PERSPECTIVE

Prevention of Mother to Child Transmission of Hepatitis B Infection

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The likelihood of developing chronic hepatitis B infection and its complications is most when infection is transmitted vertically. Awareness of the current recommendations for managing babies of mothers who are hepatitis B carriers is not universal, resulting in failure of follow up, despite the serious long term implications, including development of hepatic carcinoma. We review the current guidelines of managing babies born to mothers who are Hepatitis B carriers.

Key words: *Hepatitis B, Immunization, Perinatal prevention, Vertical transmission.*

The prevention of transmission of retroviral infection from mother to child has been a success story of our times and indeed, PMTCT is now synonymous with prevention of HIV infection. However, awareness of the current recommendations for managing babies of mothers who are hepatitis B carriers is not universal, resulting in failure of follow up, despite the serious long term implications including development of hepatic carcinoma. A review of current guidelines would help in empowering pediatricians to address this problem effectively, and ensure that vertical transmission of hepatitis B infection is prevented. Although the introduction of the birth dose of hepatitis B vaccine will go a long way to achieve this objective, there needs to be a system in place to ensure universal screening during pregnancy, timely administration of the birth dose and tracking of babies exposed to hepatitis B. Carrier mothers and their families need to be educated regarding the risks involved and the importance of preventive strategies.

BACKGROUND

It is estimated that 5% of the world's population is chronically infected with hepatitis B [1,2]. With a prevalence rate for HBsAg seropositivity 2-7 %, India has an intermediate endemicity, and a projected burden of 50 million carriers, the second largest in the world [3,4].

In India, the HBsAg prevalence rate among pregnant women varies between 0.9% and 11.2% [5-7]. Hepatitis B e-antigen (HBeAg) status, which indicates high replicative activity of the virus in the liver, was less than 30% in most earlier studies on pregnant women, though a recent study revealed HBeAg seropositivity of 56.8% [6].

Transmission

Without immune prophylaxis, in mothers who are both HBsAg and HBeAg positive, the risk for transmission to the baby is between 70 and 90% by 6 months of age, whereas in the case of mothers who are HBsAg positive, but HBeAg negative, it is less than 10% [8-11]. The increased risk of transmission with HBeAg positive status is due to high titres of HBV in these women [8]. One study found that 38% of babies born to HBsAg positive mothers, who did not acquire infection perinatally, became infected by four years of age [12]. This emphasizes the need to equip mothers with knowledge to prevent horizontal transmission of hepatitis B infection, and the importance of completion of the hepatitis B vaccination schedule.

Implications

The risk for development of chronic hepatitis B infection varies inversely with the age at which infection occurs, 90% of affected infants develop chronic infection as opposed to 30-50% of under-five children and 6% of children above five years of age [13,14]. Chronic hepatitis B infection acquired in childhood carries a 25% risk for development of chronic liver disease, cirrhosis or hepatocellular carcinoma [15]. Hence, it is imperative to prevent mother to child transmission.

PREVENTIVE STRATEGIES

Immunoprophylaxis

A combination of active and passive immune prophylaxis is the optimum strategy to prevent HBV infection in babies of HBsAg positive mothers. A combination of hepatitis B immune globulin (HBIG) and hepatitis B vaccination initiated within 24 hours of delivery has been shown to protect 85 to 95% of babies whose mothers were positive for both HBsAg and HBeAg [16]. However, studies have shown significant gaps in hospital

practices and policies to prevent vertical transmission of hepatitis B [17].

Hepatitis B vaccination is carried out using the monovalent vaccine for the birth dose. Further doses may be administered as a combination vaccine with other infant vaccines like DPT, DTaP and Hib vaccines since interference with the immunogenicity of these vaccines does not occur [2]. Hepatitis B vaccination in infancy had been adopted by 179 countries by the end of 2009 [18].

Birth dose of hepatitis B vaccine

Administration of single antigen hepatitis B vaccine soon after birth is critically important for the prevention of perinatal and early postnatal transmission of HBV infection, and is much more efficacious for this purpose than doses given after the neonatal period, since the efficacy of post exposure prophylaxis diminishes with increasing time since exposure [18].

The birth dose is recommended for all newborns since it serves as a safety net, due to the fact that errors in testing, reporting and documenting maternal HBsAg status do occur [19]. Moreover, the chance for completing the hepatitis B vaccine schedule and in fact all other immunizations, is found to improve when vaccination is initiated at birth [20].

The proportion of newborns receiving the birth dose within 24 hours has been suggested as a useful performance indicator for immunization programmes by WHO, and coordination between maternal and neonatal services is of paramount importance to achieve success in this key task [18].The CDC; however, recommends that the birth dose be given within 12 hours after delivery [2].

Vaccination schedule

Although the conventional schedule for hepatitis B vaccination consists of three doses including the birth dose, WHO stipulates that four doses may be given in concordance with programmatic requirements of National Schedules [18]. This is of enormous benefit in reducing the number of clinic visits as well as ensuring compliance, and is especially important in developing countries with resource constraints. A combination of HBIG and hepatitis B vaccination initiated within 24 hours of delivery, followed by a three dose immunization schedule initiated at 1-2 months of age, has been shown to protect 85 to 95% of babies whose mothers were positive for both HBsAg and HBeAg [16].

