

The implications of COVID-19 on the mental health of patients with treatment-resistant depression: challenges and recent strategies

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COVID-19 and consequent lockdown has increased the mental health problems in people, quite significantly affected were the patients with treatment-resistant depression [1]. Depression is the third leading cause of disability in the world. Even if successfully treated, 80 percent of patients relapse within 5 years of remission. Approximately 30 percent are diagnosed with treatment-resistant depression. The unemployment and low productivity due to COVID-19 added to the poor outcomes in these patients. Moreover, it increased the frequency of episodes of depression leading to the poor prognosis as well as poor functioning of patients in realms of work and family life. Hence, patients resort to multiple consultations, further exhausting a country's health care sources during the pandemic. A qualitative study explored deterioration of mental health of 116 patients with treatment-resistant depression during the pandemic, in multiple areas which included biological, social, and psychological domains. The patients revealed significant feelings of distress and agitation [2].

Albeit the traditional methods for the management of treatment-resistant depression like optimization, switching, augmentation by SSRIs/SNRIs/TCAs/atypical antidepressants/brain stimulation techniques remain the standard protocol. Intermittent theta burst stimulation (iTBS) has gained attention for its time-efficient profile and minimization of the chance of exposure. It is a non-invasive neurostimulation technique which shows a significant improvement in the clinical outcome of treatment-resistant depression. It ameliorates depressive symptoms by inducing changes in the organisational properties of brain networks and reducing modularity, evident as early as 4 days after treatment [3]. During the pandemic, suicidality also increased in the depressive patients as a result of emotional isolation. Ketamine's

antidepressant potential has captivated the interest of researchers here. It produces rapid action to treat suicidal ideation and behaviour in patients with major depression [4,5].

In a comparative trial, the effects of ketamine in 267 patients with treatment resistant depression (on treatment) was compared pre and post the pandemic. There was a significant reduction in depressive and anxiety symptoms with ketamine at different points in time. The sickest patients may respond to ketamine as early as a few hours in contrast to traditional antidepressants which take weeks to kick in. However, every coin has two sides. Ketamine is classified as schedule III drug by US FDA which means it has a moderate to low abuse potential. Also, it can cause extreme side effects. One of which is a short-lived state of altered consciousness immediately after the treatment with a high dose, colloquially known as the 'K-hole'. Hence, standardised procedures have been formulated to prevent it being very loosely prescribed. Ketamine may also act by reversing the damage of the connection between the brain cells which might prevent the relapse of depressive episodes. Despite many lacunas in ketamine's use and access, with apprehension comes optimism. Thus, ketamine provides a way for an era of novel drug treatments for treatment-resistant depression [6].

Since commutation and physical consultations were cumbersome, telepsychiatry gained an immense popularity during the pandemic. A randomised clinical trial supported the benefits of an online telepsychiatry adjuvant healthy lifestyle promotion program for patients with treatment-resistant depression over 8 weeks. Significant improvement on depression rating scales was observed in the treatment group as compared to the control group. Lifestyle modifications included a focus on daily exercises, nutrition,

sleep wake rhythm and sleep hygiene, appropriate exposure to sunlight and social support [7]. Another pilot study successfully evidenced a positive outcome of telephone-based behavioural activation with mental imagery in reducing depressive symptoms in older adults during the pandemic. It can be delivered in a brief format and has shown to be feasible and effective for older individuals in as few as four sessions. When we feel anxious and depressed, we should not wait for the brain to give us the motivation to get out there and do things. Instead, we need to do something in line with our values and goals that is necessary for emotions to change. One way to facilitate motivation for planned activities might be via prospective mental imagery. Coupling the two techniques successfully alleviated the depressive symptoms, delivered through telephone [8].

Clinical research shows that chronic illnesses and infections are associated with increased psychiatric distress levels. People with the medical illness or infection (like COVID-19 recently) have difficulty adjusting to the demands of the illness. It affects the person's mobility and independence. Fatigue, decreased energy, suicidal ideation due to depression worsens it further. Hence, a multidisciplinary approach is required to treat the patient as a whole and calls for rigorous and novel management techniques.

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