

216 - Faster titrations

Faster titrations

Schizophrenia and related psychoses CHAPTER 1 Alternatively, an attempt can be made to include other factors into the predictive models, such as cytochrome enzyme metaboliser status, ancestry and concurrent medication to predict target dose and corresponding titration schedule.^{2,6} The most accurate dose prediction is given by a genetic test that incorporates gene variant activity scores into a mathematical algorithm.⁷ Results from this test can be used to select a titration schedule from the four provided here by choosing the schedule with the calculated target dose closest to the final dose in the schedule. Clozapine should normally be started at a dose of 6.25mg – this is effectively a test dose for everyone. On subsequent days, the dose can be increased according to the selected schedule, provided the patient is tolerating clozapine. A flexible approach should be taken, altering schedules in response to adverse effects if needed (e.g. pausing titration, returning temporarily to a dose that was previously tolerated, or slowing the speed and/or reducing the magnitude of dose increases). Wherever possible, plasma concentration testing should be used in conjunction with adverse effect monitoring to inform dosing. Monitoring blood levels can help ensure that titration does not overshoot the target blood level. Use of point of care testing (delivering results within minutes) means this is possible without interrupting the dose regimen.^{8,9} If results cannot be obtained rapidly then levels should be checked when titration is complete or if adverse effects cause problems during titration. The dose should be divided (usually into two daily doses) and, if sedation is a problem, the larger portion of the dose can be given at night. The following tables outline four different starting regimens for clozapine. These are based on over 30 years' clinical experience and the published protocols described above. The concept behind the schedules is that every patient reaches, over 20 days, the lowest dose estimated to give a therapeutic blood concentration. The schedules should ensure that the rate of increase in clozapine plasma concentration is approximately the same for all people. This is important to note: the rate of dose increase may be very different in these schedules, but the rate of increase in blood concentration is the same. The reason we have moved away from providing a single titration schedule is because a single schedule has the opposite effect: the rate of change of plasma level will be vastly different for people with different metabolic capacities. More rapid increases than those suggested here have been used, as has an extremely slow titration (the 'Laitman protocol' allows dose increases of only 25mg per week). Slower titration may be necessary where sedation or other dose-related side effects are severe, in the elderly, the very young, those who are physically compromised or those who have poorly tolerated other antipsychotics. The target dose for patients with Asian ancestry should be around 65–75% of that given below. For older patients (>70 years), the target dose is around 50% of that given in the tables. Faster titrations The titration schedules listed here are aimed at maximising the likelihood of a successful titration – the aim is to

establish the patient on a well-tolerated and therapeutic dose of clozapine. Faster titrations can be used and have been widely used in the past. The main risk with faster titrations, assuming the patient tolerates such a regimen, is myocarditis (see section on clozapine: serious cardiovascular adverse effects in this chapter). If tolerability is not assumed, the main risk is titration failure resulting from the patient's inability or unwillingness to tolerate rapid titration.

216 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 1 Female non-smoker – target dose 225mg/day. Day Morning dose (mg) Evening dose (mg) Total daily dose (mg) – 6.25 6.25 – 6.25 6.25 6.25 6.25 6.25 12.5 6.25 12.5 18.75 12.5 12.5 6 12.5 12.5 7 25 8 25 9 50 10 50 11 50 12 50 13 75 14 75 15 75 16 75 17 100 18 100 19 100 20 100 Female smoker – target dose 300mg/day. Day Morning dose (mg) Evening dose (mg) Total daily dose (mg) – 6.25 6.25 6.25 6.25 12.5 12.5 12.5 4 12.5 12.5 5 25 6 25 7 50 8 50 9 50 10 50 11 75

Schizophrenia and related psychoses CHAPTER 1 Day Morning dose (mg) Evening dose (mg) Total daily dose (mg) 50 125 75 150 75 150 75 175 100 200 100 225 125 250 125 275 150 300 Male non-smoker – target dose 250mg/day. Day Morning dose (mg) Evening dose (mg) Total daily dose (mg) – 6.25 6.25 – 6.25 6.25 6.25 6.25 12.5 6.25 12.5 18.75 12.5 12.5 6 12.5 12.5 7 25 8 25 9 50 10 50 11 50 12 50 13 75 14 75 15 75 16 75 17 100 18 100 19 125 20 125

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