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Active Pre-exposure Immunisation against Hepatitis B Virus : Immunogenicity of Hepatitis B Vaccine in Healthy Thai Adults and Children

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SUMMARY **The immunogenicity of plasma derived hepatitis B vaccine (Hevac B®) was studied for active pre-exposure immunisation in 176 healthy volunteer adults and 162 randomised children who had no hepatitis B virus markers. All subjects received three injections of 5 μg of hepatitis B vaccine intramuscularly at one month intervals. Seroconversion at 2 months after the third dose of vaccine was 96.30 percent in the children and 92.00 percent in the adults with mean anti-HBs titres of 800 mIU/ml and 353 mIU/ml respectively. The difference of anti-HBs levels between these two groups was statistically significant ($p < 0.05$). Female adults had exhibited higher immune response to HB vaccine than male adults but there was no seroconversion difference between boys and girls. There were no serious local or systemic side effects of hepatitis B vaccination. It was concluded that active immunisation with plasma derived hepatitis B vaccine in non-immune children and adults is highly effective without any serious side effects or complications. The prevention of horizontal transmission of hepatitis B virus shold be done by vaccination in children since they have a much better immune response to hepatitis B vaccine than adults.**

In areas of hyperendemicity such as Asia and Oceania, hepatitis B virus (HBV) is transmitted from asymptomatic carrier mothers to their babies, especially when mothers are seropositive for hepatitis Be antigen.[1,2] Almost all of such babies become persistent HBsAg carriers and constitute a reservior of HBV for further horizontal and, later in life vertical spreads in the community. In order to eradicate HBV, measures must be taken not only to interrupt the mother-to-baby transmission in the perinatal period, but also to prevent horizontal transmission in later life. We have shown that either hepatitis B immune globulin (HBIG), hepatitis B vaccine alone or the combination of hepatitis B immune globulin and hepatitis B vaccine administered to infants born from HBsAg carrier with HBeAg positive mothers immediately after birth reduces the number of perinatally infected carriers by about 75, 65 and 92 percent, respectively.[3-5] It was the purpose of the present study to investigate the immunogenicity, safety, complications and side effects of plasma derived hepatitis B vaccine (Hevac B®) used in prevention of later life transmission of hepatitis B virus in Thai children and adults.

SUBJECTS AND METHODS

Between January 1984 and October 1986, 938 Thai children and adults, aged < 1-50 years, were screened for hepatitis B virus markers including hepatitis B surface antigen (HBsAg), antibody to surface antigen (anti-HBs) and antibody to core antigen (anti-HBc). Those who were negative for HBsAg, anti-HBs and anti-HBc were selected for active pre-exposure immunisation with hepatitis B vaccine. The subjects comprised 176 healthy volunteer adults, 73 males and 103 females, aged 15-50 years and 162 randomised children, 83 males and 79 females, aged 1 mo - 14 yrs. All subjects received three injections of 5 μg of hepatitis B vaccine (Hevac B®) intramuscularly at one month intervals. Follow up for side effects or complications was done after administration of each injection. The serological tests for quantitative anti-HBs were done two months after the last injection was given. The serum samples showing negative results for anti-HBs (non-responders) were further tested for HBsAg and anti-HBc.

Blood specimens were tested for HBsAg by a reverse passive haemagglutination method (RPHA Anti-

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hebsgencell, Green Cross, Osaka) and by an enzyme-linked immunosorbent assay (Behring Enzygnost HBsAg test kit), and for anti-HBs and anti-HBc by passive haemagglutination (PHA hebsgencell and core cell, Green Cross, Osaka) and by an enzyme linked immunosorbent assay (Enzygnost-anti-HBs and Enzygnost-anti-HBc, Behring). Although ELISA method is more sensitive than RPHA or PHA method, it is more expensive. For economic reasons, we therefore screened the specimens first with the RPHA method for HBsAg and PHA method for anti-HBs and anti-HBc. Those specimens with negative results were further tested by ELISA method. The quantitative measurement of anti-HBs that developed after vaccination was done by ELISA method using WHO reference standard supplied in the test kit. The statistically significant differences were tested where appropriate by either the chi-square test or the Student's *t*-test.

RESULTS

The prevalence of all three HBV markers, including HBsAg, anti-HBs and anti-HBc are shown in Table 1. Although the percentage of HBsAg carriers was rather constant (around 7-9 percent in adults), the increased percentage of anti-HBs with increasing age indicated continuous exposure to HBV among the Thai population. Consequently, the percent negativity for all three HBV markers progressively decreased with age. As shown in Table 1, 67.92 percent of the children and 38.80 percent of the adults showed serological negative results for HBsAg, anti-HBs and anti-HBc. This difference was statistically significant ($p < 0.01$).

