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Hepatitis C Screening

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ABSTRACT

Background: Hepatitis C screening is now recommended for all individuals born between the years 1945-1965 in addition to individuals who have high-risk factors. Although most clinicians have extensive experience with the diagnosis and treatment of the disease, they have limited experience screening for it.

Methods: We report current screening guidelines and methods.

Results: By identifying the disease as early as possible, screening and treatment can reduce morbidity and mortality.

Conclusion: Screening for hepatitis C leads to the appropriate evaluation and treatment of individuals chronically infected with the hepatitis C virus and prevents the progression of liver disease to cirrhosis, hepatocellular carcinoma, and the associated morbidity and mortality. Screening for hepatitis C is also cost effective.

INTRODUCTION

Hepatitis C screening is now recommended for all individuals born between the years 1945-1965 in addition to individuals who have high-risk factors. Screening for hepatitis C leads to the appropriate evaluation and treatment of individuals chronically infected with the hepatitis C virus (HCV) and prevents the progression of liver disease to cirrhosis, hepatocellular carcinoma, and the associated morbidity and mortality.

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HEPATITIS C

Of individuals infected with HCV, 15%-20% experience spontaneous recovery, while the remaining 75%-85% progress to chronic hepatitis C.[1,2] When the virus is first detected, individuals with chronic infection may have no symptoms and perhaps mild to moderate liver fibrosis. Over time, however, approximately 60% of individuals with chronic infection progress to advanced fibrosis and cirrhosis. Of individuals with advanced fibrosis or cirrhosis, approximately 5% develop hepatocellular carcinoma within a 5-year period.[3] In addition to increasing mortality,[1,2] hepatitis C infection with liver failure or liver cancer is the leading cause of liver transplantation worldwide.[4,5] Chronic hepatitis C infection in the United States affects approximately 5 million individuals[6] with an annual incidence of 17,000 new infections,[7] indicating that hepatitis C is clearly an important health problem.

Treatment of chronic hepatitis C has evolved over the last two decades, with 90%-100% of individuals now being cured.[8-13] Elimination of HCV either by the individual's natural immune mechanisms or by achieving sustained virologic response (SVR), defined as undetectable HCV ribonucleic acid (HCV RNA) in the blood for 6 months after stopping treatment, prevents progression to cirrhosis and development of hepatocellular carcinoma. Significant advances have been made in reducing adverse effects and duration of treatment. In many healthcare facilities, treatment can be administered by nurse practitioners and physician assistants as well as physicians, making treatment available to more individuals in an efficient manner. Today, once individuals with hepatitis C are identified, they are able to receive highly effective treatment.

SCREENING FOR HEPATITIS C

Although most clinicians have extensive experience with the diagnosis and treatment of disease, they have limited experience with screening for disease. Screening is characterized by interventions in a group of individuals with no signs or symptoms of disease to identify unrecognized disease. The hope is that by identifying the disease before the onset of signs or symptoms, morbidity and possibly mortality

can be reduced. Screening is not intended to be diagnostic; its main purpose is to detect the possibility of disease. The fact that screening is typically performed on healthy individuals can account for some of the limited experience on the part of clinicians.

The 2 most common types of screening are universal screening and selective screening. Universal screening involves screening all individuals in a certain category, such as all individuals above a certain age. Selective screening involves screening individuals who have a high risk for the disease, such as having family members with a known hereditary disease.

The World Health Organization has issued the following guidelines for screening:[14]

1. The condition should be an important health problem.
2. There should be a treatment for the condition.
3. Facilities for diagnosis and treatment should be available.
4. There should be a latent stage of the disease.
5. There should be a test or examination for the condition.
6. The test should be acceptable to the population.
7. The natural history of the disease should be adequately understood.
8. There should be an agreed policy on whom to treat.
9. The total cost of finding a case should be economically balanced in relation to medical expenditure as a whole.
10. Case-finding or selective screening should be a continuous process, not just a ''once and for all'' project.

Screening for hepatitis C is performed by measuring antibody to HCV (anti-HCV) in a person's serum. A positive test (detection of the antibody) is not a diagnosis of the disease; it only indicates that a person was previously exposed to hepatitis C. The currently available screening test has a sensitivity of at least 97% and a specificity of 100%.[15,16] A sensitivity of 97% indicates that the screening test will detect at least 97% of individuals who have been exposed. A specificity of 100% indicates that 100% of individuals without hepatitis C had a negative screening test with no false-positive test results. The screening test could be modified to increase the sensitivity and reduce the specificity because false-positive test results can be detected easily by measuring HCV RNA in the serum.

Currently, the US Centers for Disease Control and Prevention (CDC)[17] and the US Preventive Services Task Force[18] recommend screening for hepatitis C for 2 groups of individuals:

- All individuals born in the years 1945-1965.[17] This universal screening recommendation is based on the finding in the National Health and Nutrition Examination Survey that approximately 75% of persons with a positive screening test and chronic HCV infection were born during the years 1945-1965.[19,20]
- Individuals with at least 1 of the following risk factors.[21-23] This selective screening recommendation applies to at-risk individuals who
  1. have ever injected illegal drugs, including those who injected once or a few times many years ago and do not consider themselves drug users.
  2. received clotting factor concentrates produced before 1987.
  3. received blood or organs before July 1992.
  4. have been notified that they received blood from a donor who later tested positive for HCV infection.
  5. have ever been on chronic hemodialysis.
  6. have a persistently abnormal alanine aminotransferase (ALT) level.
  7. were born to an HCV-positive mother.
  8. have human immunodeficiency virus (HIV) infection.
  9. have had a needle-stick injury or mucosal exposure to HCV-positive blood (healthcare, emergency medical, and public safety workers).

