Clozapine Plasma Level Monitoring Guide

Clobazapine plasma level monitoring is an optional measurement of the amount of clozapine in a patient’s blood, and should not be confused with the compulsory monitoring of full blood count during clozapine treatment.

Reasons for measuring plasma clozapine/norclozapine levels:

Understanding plasma clozapine and norclozapine measurement can be helpful:

- For dose optimisation.
- To assess the effect of changes in smoking habit (tobacco and cannabis) on clozapine.
- To assess compliance – Plasma clozapine and norclozapine in the expected range only guarantees adherence over the previous few days.
- To attribute possible dose-related adverse effects, e.g. sedation, constipation, tachycardia, seizures, particularly if clozapine clearance is reduced due to hepatic dysfunction, or if drug-drug interaction.
- Investigating suspected clozapine toxicity.
- For patients who are particularly sensitive to the drug; it may be helpful to perform an assay in the very early stages of treatment.

When to take blood sample for clozapine plasma levels:

- No sooner than two to three weeks after treatment initiation and only where dose has been stable for at least the preceding 5 days.
- To ensure the result represents a trough level, take sample immediately before the morning dose or 10-12 hours post-dose where only one dose is taken per day.

Interpreting the results:

- A therapeutic window of 0.35 mg/L - 0.5 mg/L is suggested by the Maudsley Prescribing Guidelines.
- Plasma levels greater than 0.6 mg/L are related to an increased risk of convulsions. See clozapine policy for management advice.
- Levels of around 0.6-0.8 mg/L have been proposed as the upper therapeutic limit.
- There is a clearer link between seizures and plasma levels over 1.0 mg/L and other types of toxicity with levels over 0.75 mg/L.
- For levels >1mg/L, consider cautious dose reduction and LFT (Liver Function Test) measurement.
- The norclozapine level under normal circumstances is expected to be around two thirds of the clozapine level. The plasma trough clozapine: norclozapine ratio (clozapine metabolic ratio) provides a simple measure of clozapine metabolism in individuals. E.g. For a clozapine level of 0.6mg/L, a norclozapine level of 0.4mg/L would be expected.

<table>
<thead>
<tr>
<th>Norclozapine Level</th>
<th>Actions</th>
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<tbody>
<tr>
<td>2/3 of the clozapine level (and clozapine level in range)</td>
<td>Only repeat as and when needed</td>
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| >2/3 of clozapine level | Only partially compliant in the preceding days  
| | The patient is on a medication/has increased smoking. Liver enzymes induced and the metabolism of clozapine has increased  
| | The patient is a fast metaboliser |
| <2/3 of clozapine level | Only partially compliant in preceding few days  
| | The sample was not a trough  
| | The patient is a slow metaboliser/reduced smoking |

References


Kingsley Green Pharmacy and Medicines Optimisation Team, March 2019