Screening for Hepatitis B Virus Infection: A Brief Evidence Update for the U.S. Preventive Services Task Force

Methods

This brief update is based on a review of English-language articles published in MEDLINE®, the Cochrane Library, and the National Guideline Clearinghouse between 1994 and 2001. The search was further limited to Abridged Index Medicus publications. The search reviewed direct evidence on the characteristics of screening tests and the benefits and harms of routine screening for hepatitis B virus (HBV) infection, as well as the benefits and harms of screening individuals at high risk. The search identified new confirmatory evidence for the universal screening of pregnant women and for childhood immunization programs. Currently, there is limited evidence that screening and immunizing persons at high risk reduces the transmission or the population incidence of HBV infection.

The search was limited to randomized controlled trials (RCTs), meta-analyses, systematic reviews, editorials, and commentaries concerning the key questions. The populations considered were pregnant women, infants, asymptomatic individuals, and high-risk, asymptomatic persons. Studies were excluded if they did not meet the inclusion criteria or if they did not pertain to populations in the United States. No new RCTs, meta-analyses, or systematic reviews of the evidence for screening in the general population were found.

Search terms included hepatitis B, screening, pregnancy, infants, neonate, asymptomatic, immunization, general, high, risk, morbidity, mortality, liver, hepatocellular carcinoma, prevent as a truncated term, and universal. The MeSH terms hepatitis B and screening were exploded, while the remaining terms were used for free-text searches. The search yielded no RCTs meeting the inclusion criteria, 12 review articles, and 1 observational study. Only 1 article directly addressed 1 of the key questions.

Key Questions and Results

1. Is there new evidence of harms or reduced benefits from the universal screening of pregnant women?

No studies were identified that indicate new harms or reduced benefits from the universal screening of pregnant women or for the current management of infants born to hepatitis B surface antigen (HBsAg)-positive women since the U.S. Preventive Services Task Force (USPSTF) reviewed the evidence in 1996. New evidence supports

Systematic Evidence Reviews serve as the basis for U.S. Preventive Services Task Force (USPSTF) recommendations on clinical prevention topics. The USPSTF tailors the scope of these reviews to each topic. The USPSTF determined that a brief, focused evidence review was needed to assist in updating its 1996 recommendations on screening for hepatitis B virus infection.[1] This brief evidence update was written by Ramesh Krishnaraj.

To assist the USPSTF, the Research Triangle Institute-University of North Carolina (RTI-UNC) Evidence-based Practice Center, under contract to the Agency for Healthcare Research and Quality (AHRQ), performed a targeted review of the literature from 1994 to 2001. This brief evidence update and the updated recommendation statement[2] are available through the AHRQ Web site (www.preventiveservices.ahrq.gov), and in print through subscription to the *Guide to Clinical Preventive Services, Third Edition: Periodic Updates.* The subscription costs $60 and can be ordered through the AHRQ Publications Clearinghouse (call 1-800-358-9295, or e-mail ahrqpubs@ahrq.gov). The recommendation is also posted on the Web site of the National Guideline Clearinghouse™ (www.guideline.gov).

current practice of continuing to immunize such infants with the HBV vaccine and hepatitis B immune globulin (HBIG). In a cohort study in Italy, Mele and colleagues found that HBV vaccine and HBIG are effective in providing immediate and long-term protection against HBV infection in children born to HBsAg-positive mothers.[3]

2. Is there new evidence that screening and immunizing the general population for HBV infection, or that universal screening and immunizing infants and children, can reduce the morbidity and mortality associated with the chronic carrier state of HBV infection?

