garden), especially during a period of depression (Reinares et al., 2020).
	To promote healthy lifestyle choices	<ol style="list-style-type: none"> 1 Review adherence to pharmacological treatment during quarantine, and adjust or amend medication depending on the patient's current state. 2 Assess whether the patient is consuming other substances (e.g., tobacco, alcohol, drugs) and rule out the risk for substance abuse (Yatham et al., 2018). 3 Despite the COVID-19 pandemic outbreak, highlight the need to continue, and benefits of continuing, the usual treatment. To this end, establishing a good working alliance is paramount (Andrade-González et al., 2020a). 4 If deemed necessary, offer psychoeducation on the advantages of continuing pharmacological treatment and the risks associated with partial or total noncompliance (Colom and Vieta, 2006). If the patient shows a low adherence to pharmacological treatment examine the causes: lack of awareness of the illness, real or feared side effects, feeling controlled by the medication, missing periods of euphoria, prejudices about the medication, social stigma, and forgetting the scheduled doses (Reinares et al., 2020).
Social and family section	To closely monitor the risk of pharmacological interaction (if the patient is being treated for COVID-19 disease)	<ol style="list-style-type: none"> 1 If the patient is being treated for COVID-19 disease, monitor the risk of pharmacological interaction making clinical decisions based on the risk-benefit ratio (see Table 2).
	To reduce the feeling of social isolation and regularize social relations	<ol style="list-style-type: none"> 1 Assess the frequency of interpersonal contact between the patient and other people before the COVID-19 outbreak and at the present time, in order to maintain stable interpersonal stimulation. 2 Normalize the feeling of isolation caused by the health crisis, and establish a plan to maintain and strengthen the patient's social support network (e.g., by telephone or internet) (Fiorillo and Gorwood, 2020). Interpersonal contacts should be regular and of limited duration. 3 If there are outstanding interpersonal conflicts, or if the patient has lost a loved one, assess whether the patient is experiencing a complicated grief. In these cases, apply the strategies of Interpersonal and Social Rhythm Therapy (IPSRT; Frank, 2007a) or problem-solving techniques. IPSRT is a compelling therapy for BD patients aimed to improve patients' mood and level of functioning as well as diminishing interpersonal problems (Frank et al., 2000). A key aspect of this therapy is that it evaluates the regularity of the patient's routines and detect possible disruptions in rhythms to regularize them (Frank, 2007b).
Behavioral section	To provide information to the family members	<ol style="list-style-type: none"> 1 Inform the family about the risk of relapse caused by the instability of the situation provoked by the COVID-19 outbreak. 2 Point out the importance of the patient adhering to his/her pharmacological treatment and maintaining regularity in living habits. 3 Involve a family member: inform him/her about the most frequent relapse prodromes, and agree on an action plan with the family with the aim of helping the patient to deal with a possible relapse (Reinares et al., 2008). 4 Activity scheduling: plan enjoyable and meaningful activities shared in a family context, and highlight the importance of a fluent family communication (Miklowitz, 2008). 5 Validate the emotions and fears expressed within the family environment (Miklowitz, 2007). 6 Highlight the importance of not blaming the patient for possible changes in his/her behavior (e.g., if he/she is more irritable than usual).
	To reduce the stigma associated with being infected by COVID-19	<ol style="list-style-type: none"> 1 BD patients can suffer a stigma because of having a mental illness; if this is added to the fact that the patient has been infected by the COVID-19 it could lead to a double stigma (Wang et al., 2020a). To reduce stigma, normalize COVID-19 disease and the associated feelings experienced in the context of a pandemic.
	To provide the tools necessary for coping with stress	<ol style="list-style-type: none"> 1 Provide the patient with at least one stress-management technique (e.g., progressive muscle relaxation, diaphragmatic breathing, meditation) (Reinares et al., 2020). If possible, offer the patient self-guided audio so that he/she can practice it.