At two months after the third dose injection of hepatitis B vaccine, anti-HBs could be detected in 96.30 percent of the children (Table 2) and 92.00 percent of the adults (Table 3) with mean titres of 800 and 353 mIU/ml, respectively. The difference in seroconversion percentages between these two groups was not statistically significant ($p > 0.05$), but the difference in anti-HBs antibody responses between these two groups was statistically significant ($p < 0.05$). As shown in Table 2, the percentage of anti-HBs response among three children age groups were 97.90, 96.90 and 93.80%. Differences between the groups were not statistically significant ($p > 0.05$). Similarly, among 176 adults, anti-HBs could be detected in 95.60, 92.50, 83.30 and 75.00 percent in the 15-25, 26-35, 36-45 and over 45 years age groups, respectively (Table 3). These differences were not statistically significant ($p > 0.05$). Neither HBsAg nor anti-HBc could be detected in the serum samples of anti-HBs non-responder subjects.

The seroconversion in adult females (95.15 percent) was significantly higher than that in adult males (86.30 percent) ($p < 0.05$) but the mean titres of anti-HBs between these two groups was not statistically different (351 mIU/ml in females and 355 mIU/ml in males, $p > 0.05$). In children, the anti-HBs could be detected in 96.20 percent of boys and 96.38 percent of girls with mean titres of 1029 mIU/ml and 570 mIU/ml, respectively. The difference in seroconversion between these two groups was not statistically significant ($p > 0.05$).

No serious local (such as soreness or inflammation at the site of injection) or systemic side effects (such as fever, skin rash, anaphylaxis, etc.) of hepatitis B vaccination were observed.

DISCUSSION

Chronic carriers of HBsAg are at high risk of chronic liver diseases and ultimately cirrhosis and primary hepatocellular carcinoma later in life.[6,7] Thus, pre-exposure prophylaxis with the viral hepatitis B vaccine in non-immune children and adults is very important in preventing horizontal transmission of the hepatitis B virus. The present study showed that active immunisation with HBV plasma vaccine in good schedule and optimal dose was highly effective

Table 1 Prevalence of hepatitis B virus markers in normal Thai adults and children in Bangkok (by ELISA method)

Age group (Years)	Number tested	Percent positive for			Percent negative for all 3 markers
		HBsAg	anti-HBs	anti-HBc (only)	
> 45	42	9.52	61.90	11.90	16.67
36 – 45	144	7.63	50.70	15.48	26.40
26 – 35	402	7.96	40.04	9.85	42.04
15 – 25	188	8.51	33.51	21.80	35.64
Total Adults	776	8.12	41.62	13.90	38.80
< 1 – 14 (Children)	162	3.08	4.93	24.07	67.92

Table 2 Immunogenicity of hepatitis B vaccine in children, seroconversion and antibody response at 2 months after a third dose of vaccination using ELISA method

Age group (Years)	Number tested	Seroconversion (Percent)	Mean anti-HBs level ± S.D. (mIU/ml)
1/12 – 1	49	97.90	1172 ± 1538
1+ – 7	65	96.90	769 ± 1007
7+ – 14	48	93.80	445 ± 605
Total	162	96.30	800 ± 1138

Table 3 Immunogenicity of hepatitis B vaccine in adults, seroconversion and antibody response at 2 months after third dose of vaccination using ELISA method

Age group (Years)	Number tested	Seroconversion (Percent)	Mean anti-HBs level ± S.D. (mIU/ml)
15 – 25	68	95.60	408 ± 544
26 – 35	80	92.50	361 ± 419
36 – 45	24	83.30	162 ± 265
> 45	4	75.09	217 ± 204
Total	176	92.00	353 ± 463

in preventing the HBsAg carrier state in non-immune children and adults as previously described.[8,9] The seroconversion rate of 92.0 – 96.3 percent obtained in this study for both the children and adult groups was quite satisfactory. Female adults had better immune response to HB vaccine than the adult males as previously reported.[10] However, no difference in the seroconversion between boys and girls was observed in this study. It is interesting to note that the age of the vaccine recipients seemed to modulate the intensity of the immune response. With the same dose and schedule of vaccination, a higher anti-HBs antibody response was observed with younger recipients (Tables 2 and 3). The results of our quantitative anti-HBs study indicate that children have a much better immune response to hepatitis B vaccine than adults. Hence, the prevention of horizontal transmission of hepatitis B virus in children should be considered as a top priority, especially in younger age group children.

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