Monitoring Patients With Psychotic Disorders for Clozapine-Induced Myocarditis or Cardiomyopathy

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Questions or requests for information about this report can be directed to requests@cadth.ca
Key Messages

- No literature was identified regarding the diagnostic accuracy of high-sensitivity troponin I testing versus troponin T testing for detecting myocarditis or cardiomyopathy in patients receiving clozapine for psychotic disorders.
- Four evidence-based guidelines were identified regarding the use of clozapine for patients with psychotic disorders.

Research Questions

1. What is the diagnostic accuracy of high-sensitivity troponin I testing versus troponin T testing for detecting myocarditis or cardiomyopathy in patients receiving clozapine for psychotic disorders?
2. What are the evidence-based guidelines on the use of clozapine for patients with psychotic disorders?

Methods

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE, the Cochrane Database of Systematic Reviews, the international HTA database, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy comprised both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were Troponin I (cTn-I) testing and clozapine. No filters were applied to limit the retrieval by study type for question 1. CADTH-developed search filters were applied to limit retrieval to health technology assessments, systematic reviews, meta-analyses, or network meta-analyses, and guidelines for question 2. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 1, 2016 and May 17, 2021. Internet links were provided, where available.

Selection Criteria

One reviewer screened literature search results (titles and abstracts) and selected publications according to the inclusion criteria presented in Table 1. Full texts of study publications were not reviewed. Open access full-text versions of evidence-based guidelines were reviewed when abstracts were not available.

Results

Four evidence-based guidelines were identified regarding the use of clozapine for patients with psychotic disorders.1-4 No health technology assessments, systematic reviews, randomized controlled trials, or non-randomized studies were identified regarding the diagnostic accuracy of high-sensitivity troponin I testing versus troponin T testing for detecting myocarditis or cardiomyopathy in patients receiving clozapine for psychotic disorders.
testing for detecting myocarditis or cardiomyopathy in patients receiving clozapine for psychotic disorders.

Additional references of potential interest that did not meet the inclusion criteria are provided in Appendix 1.
References

Health Technology Assessments
No literature identified.

Systematic Reviews and Meta-analyses
No literature identified.

Randomized Controlled Trials
No literature identified.

Non-Randomized Studies
No literature identified.

Guidelines and Recommendations
   See: Table 3. Antipsychotic medications: available oral and short-acting intramuscular formulations and dosing considerations – Clozapine (p.37); Initiation of Treatment With an Antipsychotic Medication (p.64-65); Monitoring During Treatment With an Antipsychotic Medication (p.66-67); Myocarditis and Cardiomyopathy (p.69); Statement 7: Clozapine in Treatment-Resistant Schizophrenia (p.88-96)

   See: Pharmacological Treatments (p.32-35); Pharmacological treatments (recommendations 1.9.9 to 1.9.19) (p.68-69)

3. German Association for Psychiatry, Psychotherapy and Psychosomatics, DGPPN. S3 Guideline for schizophrenia. 2019 https://www.dgppn.de/_Resources/Persistent/b794e8f9cbdf0d761b26cb1b323b6518bc99e/038-00fe_S3_Schizophrenie_2019-03.pdf Accessed 2021 May 20.
   See: 5.3 Therapeutic Drug Monitoring (TDM) – Recommendation 20, 21 (p.25); Table 7: Recommended oral doses of various antipsychotics in acute treatment (p.27); 5.4 – Dose, determining the lowest possible dose, treatment frequency and discontinuation (p.29-30); Table 9 (p.40)

   See: 8.3.4 – Haematological effects (p.144)
Appendix 1: References of Potential Interest

Previous CADTH Reports

Systematic Reviews and Meta-analyses

Monitoring for Clozapine-Induced Myocarditis or Cardiomyopathy — Troponin Test Not Specified

Alternative Population — Patients with Psychotic Disorders Not Specified

Systematic Review of Guidelines

Non-Randomized Studies

Accuracy of High-Sensitivity Troponin I Testing for Alternative Cardiac Conditions — Not Specific to Patients with Psychotic Disorders

Guidelines and Recommendations

Alternative Methodology — Chart Reviews

Alternative Methodology — Based on Other Guidelines

Alternative Methodology — Expert Opinion

Unclear Methodology
See: Initiating clozapine; Plasma clozapine and norclozapine monitoring; Drug-drug interactions; Age, sex, body weight, and clozapine dose requirement; Myocarditis and cardiomyopathy

See: Myocarditis (p.31-35)


See: Initiating clozapine for treatment-resistant schizophrenia (p.1-2); Monitoring and managing the adverse effects of clozapine (p.2); Monitoring patients for cardiac toxicity (p.3-4); Table 2: Recommended schedule for managing patients treated with clozapine (p.6)

See: Protocols – Commencing Clozapine, Ongoing Participant Monitoring (p.5-17)

See: 5. The administration, monitoring and prescribing of clozapine therapy (p.5-19), Appendix 1 - Protocol for monitoring patients commenced on clozapine for clozapine-induced myocarditis (p.22)

**Diagnostic Accuracy of High-Sensitivity Troponin I Testing for Ruling Out Myocardial Infarction – Not Specific to Patients with Psychosis Disorders**

See: Comparative diagnostic accuracy for more than 1 test (p.20-21)

**Review Articles**

**Clozapine-Induced Myocardopathy and Myocarditis**

See: Figure 1: Proposed protocol for monitoring patients commenced on clozapine for clozapine-related cardiomyopathy, myocarditis and pericarditis


**Additional References**