(continued on next page)

Table 1 (continued)

Sections	Objectives	Clinical recommendations
	To promote both healthy sleep habits and daily activities and regularize them	<ol style="list-style-type: none"> 1 Assess sleep habits, their regularity, and the patient's daily activities (e.g., schedules and frequency of these activities). 2 If alterations in these areas are identified, promote sleep hygiene practices (Frank, 2007a), and – with the patient – decide on a behavioral activation program, to be reviewed at the subsequent consultation. 3 It may be useful to agree with the patient on some stimuli that can control other responses in order to comply with proposed schedules and activities (e.g., warnings on a refrigerator, alarms on a mobile phone).
Relapse prevention section	To train patients how to detect relapse prodromes and design an action plan	<ol style="list-style-type: none"> 1 Spend a few minutes teaching patients how to identify relapse prodromes. The four most frequent manic prodromes are sleep disturbances/decreased need for sleep, elevated mood, more talkative than usual, and increased energy/goal-directed behavior (Andrade-González et al., 2020b). The four most frequent depressive prodromes are low in energy/tired, feeling anxious/restlessness, weight loss or poor appetite, and depressed mood (Andrade-González et al., 2020b). 2 Devise an action plan. If the patient experiences prodromes of mania/hypomania, he/she will increase the hours of sleep, limit the number of activities, reduce environmental stimulation, do relaxation or mindfulness, avoid coffee and alcohol consumption, postpone important decisions, delay shopping, and contact with his/her psychiatrist and follow his/her recommendations. If the patient detects prodromes of depression, he/she will sleep about 9 hours (but avoid napping), increase activity level, set realistic goals, postpone important decisions, remember that a depressive episode is temporary, do exercise, avoid alcohol and other toxics, and contact with a psychiatrist or psychologist and follow his/her recommendations (Reinares et al., 2020).
Farewell and closure of the consultation	To ensure effective patient monitoring and offer healthcare resources	<ol style="list-style-type: none"> 1 Offer a resource to the family and/or the patient (e.g., phone number of the nearest mental health center) in case they need support for an illness episode or if they detect a risk of relapse. 2 Be available and leave a door open in case they need assistance. It may be advisable to plan future phone or online consultations (Brooks et al., 2020; Moreno et al., 2020).

2. Recommendations

The following recommendations are based on a body of scientific research and can be applied in-person or via the phone or internet. This set of recommendations contains suggestions that should consider during the first consultation of an adult patient during the COVID-19 pandemic (see Table 1).

The drug-drug interactions that should be taken into account when the BD patient is being treated for COVID-19 are presented in Table 2. It is suggested to avoid starting pharmacological treatment for BD in patients with COVID-19 treated with drugs that have shown interactions (see Table 2). In BD patients who are already under treatment, the risk-benefit of withdrawal should be evaluated (Anmella et al., 2020).

3. Discussion

The COVID-19 pandemic outbreak, the lockdown measures for weeks, and the subsequent deconfinement aimed at its containment imply an alteration in the rhythms and living habits that can present a challenge to the health of BD patients. This paper outlines the areas that mental health professionals who treat these patients should consider during this health crisis and the subsequent deconfinement. Therefore, there is a great need to provide clinical recommendations, which will necessarily have to accommodate the idiosyncrasies of each BD patient.

These recommendations should be adapted to the usual psychiatric comorbidity of the BD patient, to the degree of family support and family stress, and to the patient's current physical health. The pandemic generated by COVID-19 represents a circumstance capable of provoking intense emotions (Montemurro, 2020), which may overwhelm BD patients and thereby necessitate special professional attention. Therefore, validating the emotional experience of these patients caused by confinement is of paramount importance to successfully managing the stress reactions elicited by the COVID-19 outbreak. Adherence to social distancing, hand hygiene, and respiratory measures may be more difficult to adopt in this population, since it involves the strict establishment of new habits and the abandonment of previously established ones. Detection of relapse prodromes, monitoring of pharmacological treatment, and enhancement of medication adherence in these patients will contribute to reducing the possibility of relapses marked by the instability provoked by this health crisis. At this stage it is important that the clinicians that prescribe medication to patients with BD who are being treated for COVID-19 consider the risk of adverse pharmacological interactions. On the other hand, promoting regular healthy sleep habits and living habits will serve to normalize the emotional highs and lows brought on by the COVID-19 lockdown measures, and the subsequent deconfinement. Likewise, the reduction of social isolation feeling as well as social relationships regularization will avoid a drastic decrease and/or increase in social stimulation that could decompensate to these patients. In addition, learning a technique for coping with stressful situations will allow the BD patient not only to cope better with deconfinement but also to cope better with the possibility of a new outbreak that may necessitate another period of confinement. For the family, the COVID-19 outbreak and the changes elicited by this pandemic may raise doubts about how best to support the patient, as well as how to manage family stress arising from different types of changes (e.g., due to the loss or illness of family members or the presence of financial difficulties). In this context, ensuring patient follow-up and offering healthcare resources makes perfect sense; the fight against a pandemic in the digital era makes it necessary to have in place high-quality resources and solid recommendations that can be utilized not only face to face but also via the telephone or internet (Golinelli et al., 2020). Finally, the situation generated by COVID-19 poses new challenges for children and adolescents with BD that can represent sources of stress, such as teleschooling and the drastic change in their lifestyle habits (e.g., lack of contact with classmates and teachers, or a reduction in activity due to cancellation of extracurricular

