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Letter to the Editor

Telephonic monitoring of patients on clozapine in the resource-poor setting during the COVID-19 pandemic


Sir,

Patients of schizophrenia receiving clozapine require close clinical monitoring of their absolute neutrophil count (ANC), given the risk of neutropenia with clozapine. COVID-19 pandemic and the ensuing lockdown has come as a blow to the patients of schizophrenia, who have been receiving clozapine.

Treatment Response and Resistance in Psychosis (TRRIP) working group recently developed a consensus statement, which recommended that the frequency of monitoring of ANC can be reduced to once in 3 months, if the person has been receiving clozapine for more than one year and has never had an ANC of $<2000/\mu\text{L}$ (or $<1500/\mu\text{L}$ if a history of benign ethnic neutropenia is present) or the person has no safe or practical access to ANC testing (Siskind et al., 2020). For patients receiving clozapine for 6 to 12 months, the recommendation for monitoring of ANC needs to be decided on a case to case basis. Other recommendations include monitoring of the mental state by face to face interview or teleconsultation, and an urgent physician assessment in person or by teleconsultation along with the evaluation of ANC if the patient develops respiratory symptom (Siskind et al., 2020). While receiving clozapine, if the patient develops fever and symptoms of flu, the dose of clozapine should be reduced to about half to avoid clozapine toxicity and can be later optimized. Clozapine levels can be done, depending on availability (Siskind et al., 2020).

It is also known that acute infection, such as pneumonia can lead to clozapine toxicity, especially if the clozapine titration is done at a faster pace (Wu et al., 2019). Recent data also suggest that patients from Asia may require lower doses than used in Caucasians (de Leon et al., 2020a, 2020b).

In contrast, to the United States, where clozapine dispensing and blood monitoring is done through Risk Evaluation and Mitigation Strategy (REMS) (Leung et al., n.d.), no such strategy is available in India. The clinicians prescribing clozapine themselves have to monitor the ANC and titrate the doses of clozapine. In India, there are no national guidelines for monitoring of ANC for patients on clozapine.

It is also known that patients receiving clozapine are at increased risk of developing a respiratory infection (Wu et al., 2019).

With the COVID-19 pandemic resulting in the virtual closure of almost all the laboratory and outpatient services, it has become difficult to monitor the patients on clozapine in a major part of India. Since the lockdown, we initiated the telephonic services for the patients on clozapine to educate them about the symptoms of COVID-19, need for continuation of medications and monitoring of ANC, when to consult the treating doctor and when to contact the emergency services. Additionally, the patients and the caregivers were informed to send the ANC

reports telephonically to the treating doctor, so that the dose can be further increased or if the ANC is low, then the doses are withheld and repeat investigations are ordered.

In this background, during the subsequent follow-up, we evaluated the clinical status (both psychological and physical) of the patients on clozapine, monitoring of ANC, medication adherence, and satisfaction with the telephonic consultations. Additionally, we also evaluated the difficulty faced by the patient and families in getting the clozapine supply and difficulties in getting the ANC done. These evaluations were done by telephonic interview, during which the patient and families were also provided further information about the regular monitoring, and what to do if the patient develops symptoms of flu. We telephonically contacted, 227 patients of schizophrenia, out of whom we could reach out to 205 patients of schizophrenia, who were on clozapine, after about 6 weeks of lockdown and they were interviewed after obtaining verbal informed consent.

The mean age of the study participants was 33.7 (SD: 10.8) years, with a mean duration of education of 12.4 (SD: 3.7) years. The mean age of onset was 22.41 (SD: 8.5) years and the mean dose of clozapine use was 244.05 (SD: 107.2) mg/day. The majority of the participants were male (55.1%), currently single (70.3%), unemployed/homemakers (72.2%), belonging to the Hindu religion (71%), from nuclear families (74.6%), and urban background (74.1%). The mean duration of clozapine use was about 5 years (59.35: SD 56.02 months) at the time of assessment and 25 patients were receiving clozapine for less than one year, of whom 20 were on clozapine for <6 months.

The majority of the patients reported that they were in touch with their treating doctor (81.5%), with contact initiated by the treating team in 79% of patients. The majority (75.5%) of the patients and their family members were satisfied to a large extent, for being able to remain in touch with the treating doctor. During the lockdown period, fortunately 96.6% of the patients were taking the clozapine according to the recommended doses, while others were taking less than the prescribed doses (3.3%) and one patient discontinued the medication. Only 8% of the patients experienced worsening of their symptoms. About one-fourth of the patients had difficulty in procuring clozapine, with clozapine not being available in their locality for 15.1% of cases and 3.4% have had to switch their brand of clozapine. Only one-fourth (24.4%) of the patients were able to get the ANC done in the previous month. Fortunately, the majority of the patients (97.6%) cooperated with their family in following the rules of the lockdown, with three-fourth of the patients (77.1%) of the patients remaining inside the house. In terms of other measures, hand hygiene measures were being followed by 60% of the patients, 50.7% of patients were using the face mask and 29.8% of patients were being able to follow social distancing. Although the majority of the patients and the caregivers were aware of fever (76.6%) and cough (75.6%) as the symptoms of COVID-19, only a small proportion of the patients and caregivers were aware of other symptoms, such as sore throat (23.9%) and other flu-like symptoms (37.6%). A small proportion (4.9%) of the patients had developed respiratory symptoms in the previous month and had to visit the emergency services (2%). Only 1 patient developed severe respiratory symptoms

and was diagnosed with pulmonary tuberculosis and 1 patient had a relapse of his symptoms requiring admission to the inpatient unit. During the period of lockdown, in 6 cases, who were started on clozapine 1 month before the lockdown, the doses of clozapine could be increased, with monitoring of ANC. This led to an improvement in the clinical status of the patients. None of our patients died during this period or developed symptoms of COVID-19 infection. None of the patients, those who had access to the laboratory and had the ANC done, developed blood dyscrasia.

Clinicians across the globe are facing the clinical dilemma, in that, on one hand the monitoring of ANC is relaxed, especially for patients who were receiving clozapine for more than one year and have no infection. On the other hand, patients on clozapine are at a higher risk of developing pneumonia and at a higher risk of death (de Leon et al., 2020a, 2020b). In the ongoing pandemic, if a patient develops pneumonia, a differential diagnosis of COVID-19 or other viral infections comes into the picture (Guan et al., 2020). Hence, clinicians are often unsure about how to go about monitoring their patients.

Our experience demonstrates that in a resource-poor setting, telephonic consultations, as recommended by the TRRIP working group (Siskind et al., 2020) could be an important resource to monitor patients receiving clozapine. Accordingly, clinicians in the resource-poor setting should monitor their patients on clozapine, by using telecommunication modalities, as it is predicted that the COVID-19 pandemic is going to continue for about 1 year (Mahase, 2020).

This teleconsultation model involving voice calls, use of messages to transmit the ANC, and other reports and prescriptions can continue beyond the pandemic and emerge as a cost-effective alternative or additional monitoring model to the routine hospital visits for monitoring. Accordingly, it can be said that the clinicians should take initiative in the resource-poor setting to contact their patients, educate them about the risks of neutropenia and other infection, in the ongoing pandemic.

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Declaration of competing interest

None.

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Sandeep Grover

Department of Psychiatry, Postgraduate Institute of Medical Education & Research, Chandigarh 160012, India

Corresponding author.

E-mail address: drsandeepg2002@yahoo.com

Eepsita Mishra

Subho Chakrabarti

Aseem Mehra

Swapnajeet Sahoo

Department of Psychiatry, Postgraduate Institute of Medical Education & Research, Chandigarh 160012, India

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