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EDITORIAL

Prevention of Hepatitis B Virus Infections

Hepatitis B virus (HBV) infection and chronic carriers of the virus are common in all Asian countries. There is evidence that chronic infection with HBV is aetiologically associated with the development of primary hepatocellular carcinoma (PHC).[1,2] In areas where HBV is endemic, PHC is one of the most commonly found malignant tumours. In a study of chronic HBV carriers in Taiwan, the relative risk of PHC in carriers was over 200 times that of non-carriers.[3] More than 95 per cent of the PHC cases have developed in chronic carriers.[3,4] In our study in Thailand we found that maternal transmission plays a major role in the transmission of HVB and in the development of HBV carrier state in their children.[5] Carrier mothers who are also HBeAg-positive are more likely to transmit HBV to their newborn infants than those who are HBeAg-negative or those who have anti-HBe in their sera.[6,7] Infection at an early age, particularly maternally transmitted infection, may increase the risk of development of chronic liver disease and PHC, and decrease the age of onset of those diseases.[2] Hence, the mother-child relationship in HBV transmission is obviously important with respect to the pathogenesis of chronic liver disease and PHC in Asian countries and the Far-East.

Perinatal transmission of HBV infections

Perinatal HBV infection of infants from their HBsAg carrier mothers is most likely to occur if mothers are also HBeAg positive. About 90 percent of infants whose mothers are positive for both markers will be infected with HBV and almost all of them will become permanent carriers.[8] Infants whose mothers are HBeAg negative or who have antibody to HBeAg are at much lesser risk, but can still be infected by horizontal transmission later on.[6-8]

Infected infants usually will not become HBsAg Positive until several weeks after birth. Although clinical jaundice or acute hepatitis is rare in infected infants, elevated transaminase levels are frequent.[9] It is estimated that about one in four infants who become chronic carriers following perinatal infection will develop cirrhosis or hepatocellular carcinoma later in life. Since the infected infants who become persistent HBV carriers are also HBeAg positive in a very high percentage, they are at high risk to transmit infection to other family members, or to others later in life through sexual contact or by transfusion or inoculation of their blood and secretions. Infection of female infants may result in transmission of HBV to the next generation of infants. Indeed, transmission from mothers to infants is a major method of perpetuation of this virus in the Far-East.

Although most perinatal HBV infection occurs during delivery as the infants pass through the birth canal, intra-uterine infection of HBV may be recognised in some cases. This was characterised by the presence of at least one of the following three criteria. The first was the presence of IgM-anti-HBc in cord blood and/or in the venous blood sample after birth. Since IgM does not pass the placenta, IgM-anti-HBc which itself is a marker of recent HBV infection must have been produced by the child himself. The second was the presence and rapidly increasing titre of HBsAg and HBeAg in the venous blood at birth and in subsequent samples. Thirdly, the consumption of passively administered anti-HBs antibody has also observed in our two reported cases.[10]

Screening of women for HBsAg

The pregnant women should be screened for the presence of HBsAg and HBeAg prior to delivery. This is essential to enable those who will attend her at delivery to be aware of and to minimise the risk of exposure to her blood. It is urgent, moreover, that combined passive-active immunisation of infants born from HBV carrier mothers be accomplished promptly after birth in order to prevent HBV infection in these infants. In our study, the initial screening of pregnant women for HBsAg and HBeAg was done routinely during the first prenatal visit by reversed passive haemagglutination (RPHA) and passive haemagglutination (PHA)

tests respectively. Since 1978, more than 50,000 pregnant women have been screened for HBsAg and HBeAg at the Prenatal Clinic, Siriraj Hospital. The incidence of HBsAg positivity was approximately 6% and the incidence of chronic HBsAg carriers with HBeAg positivity was approximately 3%. We also found that the perinatal transmission of HBV in our country occurred exclusively in infants born from the HBsAg and BHeAg positive mothers. The result of our anti-HBs study in this group of infants showed that the risk of further exposure to HBV later in life (horizontal transmission) is not so high as we formerly thought, because most of the non-HBsAg carrier infants born from HBeAg positive mothers have a much better natural active immune response than infants and children in the other groups.[5]

