251 - Myocarditis

Myocarditis

Schizophrenia and related psychoses CHAPTER 1 Clozapine: serious cardiovascular adverse effects Thromboembolism Over 30 years ago a possible association between clozapine and thromboembolism was first suggested.1,2 Later, data from Sweden3 suggested the risk of thromboembolism was 1 in 2,000 to 1 in 6,000 patients treated. Thromboembolism may be related to clozapine's effects on antiphospholipid antibodies4 and platelet aggregation.5 It seems most likely to occur in the first 6 months of treatment6 but can occur at any time. The risk may be independent of dose,6 but some studies suggest a correlation with higher doses.7 Other antipsychotics are also strongly linked to thromboembolism,8 although clozapine may present the highest risk.7,9 With all drugs, the causes of thromboembolism are probably multifactorial.10 Sedation may lead to a reduction in movement and consequent venous stasis. Obesity, hyperprolactinaemia and smoking are additional independent risk factors for thromboembolism.11,12 Encouraging exercise and ensuring good hydration are essential precautionary measures.13 Myocarditis Clozapine is associated with myocarditis and cardiomyopathy. Myocarditis is a hypersensitivity response to clozapine, resulting in inflammation of the myocardium. Some debate surrounds the prevalence of myocarditis, with several Australian studies reporting an incidence of 3%14–16 and one finding a rate of 9.8%.17 Studies conducted outside Australia18–20 have suggested an incidence of 1% or less. The reason for such variation is unclear but it may be that a lack of robust monitoring leads to missed diagnoses in those countries reporting lower incidences.21 Geography, environment and higher starting doses may also play a role.17,22 A 2020 meta-analysis suggested an event rate of less than 1% – 7/1,000 patients.23 Myocarditis is potentially fatal (case fatality rate of 12.7%)23 and is most likely to occur in the first 6–8 weeks of starting clozapine treatment (median 3 weeks),24 but may occur at any time. Despite uncertainty over incidence, all patients should be closely monitored for signs and symptoms of myocarditis especially in the first few months of treatment.25 Symptoms include hypotension, tachycardia, fever, flu-like symptoms, fatigue, dyspnoea (with increased respiratory rate) and chest pain.26 Signs include ECG changes (ST depression), enlarged heart on radiography/echo and eosinophilia. Many of these symptoms occur in patients on clozapine not developing myocarditis27 and, conversely, their absence does not rule out myocarditis.28,29 Nonetheless, signs of heart failure should provoke immediate cessation of clozapine and referral to a cardiologist. Rechallenge has been successfully completed29–36 (the use of beta blockers, ACE inhibitors and mineralocorticoid receptor antagonists may help)37–39 but recurrence is also possible.29,40–43 Published cases suggest a success rate of 62%.44 Use of echocardiography, measurement of CRP and troponin are obviously absolutely essential in cases of rechallenge.45–47 Effective treatment of comorbid metabolic syndrome and diabetes may also help.23 Most cases of successful rechallenge employ a very slow rate of titration.44 One proposed schedule is to limit dose

increases to 6.25mg increments every

Revision #1
Created 2026-01-04 20:13:28 UTC by Omar Ayman
Updated 2026-01-04 20:13:28 UTC by Omar Ayman