

17 - Acting on clozapine plasma concentration results

Acting on clozapine plasma concentration results

Pharmacokinetics CHAPTER 11 Acting on clozapine plasma concentration results In most developed countries, clozapine blood concentration monitoring is widely used. Table 11.4 gives some general advice about actions that should be taken when clozapine levels are within a certain range. The ranges shown are somewhat arbitrary and convenient - the concentration at which a particular patient might respond cannot be known without a trial of clozapine. Most adverse effects are linearly or exponentially related to dose or plasma level. That is, there is no step-change in the risk of seizures, for example, at a particular dose or plasma concentration.¹ The same is broadly true of therapeutic effects. The likelihood of response in an individual increases from concentrations below the accepted therapeutic range up to around 1000mcg/L.²⁻⁴ Table 11.4 should be considered more an aid to decision-making rather than a rigorous, unbending evidence-based instruction. Note also the effect of tolerance to adverse effects - many patients have a significant adverse effect burden before therapeutic concentrations are reached,⁵ reducing over time as tolerance develops.

Table 11.4 Recommended actions in response to clozapine concentrations.*

Plasma concentration	Response status	Tolerability status	Suggested action
<350mcg/L	Poor	Poor	Increase dose very slowly to give level of 350mcg/L
350-500mcg/L	Poor	Good	Increase dose to give level of 350mcg/L
500-1000mcg/L	Good	Poor	Maintain dose. Consider cautious dose reduction if tolerability does not improve.
>1000mcg/L	Good	Good	Continue to monitor. No action required.

350-500mcg/L Poor Poor Increase dose slowly, according to tolerability, to give level of >500mcg/L. Consider prophylactic anticonvulsant.† If no improvement, consider augmentation.

500-1000mcg/L Poor Good Increase dose slowly, according to tolerability, to give level of >500mcg/L (up to 1000mcg/mL if tolerated). Consider prophylactic anticonvulsant.† If no improvement, consider augmentation.

>1000mcg/L Good Poor Maintain dose to see if tolerability improves. Consider cautious dose reduction to give plasma level of around 350mcg/L.

>1000mcg/L Good Good Continue to monitor. No action required.

>1000mcg/L Poor Poor Consider use of prophylactic antiseizure drug.† Consider augmentation. Attempt dose reduction if augmentation successful.

>1000mcg/L Poor Good Consider use of prophylactic antiseizure drug.† Slowly increase dose (up towards 1000mcg/mL if tolerated). Also consider augmentation.

>1000mcg/L Good Poor Attempt slow dose reduction to give plasma level of 350-500mcg/L unless there is known non-response at lower level. If this is the case, maintain dose and consider adding anticonvulsant.† Optimise treatment of adverse effects.

>1000mcg/L Good Good Consider use of prophylactic antiseizure drug.† Maintain dose if good tolerability continues.

(Continued)

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