

Neutropenia in patients treated with clozapine during COVID-19 infection

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INTRODUCTION

Clozapine is the most effective antipsychotic for treatment resistant schizophrenia but adverse reactions to clozapine include neutropenia. COVID-19 is the infectious disease caused by the coronavirus SARS-CoV-2.

In March 2020 clinicians raised concerns regarding continuation of antipsychotic treatment, and specifically of clozapine, in patients with COVID-19. Initially the information emerging from the Chinese experience indicated that COVID-19 was linked to lymphopenia but not neutropenia. Case series from around the same period also reported no documented neutropenia (Gee and Taylor 2020). Bonaccorso and colleagues have recently reported a series of 10 patients with COVID-19 taking clozapine which ANC values initially decline by 17% from baseline.

OBJECTIVES

We report 2 cases of neutropenia in patients treated with long-term clozapine, with no history of haematological complications, during COVID-19 infection.

METHODS

Subjects: 48 Patients diagnosed with severe mental disorder admitted to a long-stay psychiatric unit.

COVID-19 infection confirmed by positive nasopharyngeal swab for viral ribonucleic acid of SARS-CoV-2.

Hematological controls, collecting the white cell count (WCC) and the absolute neutrophil count (ANC) between March and April 2020.

CONCLUSIONS

- In our sample 2 clozapine-treated patients developed neutropenia during covid-19 infection.
- An urgent full blood count will be required to exclude severe neutropenia.
- If neutropenia is severe and clozapine has to be discontinued, it may be worth reconsidering reintroduction with caution when covid-19 has resolved and neutrophils have returned to baseline levels
- Further research will be needed to clarify the possible relationship between COVID-19, clozapine and neutropenia. To date we have case series data. We therefore advocate for studies with a larger sample size and a control group.

RESULTS

Table 1 shows the sample characteristics of the admitted patients. 16 (33%) receiving clozapine treatment. There were 18 (37.5%) cases with covid-19 infection. Clozapine-treated patients with covid-19 infection were 5 (10.4%); 2 presented neutropenia:

1- 56-year-old woman diagnosed with schizophrenia on clozapine since 2009. Begins to have a dry cough and fever with positive COVID-19 swab (day 0). Slight leukopenia without neutropenia was observed on day 1. On day 7, neutropenia was observed with an absolute neutrophil count (ANC) of 1100. We decided to suspend clozapine and to initiate daily hematological controls. The ANC on day 8 was 970. Over the next few days the ANC will progressively improve until neutropenia resolved (Table 2). The evolution of leukocytes and neutrophils is shown in figure 1.

2- 55-year-old woman who required a transfer to a general hospital because of respiratory complications from COVID-19. She presented significant leukopenia ($1.01 \times 10^3/\mu\text{L}$) and neutropenia (ANC 100). Clozapine was not withdrawn. She was treated with granulocyte colony-stimulating factor. Once the respiratory process had resolved, he returned to the psychiatric long-stay unit, maintaining her usual treatment with clozapine 300mg per day.

Table 1 Sample characteristics of admitted patients

	COVID-19 +	COVID-19 -	TOTAL
CLOZAPINE	5 (10'4%)	11 (22'9%)	16 (33'3%)
NON-CLOZAPINE	13 (27'1%)	19 (39'6%)	32 (66'7%)
TOTAL	18 (37'5%)	30 (62'5%)	48 (100%)

Table 2. Evolution of blood count and absolute neutrophil count (ANC)

	Day 1	Day 7	Day 8	Day 9	Day 10	Day 11	Day 22
Hematies $\times 10^6/\mu\text{L}$	3'98	3'74	3'28	3'49	4'07	4'02	3'55
Haemoglobin g/dl	11'3	10'8	9'4	9'7	11'2	11'3	10'1
Hematocrit %	35	32'3	28'3	29'8	36	35'5	32'6
Leukocytes $\times 10^3/\mu\text{L}$	3'61	2'90	2'99	3'01	3'50	4'15	3'90
Neutrophils $\times 10^3/\mu\text{L}$	2'03	1'10	0'97	1'46	1'28	1'85	2'00
Lymphocytes $\times 10^3/\mu\text{L}$	1'11	1'52	1'56	1'2	1'89	1'91	1'39
Monocytes $\times 10^3/\mu\text{L}$	0'42	0'26	0'43	0'33	0'28	0'35	0'42
Eosinophils $\times 10^3/\mu\text{L}$	0'03	0'01	0'02	0'01	0'03	0'03	0'07
Basophils $\times 10^3/\mu\text{L}$	0'02	0'01	0'01	0'01	0'02	0'01	0'02

leukopenia in blue; neutropenia in red. Clozapine withdrawal on day 7.

Figure 1. Evolution of leukocytes and neutrophils in patient 1



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