268 - Lithium

Lithium

Schizophrenia and related psychoses CHAPTER 1 Concurrent medications Different classes of medicines associated with haematological adverse effects are co- prescribed with clozapine. These include other antipsychotics, anticonvulsants such as sodium valproate and carbamazepine, antibacterials and GI agents such as proton- pump inhibitors. Many patients develop neutropenia on clozapine but not all are clozapine-related or even pathological. The possible contributory role of these agents should always be considered and these drugs discontinued if clozapine rechallenge is attempted.24 Management options Before treatment initiation, it is important to evaluate baseline haematological values. All patients should be genetically tested for BEN.25 In those already taking clozapine, there are three distinct patient groups: those with normal neutrophil counts, those with neutropenia unrelated to clozapine, and those with clozapine-related agranulocytosis. Here, we discuss options for the middle group – those with mild neutropenia unrelated to clozapine. The use of iatrogenic agents to elevate WCC in patients with clear prior clozapine-induced severe neutropenia or agranulocytosis (i.e. there is certainty that clozapine was the cause) is not recommended. Lithium or other medicines should only be used to elevate WCC where it is strongly felt that prior neutropenic episodes were unrelated to clozapine. Patients who have had a previous episode of agranulocytosis that is attributable to clozapine should not be rechallenged either with or without lithium. Lithium Lithium increases the neutrophil count and total WCC both acutely and chronically. The magnitude of this effect is poorly quantified, but a mean neutrophil count of 11.9×109/L has been reported in patients treated with lithium, and a mean rise in neutrophil count of 2×109/L was seen in patients treated with clozapine after the addition of lithium. This effect does not seem to be clearly dose-related, although a minimum lithium serum level of at least 0.4mmol/L may be required. The mechanism is not completely understood.26 Lithium has been used to increase the WCC in patients who have developed neutropenia while taking clozapine, allowing clozapine treatment to continue. Several case reports in adults27–31 and in children32,33 have been published. Almost all patients had plasma lithium levels of >0.6mmol/L. In a case series (n = 25) of patients who had stopped clozapine because of an apparent blood dyscrasia and were rechallenged in the presence of lithium, only one developed a subsequent dyscrasia.34 If considering lithium, discuss with the medical adviser at the relevant monitoring service to determine the optimum pharmacological strategy for the particular patient. Increased risk of neurological adverse effects such as myoclonus, ataxia and seizures should be considered when using the combination.35 Where there are valid concerns regarding neurotoxic effect, it may be prudent to use clozapine alone (off-licence) with US monitoring criteria (Figure 1.6).36

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