Table 2
Risk of drug-drug interaction between psychopharmacological drugs for bipolar disorder and COVID-19 treatments

COVID-19 treatment	Clinical recommendations and drug-drug interactions
Dexamethasone	<ol style="list-style-type: none"> 1 Monitor the occurrence of relapses, especially manic ones in short term treatment (Bolanos et al., 2004; Wada et al., 2001). Adverse effects also include depression, agitation, mood lability, anxiety, insomnia, catatonia, depersonalization, delirium, dementia, and psychosis (Bilbul et al., 2020; Warrington and Bostwick, 2006). 2 Avoid carbamazepine and oxcarbazepine (potent induction of CYP3A4 may decrease dexamethasone concentrations) (University of Liverpool, 2020). 3 Monitoring of lithium effects may be required, particularly in patients with renal impairment. 4 Caution with bupropion (lowers seizure threshold).
Remdesivir	<ol style="list-style-type: none"> 1 Totally avoid carbamazepine (University of Liverpool, 2020). 2 Risk of elevated aminotransferase levels—caution with potentially hepatotoxic psychotropics (Bilbul et al., 2020).
Tocilizumab	<ol style="list-style-type: none"> 1 Potential weak interaction with carbamazepine (Drugs.com, 2020; Esteve et al., 2020; University of Liverpool, 2020).
Favipiravir	<ol style="list-style-type: none"> 1 Possible QTc prolongation (Chinello et al., 2017).
Chloroquine/hydroxychloroquine	<ol style="list-style-type: none"> 1 These drugs may produce psychosis, mood change, mania, and suicidal ideation (Nevin and Croft, 2016). 2 Risk of QTc prolongation—caution with QT-prolonging drugs (McGhie et al., 2018). 3 Use with extreme caution sertraline, paliperidone, and mirtazapine. 4 Metabolized by CYP3A4—potential drug interactions with CYP3A4 inhibitors (e.g., fluvoxamine) and inducers (e.g., carbamazepine, oxcarbazepine, modafinil) (Bilbul et al., 2020).
Chloroquine	<ol style="list-style-type: none"> 1 Totally avoid carbamazepine, haloperidol, quetiapine, clozapine, ziprasidone, citalopram, and escitalopram. 2 Avoid as far as possible lithium salts, valproic acid, lamotrigine, topiramate, risperidone, and trazodone. 3 Use with extreme caution sertraline, paliperidone, and mirtazapine. 4 Use with caution aripiprazole, olanzapine, duloxetine, gabapentin, pregabalin, and venlafaxine (Drugs.com, 2020; Esteve et al., 2020; University of Liverpool, 2020).
Hydroxychloroquine sulfate	<ol style="list-style-type: none"> 1 Totally avoid haloperidol, quetiapine, clozapine, ziprasidone, citalopram, and escitalopram. 2 Avoid as far as possible lithium salts and risperidone. 3 Use with great caution mirtazapine, and sertraline. 4 Use with caution aripiprazole, olanzapine, paliperidone, amisulpride, venlafaxine, and trazodone (Drugs.com, 2020; Esteve et al., 2020; University of Liverpool, 2020).

Note: QTc = corrected QT.

activities; Wang et al., 2020b), which reinforces the need to provide recommendations for dealing with this population.

In conclusion, BD patients are vulnerable to experiencing stress from the profound changes in their living habits, and in addition can experience intense emotions resulting from the severe health crisis caused by the COVID-19 outbreak. Mental health professionals who are required to treat BD patients should pay special attention to this population and their families to ensure their emotional stability and reduce the likelihood of relapse.

Authors' contribution

AHG and NAG designed the study. GL and EV checked the recommendations. AHG prepared Table 1 and prepared the first draft for review. GL and EV provided input into the development of the manuscript, including the final version. EV critically revised the manuscript for intellectual content and reviewed the first and second draft. All authors contributed significantly to the discussion and approved the final draft.

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