Benefits of Screening for Hepatitis C

If individuals with chronic hepatitis C are identified before they develop advanced fibrosis, cirrhosis, or hepatocellular carcinoma, 90%-100% can now be expected to respond to treatment, whereas previously only 66%-75% of individuals responded to treatment.[8-13,24-27] Thus, detecting individuals with hepatitis C before they develop signs or symptoms of the disease can have an important impact on their subsequent clinical course. Sustained virologic clearance for more than 6 months after treatment of hepatitis C is also associated with a reduction in all-cause mortality.[28]

Drawbacks to Screening for Hepatitis C

A patient's worry or anxiety while waiting for test results, concerns about insurance coverage of evaluation and treatment, adverse effects of treatment, and complications associated with liver biopsy can limit screening for hepatitis C. However, the accuracy of HCV RNA testing, the availability of medication assistance programs for uninsured patients, and improved treatments with fewer side effects and shorter duration should allay some of the anxiety associated with the screening process.

Limitations of Screening for Hepatitis C

Barriers to screening for hepatitis C include limited access to healthcare, inadequate health insurance coverage, individuals' decreasing recall of past risky behaviors, lack of knowledge of hepatitis C prevalence, natural history, and available tests and treatments for hepatitis C at the provider level.[29-32] Moreover, nearly 42% of primary care physicians reported being unfamiliar with the CDC guidelines in a survey of community-based physicians.[33]

Evaluation of Individuals with Positive Screening Test

Patients with a positive screening test for anti-HCV antibody should be tested for serum HCV RNA. Serum HCV RNA quantifies the amount of viral RNA in serum and indicates ongoing infection. If HCV RNA is detectable, tests should be performed to determine the extent of hepatic fibrosis. These tests typically include liver biopsy or noninvasive measures, such as biochemical markers of fibrosis (ie, FIBROSpect, FibroSURE, or aspartate transaminase to platelet ratio index [APRI] score) or transient elastography.[34,35] An ultrasound of the abdomen should also be performed to identify the possible presence of cirrhosis and focal lesions in the liver suspicious for hepatic malignancy.

Patients who have a positive anti-HCV on a screening test but have no detectable HCV RNA should have a confirmatory HCV RNA test a few months later. If HCV RNA remains undetectable, these individuals should be reassured that they do not have hepatitis C infection and that the anti-HCV may remain persistently positive. Such individuals have either cleared the virus or the true specificity of the test is lower than the reported 100%[15,16] and the test result was a false positive.

Potential Sites for Screening for Hepatitis C

Screening for hepatitis C can be offered in several venues; the most likely are primary care offices, emergency rooms, urgent care clinics, and public health fairs.

Following the CDC recommendation, 3 studies were presented at the 2013 meeting of the American Association for the Study of Liver Diseases in Washington, DC. One study was conducted in an emergency department, the second in the outpatient clinics of the US Department of Veterans Affairs, and the third involved individuals undergoing screening colonoscopies for colorectal cancer at a community hospital.[36-38] All 3 studies confirmed the higher prevalence of positive serum anti-HCV in individuals born in the years 1945-1965.

Other Indications for Measuring Anti-HCV

In addition to screening, measuring anti-HCV can be useful in patients with symptoms of chronic liver disease; patients who have other viral infections, including chronic fatigue, hepatitis B, HIV, intermittently abnormal ALT, or cirrhosis found on imaging tests; or patients undergoing evaluation for organ transplantation.

COST EFFECTIVENESS

It is often difficult to know the exact cost of medical tests because of the lack of transparency and negotiated pricing by insurance companies.[39] Nevertheless, the screening test for hepatitis C, anti-HCV antibody, offered by testing facilities or advertised on the internet costs $45-$80 for uninsured individuals and less when covered by insurance.

A US study by Rein et al in primary care settings evaluated the cost effectiveness of universal screening for hepatitis C antibodies in individuals born between the years 1945-1965. The study found that compared to selective screening of subjects with at least 1 risk factor, universal screening identified nearly 800,000 additional cases of potential chronic hepatitis C at a screening cost of $2,874 per case identified.[40] Assuming that universal screening is followed by effective treatment, a study by Hagan et al[41] evaluated the cost effectiveness of treatments for chronic hepatitis C. Using a decision-analytic Markov model with a lifetime, societal perspective to evaluate the cost effectiveness of an all-oral drug regimen compared to an interferon-based regimen, the study showed the all-oral regimen dominated the interferon-based regimen across a range of willingness-to-pay thresholds with an incremental cost-effectiveness ratio of $44,514/quality-adjusted life-year. The all-oral treatment was also cost effective across all genotypes.[41]

CONCLUSION

Screening for hepatitis C is recommended for high-risk individuals as well as for everyone born between 1945-1965. Screening for hepatitis C leads to the appropriate evaluation and treatment of individuals chronically infected with the hepatitis C virus, preventing the progression of liver disease to cirrhosis and hepatocellular carcinoma and the associated morbidity and mortality. Hepatitis C screening is cost effective.

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