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Position Statement

Clozapine in COVID-19

Position

Clozapine is associated with a higher risk of pneumonia. This is most likely due to sialorrhoea and the associated increased risk of aspiration pneumonia¹. However, there is some suggestion that people on clozapine may have impaired immunological mechanisms.

Patients on clozapine presenting with any symptoms of COVID-19 infection should seek or be referred for urgent clinical assessment. A complete blood count with absolute neutrophil count (ANC) should be obtained.

If fever and/or pneumonia develop, clozapine levels should be monitored, and the dose lowered or ceased accordingly.

It has been suggested that if there are barriers to safe access to ANC testing during the COVID-19 pandemic, the frequency of ANC testing may be reduced to ensure ongoing access to clozapine. However, this is 'off-label' use and is not established as best practice.

Background

Clozapine is the most effective antipsychotic for treatment-resistant schizophrenia². However, it is associated with a high adverse effect profile. Use is reserved for people with treatment refractory schizophrenia and directed by strict guidance and monitoring.

The National Inpatient Medication Chart (NIMC) (clozapine titration) is available for patients on a [titrating clozapine regimen](#) and is accompanied by a [user guide](#).

The NIMC (clozapine titration) records the prescribing, monitoring and administration of clozapine titration for adult inpatients. The NIMC (acute) or NIMC (long-stay) should be used for initiation of patients on clozapine or maintenance of clozapine in long stay psychiatric facilities.

There is limited experience of clozapine in patients infected with COVID-19. Clozapine is associated with increased risk of pneumonia³. There is evidence that clozapine may lead to secondary antibody deficiency, which may lead to people on clozapine being more susceptible to viral respiratory infections such as influenza and COVID-19.⁴

For patients on clozapine with symptoms of infection, including cough, fever and chills, sore throat or other flu-like symptoms, an urgent physician assessment including a complete blood count (with ANC) should be obtained.

A consensus statement published in the Journal of psychiatry and neuroscience (April 2020) outlines [considerations for patients on clozapine during COVID-19](#). The statement suggests that during the COVID-19 pandemic, to ensure uninterrupted supply of clozapine, the frequency of ANC monitoring may be reduced to every 3 months for people fulfilling all of the following criteria:

- continuous clozapine treatment for >1 year;
- have never had an ANC <2000/ μ l (or <1500/ μ l if history of benign ethnic neutropenia);
- no safe or practical access to ANC testing.

Clozapine levels can increase during periods of acute infection⁵ or reductions in cigarettes smoked per day. Raised clozapine levels may be associated with clozapine toxicity, including sedation, myoclonus and seizures⁵. People on clozapine who develop COVID-19 or other respiratory infections may reduce their cigarette intake, both of which may lead to raised clozapine levels. Clozapine levels should be tested, and consideration should be given to reducing the dose of clozapine during the period of acute infection if clozapine levels are elevated.

The Royal College of Psychiatry in the UK has published [detailed guidance on the monitoring of blood dyscrasias in COVID-19](#).

For further information, South London and Maudsley NHS Foundation Trust published Clozapine and COVID-19 to cover initiation, continuation and special precautions on 30 March 2020⁶.

References

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2. Siskind D, et al. Clozapine v. first-and second-generation antipsychotics in treatment-refractory schizophrenia: systematic review and meta-analysis. *Br J Psychiatry* 2016;209:385-92
3. Dr James Paul Pandarakalam, Consultant Psychiatrist. Letter to the Editor, BMJ Online. Potential risk of COVID-19 in Clozapine Treated Patients www.bmj.com/content/368/bmj.m1071/rr
4. Ponsford M, Castle D, Tahir T, Robinson R, Wade W, Steven R, Bramhall K, Moody M, Carne E, Ford C, Farewell D, Williams P, El-Shanawany T and Jolles S. Clozapine is associated with secondary antibody deficiency. *The British Journal of Psychiatry* 2018;1-7. doi: 10.1192/bjp.2018.152
5. Clark SR, et al. Elevated clozapine levels associated with infection: a systematic review. *Schizophr Res* 2018;192:50-6
6. Gee S, Gaughran F, Taylor D. Clozapine and COVID-19. Initiation, continuation and special precautions. South London and Maudsley NHS Foundation Trust. 30 March 2020

Date of revision: 28 April 2020

The Commission gratefully acknowledges review of this position statement by the Royal Australian and New Zealand College of Psychiatrists.

If you have feedback regarding this position statement, please email: medsafety@safetyandquality.gov.au