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Mother-To-Child Transmission of Hepatitis B Virus - What's New

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Editorial

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Abbreviations: HBeAg: Hepatitis B e Antigen; HBsAg: Hepatitis B Surface Antigen; HBV: Hepatitis B Virus; MTCT: Mother-to-Child Transmission; NA: Nucleos(t)ide Analogues; TDF: Tenofovirdisoproxil Fumarate

Editorial

Chronic hepatitis B virus (HBV) infection may lead to long-term, life-threatening liver diseases worldwide. HBV is transmitted either horizontally or vertically via mother-to-child route, which is the major route of transmission in endemic areas [1]. Mother-to-child transmission (MTCT) of HBV causes chronic infection in children and is closely related the development of cirrhosis and hepatocellular carcinoma [2]. Timely administration of hepatitis B immunoglobulin and hepatitis B vaccine to newborns of HBV-infected mothers, followed by two subsequent doses of vaccine within 6 to 12 months, reduces up to 90% to 95% of MTCT of HBV [3]. However, MTCT still occurs in some infants born to highly viremic mothers positive for hepatitis B e antigen (HBeAg) with serum HBV DNA above 6 log10 IU/mL despite immunoprophylaxis [4].

Most MTCT occurs during labour or at delivery, and therefore it is also termed perinatal transmission. High maternal viral load is the most important risk factor causing MTCT and immunoprophylaxis failure. Other factors, such as maternal HBeAg seropositivity, surface gene mutants, type of birth, obstetric procedures or complications related to maternal-fetal hemorrhage and feeding practice may also affect MTCT [5].

Because of its anti-proliferative effect, interferon should be avoided in women who are currently pregnant or who wish to become pregnant within 18 months. Recently, the efficacy and safety of short-term antiviral nucleos(t)ide analogues (NAs) in highly viremic HBV-infected pregnant women to reduce maternal viral load and then MTCT have been evaluated in a growing number of studies. The NAs used in these studies included lamivudine, telbivudine and tenofovirdisoproxil fumarate (TDF). Telbivudine and TDF are preferable because of lower rates of resistance and probable better safety profiles. NA treatment usually starts from 28 to 32 weeks of gestation after careful examinations to exclude maternal systemic diseases and fetal anomalies. The target population for treatment is pregnant women with an HBV DNA level higher than 6 to 7 log10 IU/mL.

Two recent publications from Taiwan and China respectively demonstrated that pregnant mothers with high viral load, a course of antiviral treatment for 12 to 16 weeks reduced risk of mother-to-child transmission of HBV dramatically to as low as 0% to 1%. The prospective cohort study from Taiwan included 118 mother who were both positive for HBsAg and hepatitis B e antigen (HBeAg)

with serum HBV DNA ≥7.5 log10 IU/mL; 62 mothers received tenofovir disoproxil fumarate (TDF) whereas 56 mothers received no treatment [6]. Babies from mothers who received TDF had lower rate of becoming HBsAg-positive at 6 months of age (1.54% *vs*. 10.71%) compared to those from mothers received no treatment [6].

Another study from China was just published in the *New England Journal of Medicine* in June 2016. This large-scaled randomized controlled trial included 197 mothers in China who were both positive for both HBsAg and HBeAg with serum HBV DNA ≥200,000 log10 IU/mL; 97 mothers were randomized to receive TDF whereas 100 mothers received placebo [7]. In the per-protocol analysis, transmission of HBV to baby was 0% in the TDF group, whereas 7% in the placebo group.

With these new evidences, the latest international guidelines recommended proper assessment of ladies in child-bearing age or in early pregnancy. They should be tested for HBsAg, HBeAg and HBV DNA level. The American guideline published in January 2016 suggested antiviral therapy to reduce the risk of perinatal transmission of hepatitis B in HBsAg-positive pregnant women with an HBV DNA level >200,000 IU/mL [8].

Cessation of therapy 4 to 12 weeks after delivery is recommended in mothers without aminotransferase flares and without pre-existing liver fibrosis/cirrhosis. Continuation of treatment after delivery may be needed according to the status of maternal liver disease. Breast feeding is not discouraged in HBsAg-positive mothers if their newborns have received appropriate postnatal immunoprophylaxis. Despite all of the drug labels mention that breast feeding is not recommended during NA treatment because the effect to newborns is uncertain, the latest AASLD guideline did not discourage breast-feeding during TDF treatment [8].

The thing we still don't know is the long-term safety of TDF, especially on the infants. Current data show that birth defects did not increase in those infants with fetal exposure to NA therapy. However, these studies had short follow-up or only recorded defects identified at birth. Recent real-life data in Hong Kong suggested promising and comparable safety profile of all NAs for HBV in adults [9]. We look forward to the long-term safety data from these two clinical trials. The latest American guidelines published November 2015 supported the use of antiviral therapy in HBV carrier mothers with HBV DNA above 200,000 IU/mL. Together with the universal vaccination, a generation of zero HBV infection is coming.

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