09 - Clozapine

Clozapine

870 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 11 psychosis, studies suggest plasma concentrations of 20–60mcg/L may give optimal D2 occupancy and clinical response.34,35 In practice, only a minority of treated patients have ‘therapeutic’ plasma levels (probably because of poor adherence36) so plasma monitoring may be of some benefit. However, amisulpride plasma level monitoring is rarely undertaken and few laboratories offer amisulpride assays. The dose–response relationship is sufficiently robust (in trials, at least) to obviate the need for plasma sampling within the licensed dose range (although in older patients, doses of 50–100mg a day may be sufficient) and adverse effects are usually well managed by dose adjustment alone. Plasma level monitoring is best reserved for those in whom clinical response is poor, adherence is questioned or in whom drug interactions or physical illness may make adverse effects more likely. Aripiprazole Plasma level monitoring of aripiprazole is sometimes undertaken in practice. The dose–response relationship for aripiprazole is well established with a plateau in clinical response and D2 dopamine occupancy seen in doses above approximately 10mg/day.37 Plasma levels of aripiprazole, its metabolite and the total moiety (parent plus metabolite) strongly relate linearly to dose, making it possible to predict, with some certainty, an approximate plasma level for a given dose.38 Target plasma level ranges for optimal clinical response have been suggested as 146–254mcg/L39 and 150–300mcg/L,40 with adverse effects more frequent above 210mcg/L.40 Inter-individual variation in aripiprazole plasma levels has been observed but not fully investigated, although gender appears to have little influence.41,42 Age, metabolic enzyme genotype and interacting medications seem likely causes of variation.40–43 A putative range of between 150 and 210mcg/L38 has been suggested as a target for patients taking aripiprazole and these are broadly the concentrations seen in patients receiving depot aripiprazole at 300 and 400mg monthly.44 Some authorities suggest a lower threshold for clinical effect of 100mcg/L32 – a plasma level usually afforded by an oral dose of 10mg a day33,45 and around the minimum level reached during treatment with 2-monthly depot.46 Clozapine Clozapine plasma levels are broadly related to daily dose47 but there is sufficient variation to make impossible any precise prediction of plasma level. Plasma levels are generally lower in younger patients, males48 and smokers49 and higher in Asians.50 Much lower doses of clozapine are required in East Asians,51,52 Indians53 and Bangladeshis.54 The prevalence of clozapine poor metabolisers is also higher in East Asians.55,56 A series of algorithms has been developed for the approximate prediction of clozapine levels according to patient factors and these are recommended.57 Dose prediction using genetic analysis is more accurate that algorithm prediction.58 Neither method can account for other influences on clozapine plasma levels such as changes in adherence, inflammation59 and infection.60,61 The plasma level threshold for acute response to clozapine has been suggested to be 200mcg/L,62 350mcg/L,63–65 370mcg/L,66 420mcg/L,67 504mcg/L68 and 550mcg/L.69 Limited data suggest a

level of at least 200mcg/L is required to prevent relapse.70 Substantial variation in clozapine plasma level may also predict relapse.71 Changes in

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