[総説］Vaccination practice for perinatal hepatitis B virus infection

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ABSTRACT

According to the national prevention program, passive-active immunoprophylaxis with hepatitis B immune globulin (HBIG) and hepatitis B (HB) vaccine have been carried out for infants born to HB virus (HBV) carrier mothers positive for hepatitis Be (HBe) antigen since 1986 in Japan. Twenty-six thousand and ninety-nine infants born to the HBV carrier mothers received HBIG at birth and 24,065 of the infants further received 3 doses of HB vaccine in all of Japan. From 1995, the program was expanded to include infants born to carrier mothers negative for HBe antigen. In the present article, vaccination practice for perinatal HBV infection was reviewed from the view point of child health. In addition, the vaccination practice in a clinic was surveyed. *Ryukyu Med. J., 17(3)127~129, 1997*

Key words: HB vaccination practice, HB virus carrier, perinatal infection

INTRODUCTION

HBV has a worldwide distribution. The prevalence of the carrier state is high in China and Southeast Asia, but low in the western countries of North America, Europe, and Australia. Most of the carrier state in adulthood are due to infection during infancy, especially from carrier mothers. Passive-active immunoprophylaxis with HBIG and HB vaccine has been recommended as an effective public health means of preventing perinatal HBV infection since the 1980's. With regard to the vaccination practices, targeted immunoprophylaxis or universal/mass immunization has been carried out in endemic countries and in those with low prevalence of carriers. Therefore, vaccination schedules are different around the world. In the Republic of China, a nationwide vaccination program against HBV for high risk infants was initiated in 1984[1]. In the western countries such as Italy and United States, vaccination has been extended to all newborns, regardless of mother's serologic status for HBV infection since the 1990's[2]. In Japan, the prevalence of HBV surface (HBs) antigen carrier in pregnant women was 1.1% from 1986-1993, of which the positive rate of HBe antigen was about 25%[3]. The national prevention program of perinatal HBV infection was launched in 1985. HBIG and HB vaccine have been administered to infants born to HBV carrier mothers positive for HBe antigen (high risk infants) since 1986. The program was expanded to include infants born to HBV carrier mothers negative for HBe antigen (low risk infants) in 1995, to prevent development of acute hepatitis or fulminant hepatitis. There is concern that vaccination compliance might be decreased by the expansion of the program. Vaccination practice for perinatal HBV infection in Japan so far, is reviewed from the view point of child health. Additionally, the result of a survey at a clinic is reported and vaccination compliance is discussed.

NATIONAL PREVENTION PROGRAM IN JAPAN

Since 1986, all pregnant women undergo prenatal screening for HBs antigen as one of their health check-ups. Pregnant women positive for the HBs antigen further received an HBe antigen test. If the results of both tests are positive, the woman is considered to be at high risk of transmitting HBV to her baby. High risk infants received two shots of HBIG intramuscularly, at birth and two months of age, and 3 shots of HB vaccine intracutaneously, at 2, 3 and 5 months of age as shown in Figure. From 1995, low risk infants were also included for treatment with HBIG at birth and the HB vaccine at the age of 2, 3 and 5 months. Plasma derived vaccine was used until May 1987, after which recombinant vaccine has been in use.

According to the revised protocol in 1995[4], serological testing for HBs antigen in cord blood at birth is not needed, whereas serological testing for HBs antibody in serum is recommended at the age of 6 months to estimate the efficacy of vaccination. HBs antigen was measured by reverse passive hemagulutination or radioimmunoassay method, and antibody to HBs was measured by passive hemaggulutination or radioimmunoassay method. From

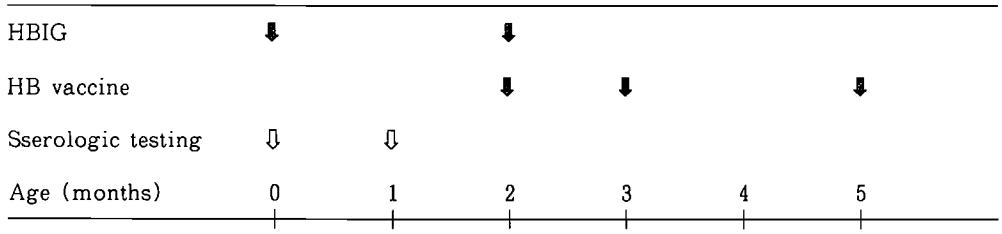

Fig. 1 Schedule of the administration of HBIG and HB vaccine, and serologic testing of HBs antigen by the national prevention program from January 1986 to March 1995.

