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Original Article

Effectiveness of Macau Hepatitis B Vaccination Programme for Newborns from Hepatitis B Carrier Mother

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Abstract

Aims: First: To evaluate the effectiveness of Hepatitis B vaccine (HepB Vaccine) and Hepatitis B immunoglobulin (HBIG) on preventing vertical transmission of hepatitis B virus from hepatitis B carrier mother. Second: To assess the effectiveness of HepB Vaccine in providing adequate immune protection. ***Methods:*** It is a retrospective study from 1st January 2009 to 31st December 2013 which includes newborns from hepatitis B carrier mother delivered at Centro Hospitalar Conde de Sao Januario (CHCSJ) hospital of Macau. There were total 1315 newborns involved in the study. Hepatitis B carrier status was defined as patient who has hepatitis B surface antigen (HBsAg) during blood test. According to CHCSJ hospital hepatitis B vaccination protocol, all subjects should receive both HBIG and first dose of HepB Vaccine during birth, followed by second and third dose of HepB Vaccine at first and sixth month of age. For preterm baby with birth weight less than 2 kg, an additional dose of HepB Vaccine was required during second month of age. Blood test for HBsAg and hepatitis B surface antigen antibody (Anti-HBs) were performed after nine months of age to check for hepatitis B infection and immunity post vaccination. For non-infected subjects who did not develop adequate immune protection, a second course (three doses) of HepB Vaccine will be offered. ***Results:*** Out of the 1315 subjects, only 980 subjects had post vaccination blood test and HepB Vaccine given according to CHCSJ hospital hepatitis B vaccination protocol. Therefore, hepatitis B vertical transmission rates and post vaccination immune protection can only be assessed on the 980 subjects. Twenty-two out of 980 subjects were tested positive for HBsAg. That equals to an overall vertical transmission rate of 2.24% (95% confidence interval 1.29 to 3.18%). As an additional finding, based on the 570 subjects' mothers who had hepatitis B envelope antigen (HBeAg) tested, 176 were positive for HBeAg. The vertical transmission rate for HBeAg positive mothers were much higher reached 12.5% (95% confidence interval 7.5 to 17.5%). Eight hundred and sixty-four out of 980 babies developed adequate immune protection (as defined by antibodies level more than 10 mIU/ml) from hepatitis B virus after first course of HepB Vaccine. For the remaining 94 babies without adequate protection, 74 agreed to have second course of HepB Vaccine. However, only 29 babies had antibodies level tested after vaccination and follow up blood test revealed all of them to have immune protection. ***Conclusion:*** Active and passive immunisation with HepB Vaccine and HBIG for newborns of hepatitis B carrier mother are highly effective in preventing vertical transmission of hepatitis B virus and also provide adequate immune protection for

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most subjects. For subjects who did not develop adequate immune protection after first course of HepB Vaccine, it is worth giving a second course of HepB Vaccine. The compliance rate to CHCSJ hospital hepatitis B vaccination programme is not satisfactory and improvement has been made after the study period. Follow up study will be needed in the future to look for any improvement in compliance rates.

Key words Hepatitis B; Hepatitis B immunoglobulin; Hepatitis B vaccine; Newborns; Vertical transmission

Introduction

Hepatitis B virus infection is a worldwide health problem. It is estimated that there are about 248 million hepatitis B carriers in the world. Approximately 600,000 die annually from hepatitis B virus related liver disease.[1,2] The prevalence of hepatitis B infection varies greatly with different geographic locations. High prevalence areas include Macau, China and South-East Asia have rates >8%. As compare to low prevalence areas like United states, Canada and Australia which have rates around 0.1-2%.[1-3] The principle mode of virus transmission varies from high to low prevalence areas. In high prevalence area like Macau, the principle mode of transmission is perinatal. If babies acquire the virus during perinatal period, almost 90% will develop chronic carrier status. On the other hand, if adult acquire the infection, only 5% will become chronic carrier.[4-6] It was shown that Chronic Hepatitis B carrier have higher risk for developing chronic hepatitis, liver cirrhosis and even hepatocellular carcinoma. Thus, it is important to prevent the transmission of hepatitis B virus during the perinatal period. From the previous studies, we knew that the combination effect of Hepatitis B Vaccine (HepB Vaccine) and Hepatitis B immunoglobulin (HBIG) could reduce the rate of hepatitis B perinatal infection by more than 90%.[7,8] In regards to Macau, it has commenced its own hepatitis B vaccination programme since 1989. All newborns in Macau will receive HepB Vaccine and newborn from hepatitis B carrier mother will receive an addition of HBIG within 24 hours after delivery. Local protocol in Macau requires newborns delivered by hepatitis B carrier mother to be tested for hepatitis B surface antigen (HBsAg) and Anti-HBs after 9 months of age or 1-2 months after third dose of HepB Vaccine.[9] Despite the fact that Macau has its own hepatitis B vaccination programme since year 1989, there has not been any formal study conducted on the effectiveness of this programme in the prevention of hepatitis B virus perinatal transmission. This study will evaluate the effectiveness of the HepB Vaccine and HBIG in preventing vertical transmission of Hepatitis B virus and also determine the immune protection rate after vaccination. In addition, for those babies who do not develop immune protection after first course of HepB Vaccine. A second course of vaccination will be offered follow up by antibodies level testing.

