

Can You Cross the Red Line?

A Case of Safely Continuing Clozapine Despite Neutropenia



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Background

- Clozapine is the most effective of the antipsychotics but potentially has the most dangerous adverse effects, including fatal neutropenia.
- Around 2.7% of patients treated with clozapine develop neutropenia.
 - Not all are clozapine-related or even pathological.

Objective

- To inform clinicians of a case where clozapine therapy was safely continued, despite mild neutropenia, avoiding the risk of relapse in mental state from cessation of clozapine.

Clinical Presentation

- Mr TR is a 37 year old man with hebephrenic schizophrenia. He was referred from his community psychiatrist to a specialist mental health Hospital in the Home (HiTH) service to circumvent an inpatient admission and avoid relapse secondary to multiple stressors.
- A notable stressor was Mr TR's anxiety about the prospect of clozapine being ceased if his neutrophil count dipped into the "red" range ($<1.5 \times 10^9/L$). He felt guilty about becoming a burden to his family should the clozapine cessation result in a relapse.

Patient Information

- Medical History:
 - Nil significant
- Other medications:
 - Nil
- Allergies/adverse drug reactions:
 - Nil known
- Mr TR found clozapine effective in maintaining his mental state and was very keen to remain on it.

Clozapine Treatment History

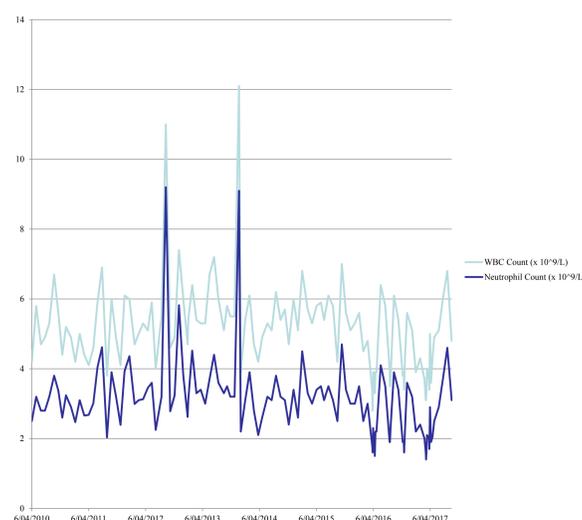
- Clozapine commenced: 1/4/1997.
- Current clozapine dose: 300 mg nocte.
- This dose has been unchanged since at least September 2010 (the earliest record readily available).

Interventions

- The pharmacist played a key role in the coordinating following strategies:
 - ✓ Psychiatrist and Clozapine® haematologist consultation
 - ✓ Daily HiTH clinician home visits, monitoring physical and mental states
 - ✓ Twice-weekly FBP blood tests while in the "amber" range
 - ✓ Daily FBP blood tests while in the "red" range.

Clozapine® Protocol		
	WBC	Neutrophil
Green	$>3.50 \times 10^9/L$	$>2.00 \times 10^9/L$
Amber	$3.00 - 3.50 \times 10^9/L$	$1.50 - 2.00 \times 10^9/L$
Red	$<3.00 \times 10^9/L$	$<1.50 \times 10^9/L$

White Blood Cell and Neutrophil Counts



- Mr TR's white blood cell and neutrophil counts have been frequently close to the lower limits over the past few years.

Case Progress

Date	Investigation	Comment
10/3/2017	Neutrophils: $1.4 \times 10^9/L$	Red range
13/3/2017	Neutrophils: $1.7 \times 10^9/L$	Spontaneous return to Amber range
16/3/2017	Neutrophils: $2.1 \times 10^9/L$	Spontaneous return to Green range

- The literature suggests some people may have a consistently lower neutrophil count than the reference range without evidence of increased susceptibility to infection or any other adverse effect.¹

When would it have been a bad idea to continue?

- If the first blood dyscrasia:
 - Was inconsistent with previous WBC or neutrophil counts (ie not part of a pattern of repeated low WBCs);
 - Occurred within the first 18 weeks of treatment;
 - Was severe (neutrophils $<0.5 \times 10^9/L$); and
 - Was prolonged.
- The above would indicate a very high risk of bone marrow toxicity if clozapine is continued.
- In such a case, continuation of clozapine would generally not be advised.²

Outcomes

- Following discharge from HiTH, Mr TR was able to travel to New Zealand, along with his wife and two children. The stability afforded to him by safely remaining on clozapine ameliorated his anxiety, while preventing potential rebound psychosis and disruption to his family life.



Conclusion

- With cautious monitoring and specialist consultation, it is possible to safely continue clozapine therapy in a patient with mild neutropenia.

Reference

1. Haddy TB, Rana, SR, Castro O. Benign ethnic neutropenia: What is a normal absolute neutrophil count? J Lab Clin Med. 133(1); 1999:15-22.
2. Taylor D, Paton C, Kapur S. The Maudsley Prescribing Guidelines in Psychiatry. 12th ed. West Sussex, UK: Wiley Blackwell; 2015.

More information?

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