



Myocardial complications of clozapine

VCCAMM has recently received a report of a patient who had been taking clozapine and developed persistent, drug resistant hypotension after induction of anaesthesia. It would appear that the association between clozapine and myocardial damage is not widely known and the following review is therefore provided.

The association between clozapine and myocardial complications was first reported in the Lancet by Australian doctors in 1999 (1). Since then this association has been confirmed in a review article in the NEJM 2001(2). Clozapine is a unique antipsychotic acting weakly at D2 receptors, strongly at D4 and exhibiting potent serotonin and noradrenergic antagonism. Its main indication is for patients with schizophrenia who do not respond adequately to other antipsychotics. It was recognised initially that clozapine can cause agranulocytosis and all patients have regular blood count screening, especially within the first 18 months of treatment.

The myocardial sequelae of clozapine appear to involve at least two discernible patterns. Myocarditis occurs in the first month of treatment and is found in about 1:500 young adult patients. This is about 80 times more common than in the general population. The median time to onset of symptoms is 15 days and corresponds to acute hypersensitivity myocarditis with eosinophilic infiltrates seen histologically.

The second pattern seen is that of dilated cardiomyopathy that may have resulted from previously unrecognised acute myocarditis. It is more commonly seen after 8 weeks of treatment. The incidence appears to be about 5:10,000 and is about five times more common than in the general population.

MIMS contains a boxed warning in its section on clozapine.

Myocarditis/ cardiomyopathy. Cases of myocarditis, some of which have been fatal and cardiomyopathy have been reported in patients on clozapine (see Precautions and Adverse Reactions, full PI).”

Patients commenced on clozapine must be in a monitoring program. This was commenced to monitor the onset of agranulocytosis but now includes cardiac complications. Recommendations from the Western Australian Psychiatric Drugs Committee 2006 include an ECG at 14 days and thereafter as indicated, troponin at day 7 and 14 as then as indicated, and echocardiogram at baseline and at 6 months. Full blood count is recommended weekly for 18 months and then monthly.

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In conjunction with and endorsed by VCCAMM.

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References:

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