TITLE: Hepatitis C Polymorphism Testing: A Review of the Clinical Evidence

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CONTEXT AND POLICY ISSUES

Hepatitis C infection is a considerable public health problem worldwide,[1] with considerable costs associated with treatment of the disease and its sequelae.[2] In Canada, the prevalence of hepatitis C infection was estimated to be 0.78% in 2007, with the expectation that this rate would continue to increase.[3] Most commonly transmitted through injection drug use,[3] 75 to 80% of infected individuals develop chronic hepatitis C (CHC).[4] Though infected individuals are largely asymptomatic, chronic hepatitis C can progress to liver cirrhosis, hepatocellular carcinoma, decompensated liver disease and premature death.[1,4] In persons aged 35 to 59 who received a liver transplant, the most common primary diagnosis for transplantation was hepatitis C[5] Therefore, effective management of chronic hepatitis C is essential to overcoming this growing health care burden[6].

The hepatitis C virus (HCV) has six major genotypes, with genotype 1, and its subtypes 1a and 1b, being primarily found in North America.[6,7] In the past, treatment of genotype 1 HCV with a combination of peginterferon alfa and ribavirin was suboptimal, with sustained virological response (SVR) rates of approximately 40%.[8] Recent major advances in the treatment of hepatitis C, with the introduction of direct-acting antivirals (DAAs) being used in triple combination therapy, have changed the treatment landscape.[9] Simeprevir (brand name: Galexos), a NS3/4A protease inhibitor like the already available DAAs telaprevir and boceprevir, was recently approved by Health Canada for the treatment of chronic hepatitis C genotype 1 infection, in combination with peginterferon alfa and ribavirin in adults with compensated liver disease, including cirrhosis, who are treatment-naïve or who have failed previous interferon therapy (peglyated or non-pegylated) with ribavirin.[10] Phase 3 studies in patients with genotype 1 chronic hepatitis C, simeprevir in combination with peginterferon alfa and ribavirin has shown significantly higher SVR at week 12 of treatment (SVR12) rates as compared to placebo in combination with peginterferon alfa and ribavirin.[11]

Genetic polymorphisms, more specifically the Q80K mutation, have been found to affect SVR12 rates of simeprevir.[12] Found primarily in HCV subtype 1a with prevalence up to 48% in North America,[10,12,13] the Q80K mutation is a naturally occurring amino acid substitution in the viral

NS3 region.[6] In a pooled analysis of phase 3 studies of treatment-naïve genotype 1a HCV patients treated with simeprevir in combination with peginterferon and ribavirin, those with Q80K polymorphism at baseline had lower rates of SVR12 compared to those who did not have the polymorphism (58.3% vs. 83.6%, respectively).[12] Given the impact of this polymorphism on simeprevir efficacy, the product manufacturer for simeprevir recommends that, when accessible, testing for Q80K polymorphism in patients with HCV genotype 1a be considered.[10]

This report will review the diagnostic accuracy of laboratory tests for the Q80K polymorphism.

RESEARCH QUESTION

What is the accuracy of laboratory tests for the identification of Q80K polymorphism in patients with hepatitis C virus genotype 1?

KEY FINDINGS

No evidence regarding the diagnostic accuracy of laboratory tests for hepatitis C Q80K mutation was identified.

METHODS

Literature Search Strategy

A limited literature search was conducted on key resources including PubMed, The Cochrane Library (2014, January), University of York Centre for Reviews and Dissemination (CRD), OVID's Medline and Embase databases, Canadian and major international health technology agencies, as well as a focused Internet search. No methodological filters were applied to limit retrieval. Where possible, retrieval was limited to the human population. The search was also limited to English language documents published between January 01 2009 and January 23 2014.

Selection Criteria and Methods

One reviewer screened the titles and abstracts of the retrieved publications and evaluated full-text publications for the final article selection, according to the selection criteria presented in Table 1.

Table 1: Selection Criteria

Population	Patients with Hepatitis C virus genotype 1
Intervention	Tests for Hepatitis C Q80K mutation (e.g. HCVGenoSure)
Comparator	None specified
Outcomes	Diagnostic accuracy
Study Designs	Health Technology Assessments, systematic review, meta-analysis, randomized controlled trials, and non-randomized studies

Exclusion Criteria

Studies were excluded if they did not meet the criteria described in Table 1. Furthermore, they were excluded if they were duplicate reports of the same study or were published prior to 2009.

SUMMARY OF EVIDENCE

Quantity of Research Available

There were 39 studies identified in the literature search and 26 reports retrieved from the grey literature search. Thirty potentially relevant reports were retrieved for scrutiny. No publications were selected for inclusion into the report. Appendix 1 describes the PRISMA flowchart of the included studies in the report.

Summary of Findings

No relevant literature was found regarding the diagnostic accuracy of laboratory tests for hepatitis C Q80K mutation. Therefore, no summary can be provided.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING

No conclusions can be made regarding the diagnostic accuracy of hepatitis C Q80K mutation testing due to the lack of evidence.

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APPENDIX 1: Selection of Included Studies