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Cardiomyopathy

254 The Maudsley® Prescribing Guidelines in Psychiatry CHAPTER 1 4 days until a daily dose of 75mg is reached.22 Dose increases (of 6.25mg) can then be made every 3 days after this point, and every 2 days after reaching a daily dose of 150mg. Autopsy findings suggest that fatal myocarditis can occur in the absence of clear cardiac symptoms, although tachycardia and fever are usually present.48 A monitoring programme which is said to detect 100% of symptomatic cases of myocarditis49 using measurement of troponin I or T and CRP has been developed (Table 1.56). The additional measuring of NT-proBNP (an indicator of cardiac failure) and continuing cardiac and blood marker monitoring for 8 weeks have also been suggested50 (5-8% of cases occur in the second month of treatment,50,51 almost all of these in weeks four to six).52 Echocardiography at baseline, 6 months and yearly thereafter is routine practice in Australia, although the benefit of this monitoring in the absence of other symptoms has been questioned.53 Baseline echocardiography may at least be useful to establish a comparator if concerns arise later, especially in those with known cardiac disease, structural abnormalities or other cardiac risk factors.54 The absence of resources to provide monitoring beyond routine blood tests (including CRP and troponin) and ECG should not be a barrier to prescribing for most patients.20 Factors that may increase the risk of developing myocarditis include rapid titration, concurrent use of sodium valproate55 and older age (31% increased risk for each additional decade).56 Other psychotropics, including lithium, risperidone, haloperidol, chlorpromazine and fluphenazine, have also been associated with myocarditis.57 It is probably preferable to avoid concomitant use of other medicines that may contribute to the risk, but this may be practically difficult. Any pre-existing cardiac disorder, previous cardiac event, use of illicit drugs15 or family history of cardiac disease should provoke extra caution. Cardiomyopathy Cardiomyopathy is usually diagnosed from echocardiography to establish left ventricular dilatation (resulting in a reduced ejection fraction) and/or hypertrophy. It may develop following myocarditis (if clozapine is not stopped), but other causative factors may include persistent tachycardia, obesity, diabetes and previous personal or familial cardiac events.21 Long-term clozapine seems to induce cardiac myocyte autophagy and structural remodelling of the heart.58 Most incidence data originate from Australia and range from 0.02 to 5%.16,59 Meta-analysis suggests an event rate of 6 per 1,000 patients, with a case fatality rate of 7.8%.23 Cardiomyopathy occurs later in treatment than myocarditis (median 9 months)24 but, as with myocarditis, it may occur at any time. Cardiomyopathy should be suspected in any patient showing signs of heart failure, which should provoke immediate cessation of clozapine and referral. Presentation of cardiomyopathy varies somewhat60,61 and is often asymptomatic in the early stages,16 so any reported symptoms of palpitations, chest pain, syncope, sweating, decreased exercise capacity or breathing difficulties should be closely investigated. Successful

rechallenge with rigorous cardiac monitoring (including ECHO) and instigation of disease-modifying cardiac medications may be possible,39,62–66 including in cases of pre-existing cardiomyopathy or heart failure (as opposed to clozapine-induced cardiomyopathy). Despite an overall reduction in mortality, younger patients may have an increased risk of sudden death,67 perhaps because of clozapine-induced ECG changes.68 There may, of course, be similar problems with other antipsychotics.57,69,70

Schizophrenia and related psychoses CHAPTER 1 Table 1.56 Suggested monitoring for myocarditis.22,49,71,72 Baseline* Pulse, BP, temperature, respiratory rate FBC CRP Troponin Echocardiography (if available) ECG Daily, if possible Pulse, BP, temperature, respiratory rate Ask about: chest pain, fever, cough, shortness of breath, exercise capacity On days 7, 14, 21, and 28 CRP Troponin FBC ECG if possible If CRP >100mg/L or troponin > twice upper limit of normal Stop clozapine; repeat echo NT-proBNP If fever + tachycardia* + raised CRP or troponin (but not as above) Daily CRP and troponin measures NT-proBNP * Tachycardia is not a good indicator of myocarditis – almost all cases have tachycardia, but tachycardia is very common in people who do not have myocarditis.52 CRP, C-reactive protein; NT-proBNP, N-terminal pro b-type brain natriuretic peptide.

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