Methods

Newborns from hepatitis B carrier mother delivered at Centro Hospitalar Conde de Sao Januario (CHCSJ) hospital of Macau were selected for this retrospective study. There were 1315 newborns during the period from 1st January 2009 to 31st December 2013. Ethics approval from CHCSJ hospital Medical Ethic Committee has been obtained for this research project. Hepatitis B carrier status was defined as patient who has HBsAg during blood test. According to CHCSJ hospital hepatitis B vaccination protocol, all subjects should receive both HBIG and first dose of HepB Vaccine during birth, followed by second and third dose of HepB Vaccine at first and sixth month of age. For preterm baby with birth weight less than 2 kg, an additional dose of HepB vaccine was required during second month of age. Blood test for HBsAg and Anti-HBs were performed after nine months of age. For subjects with Anti-HBs level less than 10 mIU/ml, a second course of HepB Vaccine will be offered follow up by repeat antibodies level testing.

Results

Out of the 1315 subjects, only 980 subjects had post vaccination blood test and hepatitis B vaccination given according to CHCSJ hospital hepatitis B vaccination protocol. Thus, hepatitis B vertical transmission rates and post vaccination immune protection can only be assessed on the 980 subjects. Twenty-two subjects out of 980 were tested positive for HBsAg. That equals to an overall vertical transmission rate of 2.24% (95% confidence interval 1.29 to 3.18%). All infected subjects were delivered by hepatitis B envelope antigen (HBeAg) positive mother. As an additional finding, 570 out of 980 subjects' mothers actually

had HBeAg blood test performed and 176 mothers were positive for HBeAg. Out of the 176 HBeAg positive mothers, 22 have infected infants and 154 have non-infected infants. This equals to vertical transmission rates of about 12.5% (95% confidence interval 7.5 to 17.5%) for HBeAg positive mother despite HepB Vaccine and HBIG injection. 864 out of 980 babies developed adequate immune protection (as defined by antibodies level more than 10 mIU/ml) from hepatitis B virus after first course (three doses) of HepB Vaccine. That equals to 88% (95% confidence interval 86 to 90%) of immune protection rates. In regards to the non-infected 94 babies without adequate immune protection, 74 agreed to have second course (three doses) of HepB Vaccine given. However only 29 of them had repeated antibodies level testing and result revealed all of them to be immune protected.

Discussion

According to previous studies, the risk of maternal-infant transmission of hepatitis B virus is about 85-90% in infant born to HBeAg positive mother and 32% in infant born to HBeAg negative mother. Overall risk of transmission is about 40%.[10,11] In contrast, when both HepB Vaccine and HBIG are given, less than 5% of infant become infected.[7,8] In this study, only 2.24% (95% confidence interval 1.29 to 3.18%) of infant become infected. According to Australian immunisation handbook, a single course three doses of HepB Vaccine will provide immune protection for about 90% of subjects.[4] For non-responders to first course of HepB Vaccine, repeat second course of HepB Vaccine will provide adequate protection for most subjects.[12] In this study, about 88% (95% confidence interval 86 to 90%) of subjects developed adequate antibodies level after first course of HepB Vaccine. For the non-responders who participate in the second course of HepB Vaccine, those who agreed to have repeat blood test had all responded well with production of adequate antibodies level. These results are consistent with the data from Australian immunisation handbook and international studies. This means for non-responders after first course of HepB Vaccine, it is worth giving a second course of HepB Vaccine.

During the study period, there were 1315 newborns delivered by hepatitis B carrier mother, however only 980 complied to CHCSJ hospital hepatitis B vaccination protocol. That give us a compliance rates of 74.5% and non-compliance rates of 25.5%. This is one of the deficiency of CHCSJ hospital hepatitis B vaccination programme. On further investigation into the 335 non-compliance subjects, we noticed that 312 subjects failed to have appropriate post-vaccination serology performed and 23 subjects did not have hepatitis B vaccination given appropriately. After further investigations, we noticed that 246 out of the 312 subjects were regularly followed up by Macau health centre (which is responsible for primary health care in Macau public health system) and 66 out of 312 subjects had missed the follow up after birth. Among the 246 subjects, possible explanations for not having post-vaccination serology perform include 1) patient's parent refuse to have the blood test, 2) the health centre doctor might have forgotten to order the blood test, 3) the patient might have blood test done outside the public health care system like in private or in China. Therefore, it was not shown in the health information system. In response to this finding, a new Health Centre Paediatric Guideline was issued in year 2016 which emphasised the importance of performing post-vaccination serology for baby from hepatitis B carrier mother and the guideline also provided patient education information for the baby's mother to learn about the importance of having the blood test.[13] In the future, we are trying to incorporate a computer alert system in the current health information system. It will alert the health centre doctor to perform post-vaccination serology for baby from hepatitis B carrier mother.

During the study, all infected subjects were delivered by Hepatitis E antigen positive mother and this is likely due to the fact that baby deliver by HBeAg positive mother had much higher vertical transmission rates which was about 12.5% (95% confidence interval 7.5 to 17.5%) in this study. However, testing for HBeAg during the antenatal period is not compulsory in Macau. If testing for HBsAg as well as HBeAg antigen are performed during the antenatal period, we will be able to isolate this group of higher risk patients and look for further ways to decrease the vertical transmission rate of Hepatitis B virus by additional intervention like anti-viral treatment. That is something we can consider in the future.

As the result of this study, we found out that the compliance rate to CHCSJ hospital hepatitis B vaccination protocol was not satisfactory and further action has been taken to improve the situation. On the positive side, Macau hepatitis B vaccination programme has successfully reduced the risk of hepatitis B vertical transmission and also provided adequate immune protection to most of the subjects. For non-responder to first course of HepB Vaccine, it is worth giving a second course of HepB Vaccine

as it has already done in Macau. In the future, we should anticipate a fall in the prevalence of hepatitis B infection in Macau.

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Declaration of Interest

The authors declare that there is no conflict of interest.

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