No studies were identified that address the question of whether routine screening of asymptomatic persons in the clinical setting is an effective method of reducing HBV infection in the general population. However, McQuillan and colleagues showed that the prevalence of HBV infection has not significantly decreased despite the availability of the HBV vaccine.[4]

No studies were identified that address the question of whether early screening and detection of HBV infection in the general population reduces the morbidity and mortality associated with the chronic carrier state of HBV infection. New evidence does support the potential benefits of universal screening and immunization programs in reducing the chronic carrier state and the new infection rate in children and adolescents.[5] This descriptive analysis in Taiwan showed that since the universal vaccination program began in 1984, the prevalence of HBsAg among persons younger than 15 years of age was reduced from 9.8% in 1984 to 0.7% in 1999. (Taiwan's universal program includes vaccinating children through adolescence.) Chang et al,[6] in a retrospective population study using a national cancer registry, showed that the incidence of hepatocellular carcinoma (HCC) in children has declined since Taiwan instituted its program of universal hepatitis B vaccination. Incidence declined from 0.52 among children born between 1974 and 1984 to 0.13 among children born between 1984 and 1986 ($P < 0.001$, rates reported per 100,000 children aged 6–14 years). However, these studies were conducted in an area hyperendemic for HBV infection and may not be generalizable to the United States, where the true prevalence of HBV infection has been difficult to assess.

3. Is there new evidence of the benefits or harms associated with screening adolescents and high-risk individuals so they can be immunized against HBV infection?

No studies were identified that address the effectiveness of routine screening of adolescents and high-risk individuals for the purposes of referral for HBV vaccination. Some studies (including Osterholm et al[7]) support the assertion that selective vaccination of high-risk persons does not significantly reduce HBV transmission in the general population. One review article noted that most new cases of HBV infection were occurring in individuals who did not acknowledge any risk factors, even after the vaccine was introduced.[8] The Centers for Disease Control and Prevention (CDC) found that roughly one-third of all new cases of acute HBV infection occur in individuals with no identifiable risk factors and in which the mode of transmission is unknown.[9] Nevertheless, a review article from the Hepatitis Branch of the CDC suggested that efforts to target adolescents, young adults, and high-risk individuals for screening and selective immunization may help to accelerate the elimination of HBV transmission in the United States.[10] Recent data indicate that the majority of HBV transmission and the morbidity associated with acute HBV infection in the United States occur among older adolescents and young adults and result mostly from sexual transmission.[11]

4. Is there evidence indicating that risk assessment tools to identify persons at high risk for HBV infection are valid?

There is no compelling evidence validating the accuracy of the risk assessment tools used to define persons at high risk for HBV infection. There are no studies describing different tools. Most studies include high risk as a self-reported value, making it difficult to discriminate between truly high-risk individuals and those not disclosing their risk factors. This, in turn, makes it difficult to discriminate between absolute risk and relative risk for HBV infection when evaluating the cost-effectiveness of pre-immunization screening for HBV infection.[12]

Summary

An estimated 2 billion people worldwide are infected with the hepatitis B virus, 350 million of whom are chronic carriers. Many will go on to develop progressive liver disease, with significant morbidity and mortality associated with the disease. In the United States, the burden of suffering remains substantial and may be underestimated for the very reason that screening is performed in unidentified carriers. The recommendations of the USPSTF aim to reduce the incidence of new disease and the transmission of the virus through a concerted effort by clinicians, the public health service, and the general public. Universal immunization of infants appears to be the most effective means to reduce the pool of potential transmitters of disease, although there remains an adult and adolescent population at high risk for infection. No ongoing research on screening or immunization for HBV infection was identified.

Recommendations of Other Groups

The Advisory Committee on Immunization Practices (ACIP) and the American Academy of Family Physicians recommendations on screening for HBV infection can be accessed at: http://www.cdc.gov/nip/ACIP.

The American College of Obstetricians and Gynecologists recommendations on screening for HBV infection were published in: *Guidelines for Perinatal Care.* American Academy of Pediatrics/ACOG. 5th ed. Elk Grove Village, IL; American Academy of Pediatrics. 2002.

The American Academy of Pediatrics recommendations on screening for HBV infection can be accessed at: http://search.aap.org/aap/CISPframe.html?url=http://www.cispimmunize.org/fam/hepb/whofact.html and http://www.aap.org.

The American College of Physicians-American Society of Internal Medicine recommendations on screening for HBV infection can be accessed at: http://www.acponline.org/aii/hepb.htm and http://www.acponline.org/index.html.

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