Immunisation of infants

The greatest protection of infants is achieved by using a combination of active immunisation of infants with three doses of hepatitis B vaccine and passive immunisation with hepatitis B immune globulin (HBIG). It is important that HBIG must be administered as soon after birth as possible, but the vaccine administration may be delayed if necessary. However, giving the first dose of vaccine simultaneously with HBIG at birth or prior to discharge from the hospital eliminates an additional return visit. Infants must be immunised whether they are delivered vaginally or by Caesarean section. Among the various combined immunoprophylaxis regimens which we have tried in our department, the best one is the regimen consists of giving the first dose of HBIG (200 IU/ml-Gamma protect®) intramuscularly in conjunction with hepatitis B vaccine (5 μg Hevac B Pasteur®) intramuscularly, each in separate thighs within 72 hours after birth, and followed by Hevac B 5 μg intramuscularly at thirty and sixty days. Persistent HBs antigenaemia did not develop in any of 20 infants receiving this combined prophylaxis regimen.[11] Simultaneous administration of hepatitis B vaccine with DPT-polio vaccine at two months of age has not led to increased reaction. Antibody to HBsAg was similar in infants who received hepatitis B vaccine with or without DT-polio vaccine.[12] By serial determinations of HBV markers in vaccinated infants, it is possible to evaluate the success or failure of the immunoprophylaxis program. The absence of HBsAg after 12 months of age is indicative of successful prevention of perinatal transmission. The presence of anti-HBs in the absence of anti-HBc after 6 and/or 12 months of age is indicative of successful immunisation. The presence of anti-HBc with or without the presence of anti-HBs after 6 and/or 12 months of age is indicative of natural HBV infection. Children should be tested for HBeAg, anti-HBs and anti-HBc at 2 months after the last vaccination or later. Those who are found to be negative for all three HBV markers should receive another dose of hepatitis B vaccine and be retested. Our study showed the presence of anti-HBs and anti-HBc alone at 12 months of age in eighty and twenty percent respectively.[11]

Precautions for infants of HBsAg-positive mothers

Infants born to mothers who are HBsAg and HBeAg positive should be admitted in the septic ward. They should be cleaned by a gloved attendant. Their blood shold be handled with appropriate precautions.[13] We have collected the venous blood sample for testing HBsAg and IgM anti-HBc before giving HBIG and the first dose of vaccine. If HBsAg and/or IgM anti-HBc is positive, intra-uterine HBV infection has been proved.[11] Testing of cord blood is unreliable because of the contamination of HBsAg in vaginal secretion and/or maternal blood due to micro-materno-foetal transfusion. There appears to be no reason to withhold breast-feeding. In three studies in which infants were and were not protected by immunisation, there was no increased risk of HBV infections in those who are breast-fed.[14-16]

Immunisation of contacts of carrier mothers or infants

Susceptible personnel who are likely to be exposed to the blood of infants or mothers with HBV infection shold be considered at increased risk of contacting hepatitis of all forms. All such contacts should be screened, and those who are negative for HBsAg, anti-HBs and anti-HBe should be immunised with three doses of HBV vaccine. Household members and sexual contacts of those who are HBsAg positive should receive hepatitis B vaccine if testing indicates that they are negative for HBsAg, anti-HBs and anti-HBc. Half adult dose can be given to children less than 10 years of age. The interval between each dose depends on the type of vaccine used.

Safety of hepatitis B vaccine and hepatitis B immune globulin

To date, approximately 1.5 million doses of hepatitis B vaccine have been distributed; it is estimated that about 0.5 million individuals have received two or more doses. Approximately 35 significant reactions have been recorded following receipt of the vaccine. These have included arthritis and arthalgia, some neurologic reactions, and others. The rate of Guillain-Barre syndrome following administration of hapatitis B vaccine does not appear to be increased above the expected level.[17] In our study, we did not find any significant or temporally associated reactions in both pre-exposure and post-

exposure hepatitis B vaccine and hepatitis immune globulin injections both intramuscularly and intravenously.

Although the vaccine is prepared from plasma obtained from HBsAg carriers, one and usually more than one of the following virus inactivating procedures have been employed:heat, urea, formalin, proteolytic enzymes, etc. To date, there have been no cases of acquired immunodeficiency syndrome (AIDS) in vaccine recipients.

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