Table 1 Administration of HBIG and HB vaccine (1986-1994)

	HBs serological test	HBIG		HB vaccine			Completion rate (%)
		First	Second	First	Second	Third	
All Japan[3]	26813	26179	26099	26269	26053	24065	91.6
Okinawa Prefecture[6]	256	255	256	256	251	223	87.1
Hospital I	13	13	12	12	12	12	100.0

1986 to 1994, 26,813 high risk infants were tested serologically for HBs antigen in cord blood and 26,179 of them who were negative for HBs antigen received HBIG. After a second serological testing at the age of one month, 26,099 infants received the second HBIG and 26,269 infants received the first HB vaccine (Table). Although the number should be the same, the later number was slightly increased. This difference might be due to double or missing report from the municipalities since the data is calculated from the report of each municipality. Satogaeri delivery makes report in the registered municipality complicated, because mothers with newborns or infants return to their own homes, one or a few months after delivery at their mother's home town.

PROBLEMS IN THE VACCINATION PRACTICE

One of the problems in the prevention program is HBV infection which occurred before or during the program i.e. failure of prevention. Shiraki et al[5] reported that 3.4% of infants became carriers soon after birth before vaccine administration, during or soon after the third vaccination. An infant born to a high risk mother at our clinic became a carrier before the vaccine administration and was therefore excluded from the program according to the protocol. HBs antigen in his cord blood was negative. The dose of HBIG might be insufficient to neutralize the virus transmitted or infected HB virus might have low affinity for HBIG because of escape mutant. It is important to support these infants who became carriers in spite of the administration of HBIG and HB vaccine.

Another main problem in the prevention program is the low or poor response to vaccination. An infant who was born to a high risk mother became positive for anti-HBs antigen antibodies after five doses of the vaccine. The vaccine was plasma derived vaccine at that time. It is necessary to recommend four or five doses of administration of vaccine for such a low or poor responder case. In our clinic, however, the rate of seroconversion to HBs antigen in infants who received three doses of HB vaccine, was 100% from June 1987 when recombinant vaccine was introduced.

ADVERSE EFFECTS

Adverse effects such as fever, local redness and irritability have been reported. However, there were no infants with adverse effects of HB vaccine in our cases. Health examination is important to prevent coincidental complication especially at the third doses of vaccine.

VACCINATION COMPLIANCE

More than 90% of infants born to high risk mothers in Japan were administered HB vaccine after the program started. As aforementioned, about 3.4% of infants were excluded from the program because of HBV infection. Therefore, the completion rate of HB vaccination seems to be high relative to other vaccinations. It is considered that the Japanese integrated health care system and universal access to health care resulted in high completion rate of HB vaccination. With regard to the vaccination compliance, the completion rate of HB vaccination was calculated arbitrary as the number of infants with 3 doses of vaccine/number of infants administered

the first dose of vaccine ×100. The completion rates in Japan, Okinawa prefecture and Hospital I were 91.6, 87.1 and 100%, respectively. In Okinawa prefecture, the completion rate is low relative to the whole Japan. This may be partially due to the high incidence of satogaeri delivery in which infants receive the second or third vaccine at their registered municipality, because the data are based on the report of each prefecture. We usually refer newborns to a pediatric clinic for the vaccine when they return to their registered municipality in satogaeri delivery. It is also important to emphasize the need for the prevention program to the parents.

One of the main reasons for dropping out from the program seems to be complexity of vaccination. Administration of first doses to newborns before they leave hospital should be discussed in order to improve vaccination compliance by minimizing the number of HBIG injection in future.

CONCLUSION

Though it may take a long time to see substantial decrease in morbidity and mortality associated with HB virus infection, the prevalence of HBV carrier in children who were born after 1986 will be decreased by the national prevention program. We should make the effort to maintain a high completion rate of HB vaccination to prevent perinatal infection.

In conclusion, follow up and support systems for satogaeri delivery is important to improve vaccination compliance of HB vaccine in Japan. In addition, vaccination schedules should be discussed to maximize compliance.

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