The Impact of COVID-19 on Clozapine Therapy in a Forensic Service

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BACKGROUND

Clozapine is the most effective antipsychotic in treatment-resistant schizophrenia[1], but treatment with this medication requires regular full blood count monitoring due to the risk of serious haematological complications, including neutropenia which can progress to life-threatening agranulocytosis. However, when they do occur, such complications are most commonly seen during the first 18 weeks of treatment. Early in the pandemic it was established that leukocytopenia also occurs in acute COVID-19 infection; however, this appeared to be driven by lymphocytopenia in the general population, with neutrophil counts being persevered or even slightly raised[2]. It was not until later in the pandemic that it was demonstrated that, contrary to these findings, transient neutropenia was being observed in acute COVID-19 infection in patients taking clozapine[3]. In November 2020, as these data began to emerge, South London and Maudsley NHS Foundation Trust published guidelines on how to respond to neutropenia in patients taking clozapine with acute COVID-19 infection[4].

AIMS

In light of this discovery, we set out to retrospectively examine whether this transient neutropenia had been observed in any of the patients taking clozapine in the North London Forensic Service in the presence of acute COVID-19 infection. Also, if this was indeed found to be the case, we wanted to assess whether treatment had consequently been interrupted and, if so, what the implications of this were.

METHODS

We retrospectively examined records in the North London Forensic Service dating from January 2020, when SARS-CoV-2 was first detected in the UK, to June 2021, when we conducted this study. Of 42 patients that were taking clozapine during this period, we identified 15 patients who acquired COVID-19 infection. Of these, 3 were found to have experienced neutropenia and were explored in more detail using blood test results and electronic clinical records.

RESULTS

Case 1

Diagnosis and status: Paranoid schizophrenia treated in community under Section 41 since 2014.

Duration on clozapine: Since 2007 with no previous red or amber results .

Red result: 12 January 2020.

COVID-19 status: Negative on lateral flow at time of red result but SARS-CoV-2 detected on PCR when recalled to hospital 14 days later.

Outcome: Clozapine stopped. Sleep disturbance and increased hostility noted in first week and return of persecutory delusions in second week. Recalled to hospital and Section 37/41 reinstated. Refused to restart clozapine and unprovoked assaults of staff commenced. Remained unwell in long-term segregation (LTS) at the time of this study.

Case 2

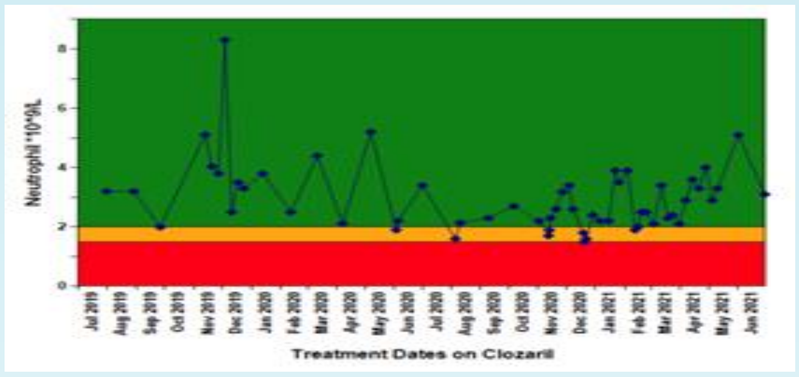
Diagnosis and status: Schizoaffective disorder treated as an inpatient under Section 3.

Duration on clozapine: Since 2013 with no previous red results but intermittent amber results .

Red result: 18 December 2020.

COVID-19 status: SARS-CoV-2 detected on PCR when swabbed 4 days after red result.

Outcome: Clozapine stopped but restarted within 4 days in accordance with South London and Maudsley NHS Foundation Trust guidance[4]. Persecutory delusions and generally disorganised behaviour became apparent within days but began to abate 5 days after clozapine was recommenced.



Case 3

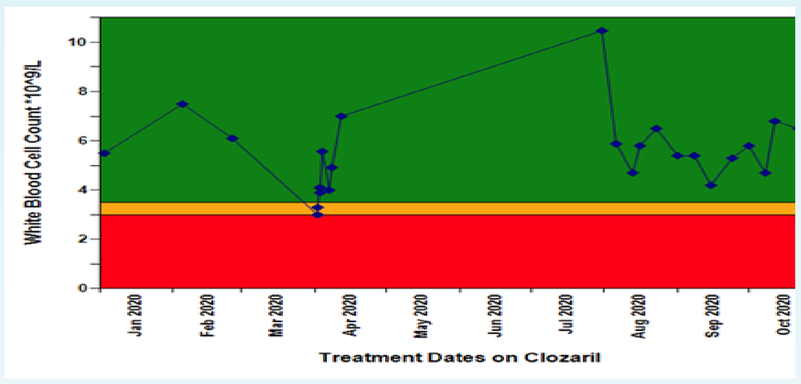
Diagnosis and status: Paranoid schizophrenia treated as an inpatient under Section 3 since 1998.

Duration on clozapine: Since 2016, and previously 2004-2008, with one isolated amber result in 2018.

Red result: 02 April 2020.

COVID-19 status: Refused testing. COVID-19 was present on the unit at the time.

Outcome: Clozapine stopped. Increase in persecutory delusions within days and became thought disordered soon after. Secluded 4 days after stopping for assaulting another patient. Aggressive behaviour continued and LTS was commenced. Despite a number of later attempts, compliance with clozapine was never re-established. Risk to others continued to escalate culminating in his secreting weapons (no prior history of use of weapons) and attempting to assault a junior doctor during an LTS review. Transferred to Broadmoor Hospital (high security) in April 2021.



DISCUSSION

- Our small retrospective study supported the findings of others studies[4,5] in demonstrating that acute COVID-19 infection can produce a transient neutropenia in patients treated with clozapine.
- Cessation of clozapine treatment can result in a rapid and catastrophic relapse in patients with treatment-resistant schizophrenia, as we observed in 2 of the 3 patients studied here.
- The unnecessary stoppage of clozapine treatment, and the associated risk of catastrophic relapse that this entails, can be averted by following the *COVID-19 and Clozapine* guidelines published by South London and Maudsley NHS Foundation Trust[4]. This was successfully done in 1 of our 3 cases and could have also been done in the other 2 had such knowledge been available at the time.
- With COVID-19 likely to remain endemic, in the presence of red or amber results, particularly in patients established on clozapine for extended periods without prior complications, PCR testing for SARS-CoV-2 should be undertaken without delay in order to inform immediate management decision.

REFERENCES

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