Preventing Hepatitis B in People in Close Contact with Hepatocellular Carcinoma Patients

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SYNOPSIS

Objective. To determine the prevalence of testing for hepatitis B virus (HBV) infection in the clinical management of primary liver cancer (hepatocellular carcinoma).

Methods. The authors reviewed the records of 78 patients treated for hepatocellular carcinoma in hospitals in the Puget Sound area in 1988 and early 1989 and reviewed all 1990 U.S. death certificates on which primary liver cancer was listed.

Results. The records of 50 (64%) of 78 hepatocellular carcinoma patients contained no evidence that the patient's hepatitis B surface antigen (HB_sAg) status had been determined. In addition, of 4353 people who died in 1990 for whom the diagnosis of primary liver cancer was listed on the death certificate, HBV infection was also listed for only 136 (3%), much less than expected based on case series.

Conclusions. Many patients with hepatocellular carcinoma are not tested for HBV infection, suggesting that their close contacts are also not evaluated for HBV infection and the need for vaccination. Hepatitis B vaccination of close personal contacts of HBV-infected hepatocellular carcinoma patients is an important strategy for preventing HBV transmission.

Because of the association between hepatitis B virus (HBV) infection and the development of primary liver cancer (hepatocellular carcinoma), hepatitis B screening and vaccination of close contacts of patients with primary liver cancer provide a unique opportunity to prevent the spread of HBV. However, many clinicians who treat patients with hepatocellular carcinoma may not recognize the causative role of hepatitis viruses—including HBV and hepatitis C virus—and thus the potential for disease prevention.[1]

In the United States, an estimated 15% to 36% of hepatocellular carcinoma cases are associated with prior HBV infection.[2–4] In some subgroups of the population—for example, Alaska Natives—80% of patients with hepatocellular carcinoma are also infected with HBV.[5] Clinicians may not consider this association to be clinically relevant since it does not impact on the immediate management of patients with hepatocellular carcinoma; however, because any car-

rier of HBV can potentially infect close personal contacts, vaccination of people who are in close contact with these cancer patients is an important preventive measure.

Methods and Results

Given the potential for preventing HBV transmission, we decided to examine how frequently HBV infection was documented among hepatocellular carcinoma patients in clinical practice. We reviewed the hospital records for 1988 and early 1989 of the 78 patients newly diagnosed with hepatocellular carcinoma who were detected by the 13-county Puget Sound Surveillance, Epidemiology, and End Results (SEER) cancer surveillance system. We systematically abstracted key data items from the laboratory records and physician notes. The records of 50 (64%) of the 78 patients whose records we reviewed contained no evidence that the patients' hepatitis B surface antigen (HB_sAg) status had been determined. Although some patients may have been tested for HB_sAg prior to their hospitalization for hepatocellular carcinoma, there was no indication in any of the hospital records that an attempt had been made to screen household members and other close contacts with HBV serologic tests or to offer them appropriate counseling and immunization.

Many patients with hepatocellular carcinoma are not tested for HBV infection, suggesting that their close contacts are also not tested for susceptibility to HBV.

Further evidence of the lack of recognition among clinicians of the association of HBV infection with hepatocellular carcinoma was provided by an analysis of death certificate data from national vital statistics mortality data.[6] We reviewed U.S. death certificates for 1990 for which primary liver cancer (International Classification of Diseases [ICD-9] code 155.0) was listed as either an underlying cause of death or contributory cause of death and analyzed whether HBV infection (ICD-9 code 070.2 or 070.3) was listed as a contributory cause of death. For 1990, the diagnosis of primary liver cancer was listed on 4543 death certificates; among these, HBV infection was listed on only 136 (3%), which is much less than expected based on case series.[2–4]

Discussion

The lack of evidence of HBV status in hospital charts and death certificates does not prove that clinicians are unaware of the relationship between HBV infection and hepatocellular carcinoma. However, the omission does suggest that clinicians did not consider HBV to be important enough in their management of hepatocellular carcinoma to warrant either obtaining blood tests and histories of HBV infection or documenting HBV status.

The Centers for Disease Control and Prevention (CDC) and national immunization advisory groups recommend that susceptible household and sexual contacts of people with HBV infection receive hepatitis B vaccine.[7,8] Because many patients with hepatocellular carcinoma are HBV-infected, vaccination of people with whom they are in close contact represents an opportunity to prevent HBV transmission. Vaccination of household contacts of HBV-infected hepatocellular carcinoma patients is especially important because such patients may experience bleeding episodes that expose household members and caregivers to infection with HBV. Screening of adults prior to vaccination may be cost-effective; however, screening of children and most adolescents prior to vaccination is not indicated because of their relatively low rates of infection and the relatively low costs of vaccines.[7]

HBV status should be included routinely as part of the evaluation of patients with hepatocellular carcinoma. Although screening and counseling of household contacts would most likely take place in an outpatient setting, primary care practitioners can obtain helpful guidance on appropriate approaches to HBV prevention from hospital-based specialists who treat hepatocellular carcinoma.

With the implementation of routine childhood and adolescent hepatitis B vaccination, liver cancer associated with HBV infection will be largely prevented at some point in the future.[7] However, for many decades, prophylaxis of contacts of HBV-infected people will remain an important prevention strategy. Economic analyses based on infection rates in the general U.S. population have shown that routine hepatitis B vaccination of infants is cost-effective and that the cost of routine vaccination of adolescents compares favorably with the costs of various commonly accepted medical interventions.[9] While these analyses have not formally included screening and vaccination of household members and close contacts of HBV carriers, one would expect this strategy to be highly cost-beneficial given that the lifetime risk of infection among close contacts is much higher than the risk among the general population.

Two other serological tests related to hepatocellular carcinoma—alpha-fetoprotein (AFP) screening and hepatitis C serology—may offer the opportunity to further expand prevention efforts. Clinicians need to be aware of the usefulness of alpha-fetoprotein (AFP) measurement both for the early detection of hepatocellular carcinoma in asymptomatic

people at high risk for the disease and as an initial laboratory test in the diagnosis of hepatocellular carcinoma in symptomatic individuals.[10,11] In 1989, an international group at a workshop on screening for hepatocellular carcinoma in Anchorage, Alaska, concluded that AFP screening of HBV carriers should optimally be done every 6 to 12 months.[12] A preliminary analysis showed that the five-year relative survival rate had improved from zero (no five-year survivors) to 37% for Alaska Natives diagnosed with hepatocellular carcinoma after the institution of a statewide AFP screening program for all Alaska Native HBV carriers. Although AFP screening of HBV carriers is standard practice in the sense that it is recommended by experts, it is by no means uniformly practiced across the country. Furthermore, pressures from managed care administrators to control costs may persuade clinicians to limit the use of such screening tests in the future.

Finally, several case-control and laboratory studies have demonstrated a strong association between hepatitis C virus infection and hepatocellular carcinoma.[13,14] Strategies for the prevention, early detection, and diagnosis of hepatocellular carcinoma may expand as this association is better understood.

Serologic testing of close personal contacts of HBV-positive hepatocellular carcinoma patients, followed by immunization when appropriate, is an important strategy for preventing HBV transmission.

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