THE ROLE OF ANTIBODIES TO HEPATITIS B CORE ANTIGEN IN THE ASSESSMENT OF SEROLOGICAL STATUS TO HBV INFECTION IN SINGAPORE

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SYNOPSIS

We looked at the role of total immunoglobulin to hepatitis B core antigen (total anti-HBc) in the screening of individuals before hepatitis B vaccination. Enzyme-linked immunosorbent assay (ELISA) of total anti-HBc was performed on the sera of 124 children of asymptomatic hepatitis B carrier mothers who were found to be negative to hepatitis B surface antigen (HBsAg) and hepatitis B surface antibody (anti-HBs). 3.2% were found to be positive for total anti-HBc. We found that it would not be cost effective to screen for total anti-HBc on top of screening for anti-HBs and HBsAg before vaccination of the individuals at risk.

The role of IgM antibodies to hepatitis B core antigen (IgM anti-HBc) in the management of asymptomatic carrier mothers and their children was also discussed.

INTRODUCTION

Routine screening for exposure to the hepatitis B virus (HBV) has been largely through the use of hepatitis B surface antigen and antibody (HBsAg and anti-HBs). The absence of both markers is taken to indicate non-exposure to HBV. False positives and false negatives to these screening procedure do occur (1,2) and efforts have been made to look at other serological markers of the infection as a means of identifying individuals at risk who would benefit from vaccination.

This study, which is part of a larger epidemiological study on household contacts of asymptomatic HBV carriers in Singapore, was done to see whether antibodies to hepatitis B core antigen have a role in the management of children of HBV carriers. We looked at the use of total immunoglobulin to hepatitis B core antigen (total anti-HBc) in identifying individuals who may benefit from hepatitis B vaccination. We also measured the IgM subclass of the antibody (IgM anti-HBc) to see if we can distinguish long term carriers of HBsAg from those suffering from acute but asymptomatic HBV infection.

Subjects of this study were asymptomatic hepatitis B carrier mothers and their children. The women were identified to be HBV carriers at antenatal screening at Kandang Kerbau Hospital, the main maternity hospital in Singapore. 90.8% of the women were Chinese with a mean age of 29. 81% of the children were Chinese and 79% of the children were aged between 2 and 7 while the rest were older. Children found to be negative for HBsAg and anti-HBs were subsequently vaccinated since they are close contacts of HBV carriers, namely their mothers.

Part I: Total Anti-HBc

MATERIALS AND METHODS

Sera of 124 children who were found to be negative to HBsAg and anti-HBs was stored at −70°C for 6 to 27 months before assay. ELISA of total anti-HBc was done using the Abbott Corzyme diagnostic test. Where the results were borderline the test was repeated, otherwise a single assay was done.

Part II: 1 gm Anti-HBc

RESULTS AND DISCUSSION

Out of 124 sera negative for HBsAg and anti-HBS, 4 were found to be positive for total anti-HBc (3.2%). This is consistent with the findings of Deinhardt (3,4) who found that 2-4% of HBV exposure can be identified with the addition of anti-HBc to routine HBV screening with HBsAg and anti-HBs.

We stored our sera for up to 27 months before assay and we do not know the biodegradability of the total anti-HBc in frozen serum. The figure of 3.2% may be an underestimate. But we can assume that at least 3.2% of the 'non-exposed' category using just HBsAg and anti-HBs were actually positive for total anti-HBc.

Possible explanations for a positive total anti-HBc with negative HBsAg and negative anti-HBs include (a) presence of a 'serological window' during the early phase of HBV infection when HBsAg has disappeared from the serum but before the appearance of anti-HBs; (b) an unusually low titre of anti-HBs, below the level of detection by the assay; (c) a true false positivity to total anti-HBC.

If the 3.2% of individuals found to be positive for total anti-HBc are truely immune to HBV infection, the vaccinations given to those children would have been wasted. We did a simple cost-benefit analysis of this situation. The cost of performing 100 total anti-HBc tests at S$50.00 per test (test charge at the WHO immunology centre, NUS) is S$5,000.00. Assuming that all 100 individuals screened were negative for HBsAg and anti-HBs the cost of unnecessarily vaccinating 3.2% of them at $60.00 per course for children and S$120.00 per course for adults would be S$60 × 3.2 = S$192.00 and S$120 × 3.2 = S$384.00 respectively. Looking at our simple analysis, it would not be cost-effective to screen for total anti-HBc in addition to HBsAg and anti-HBs before vaccination. But, for the individual who does not wish to be vaccinated unnecessarily, the total anti-HBc test has its place. We have not taken into consideration the cost of travelling and taking time off work for clinic visits, and the cost of any complications due to vaccination. Those unaccounted-for factors may indeed be more pertinent on an individual basis. But such cost-benefit estimates are beyond the scope of this report.

Part I: Total Anti-HBc

MATERIALS AND METHOD

Fifty-eight mothers and 60 children who were all positive for HBsAg were included in this part of the study. Two blood samples were taken from all the mothers and 46 of the children while only one sample was available from the other 14 children. Paired sera were taken at least six months apart. All sera were frozen and stored at −70°C for 2 to 32 months and assayed simultaneously. ELISA of IgM anti-HBc was done using the Abbott Corzyme-M Kit.

Part II: Igm Anti-HBc

RESULTS AND DISCUSSION

We wanted to see whether all these individuals who were positive for HBsAg acquired their HBV infection recently or were long-term carriers. IgM anti-HBc results showed that all the sera tested were negative for this subclass of anti-HBc. This indicates that none of the mothers nor their children acquired the infection recently. With our small sample size, we were not able to demonstrate how many in our pool of mothers with HBsAg at antenatal screening were due to recent infection. For the children, there is evidence to indicate that they probably acquired their infection early in life. Chan et al (5) showed that 46.4% of the newborn of hepatitis B carrier mothers in Singapore became infected with HBV within the first year of life and 76% of them remained chronic carriers of HBV. Our sample of HBsAg positive children are likely to consist entirely of children who acquired the infection much earlier in life as none of them were below the age of 2. Our sample size was again so small that we could have missed sampling any recent HBV infection among these children.

Measurement of IgM anti-HBc has its use in the diagnosis of acute hepatitis B infections. In the jaundiced patient positive for HBsAg, it may be used to distinguish acute from chronic hepatitis B. In asymptomatic HBsAg carriers, the chance of picking up an acute HBV infection is so small that IgM anti-HBc probably has no role.

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