The widely spaced schedule with the third dose of hepatitis B vaccine administered at least 6 months after birth, is recommended by the CDC for vaccination of babies of HBsAg positive mothers (2), since the last dose mainly acts as a booster, and is responsible for providing long term protection. However, WHO differs on this point, and recommends the closely spaced schedule, asserting that longer dose intervals may increase the final anti-HBs titres, but not the seroconversion rates [1].

Special situations

In mothers with an unknown HBsAg positivity status at delivery, the birth dose of hepatitis B vaccine is administered within 24 hours of birth, and HBIG is administered as soon as possible if the mother tests positive, ideally within 72 hours of delivery [2,18].

In the case of preterm babies of HBsAg positive mothers, the birth dose is indicated even if the baby weighs less than 2 kilograms, but should be followed by a further three doses starting at six weeks of age [21,22]. This is due to the reduced immunogenicity of hepatitis B vaccine in preterms weighing <2 kilograms in the first month of life [23].

The immunogenicity of hepatitis B vaccine is suboptimal in conditions associated with immuno-suppression, including advanced HIV infection, and is influenced by the viral load, CD4 count, age, duration of HAART and the presence of AIDS defining conditions [18]. Hence, early administration of the hepatitis B vaccine starting at birth is imperative, since immunosuppression increases over time [18].

Interruption of the vaccine series does not warrant revaccination, but rather completion of the missed dose as early as possible with a minimum interval of four weeks between two doses [24].

Women who are HBsAg negative in pregnancy, but who are at high risk of acquiring hepatitis B infection, including those with a history of multiple sexual partners or of drug abuse, should receive hepatitis B vaccine [24].

Passive immunization

HBIG is used as an adjunct to the hepatitis B vaccine to prevent vertical transmission. It provides temporary protection that lasts for 3 to 6 months. A combination of HBIG with HBV is more effective than HBV alone in prevention of transmission of hepatitis B [26]. Studies have shown that HBIG is effective when administered as late as 72 hours after birth [2].

Administration of a 3 or 4 dose series of hepatitis B vaccine starting within 12 hours after birth without passive immunization with HBIG has shown to have a protective efficacy of 70 to 95 % in mothers who were both HBsAg and HBeAg positive [27-30]. The addition of HBIG to active immunization is particularly beneficial when the mother is both HBsAg and HBeAg positive.

Some studies have shown that when HBIG is unavailable, vaccination alone can prevent vertical transmission in 66% to 90% of cases [31]. Moreover, in full-term newborns, the protection against perinatally acquired infection achieved by immediate (<24 hours) hepatitis B vaccination is not significantly improved by the addition of HBIG [1]. This is highly pertinent in settings like ours where financial constraints often preclude the use of HBIG.

Breastfeeding

Breastfeeding by an HBsAg positive mother does not increase the risk of transmission to the baby, and is therefore not contraindicated , provided the baby is given immunoprophylaxis [32].

Follow up

Although routine post-vaccination testing is not necessary, it is recommended for high-risk groups including babies born to mothers who are HBsAg positive, and should commence at 9 to 18 months of age, atleast 1 month after the last dose of vaccine [18]. HBsAg status and the anti HBs titre should be checked. The anti HBs levels done earlier than 9 months of age may reflect passive immunization with HBIG [2]. Anti HBs levels of more than 10 mIU/l indicate adequate protection, whereas babies with anti HBs levels of less than 10 mIU/l need to be revaccinated with the entire 3 dose schedule. Babies who are HBsAg positive are infected and need to be followed up. Anti HBc testing is not advised since it may remain positive upto 2 years of age in babies of infected mothers [2].

More than 95% of healthy newborns respond to a 3 dose vaccine series, while almost all respond to revaccination [33]. However, there is no data to suggest any benefit in revaccinating a baby who has no detectable antibody after 6 doses of vaccine.

CONCLUSIONS

The importance of public awareness and education of medical professionals is well recognized [34]. Education about the importance of administering the birth dose within 24 hours of birth is vital [35]. Universal screening of all pregnant women for hepatitis B is thus a pre requisite for effective preventive services and follow up care to be put in place.

Newer heat and freeze resistant vaccines are under development, raising hopes of vaccination on site in the case of home deliveries [33]. Evidence is emerging to suggest that the antiretroviral drugs, lamivudine and telbivudine may further prevent vertical transmission when administered to women with a high HBV viral load in the third trimester, and a beneficial effect with maternal HBIG has also been shown to occur [36-39]. Research is being carried out to develop a vaccine suitable for non-responders to the currently available vaccine.

In conclusion, the differences in the recommendations of the WHO and CDC are a reflection of the diverse population groups they represent, the high-prevalence countries with the added burden of resource and logistical constraints on the one hand, and the low-prevalence, resource- rich nations on the other.

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