ORIGINAL ARTICLE

Immunogenicity of a Plasma-derived Hepatitis B Vaccine in Children and Adults

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Summary

Immunisation of health care workers and staff working in laboratory and hospital settings has been implemented since 1988. However due to the high cost of currently available HBV vaccine, many health personnel outside the Ministry of Health are not being immunised. This study sought to determine the immunogenicity of three doses of a low cost plasma-derived Korean HBV vaccine on employees of an institute for mentally handicapped and their spouses and children. We found that the Hepatitis B Vaccine-KGCC to be safe and immunogenic. The response to 10 mcg and 20 mcg Hepatitis B Vaccine-KGCC after third dose was good with 100% seroconversion.

Key Words: Hepatitis B Vaccine, Seroconversion, Immunisation

Introduction

Hepatitis B is a viral infection of the liver transmitted through infected blood and body fluids. Among those infected as adults, 6% to 10% become lifetime carriers of the virus[1]. Hepatitis B virus (HBV) carriers run the risk of not only developing chronic hepatitis but also a 300 times greater risk of hepatic cirrhosis and primary liver cancer as compared to non HBV carriers[2].

The carrier rates of Hepatitis B surface antigen (HBs Ag) in Malaysia were reported to be 3.1% in the normal population[3] and 6.9%[4] in adult healthy blood donors with higher prevalence rates in certain risk populations like intravenous drug abusers[5], promiscuous heterosexuals[6] and health care personnel[7]. It is also known that inmates of institutions for mentally handicapped have a high HBV carrier rate[8].

Routine HBV immunisation has been recommended in Malaysia for all health care workers and staff working in a variety of laboratory and hospital settings since 1988. The cost of vaccination of the Ministry's health personnel is borne by the Ministry of Health. Despite this recommendation, many health care personnel outside the Health Ministry are not being immunised.

Given that cost appeared to be the major barrier to HBV immunisation outside the Ministry of Health,

this study was conducted to determine the immunogenicity of three doses of a low cost plasma derived Korean HBV vaccine. The study population comprised employees and their dependants of a national institute for mentally handicapped children in Kuala Kubu Baru (Rumah Taman Sinar Harapan) which is run by the Ministry of Social Welfare.

This project was organised by the Community Services Division of the Damansara Rotary Club. Korea Green Cross Corporation donated their Hepatitis B vaccine-KGCC for this project, which spanned October 1991 to October 1992.

Materials and Methods

In October 1991, 90 employees of the National Institute for the Disabled and Mentally Handicapped volunteered for HBV screening and vaccination. They also brought along their children or household members, comprising 60 children below 18 years of age.

Of the 150 individuals in our study, 76 were male and 74 female. The racial composition was Malays (136), Indians (14) and Chinese (0).

Prior to vaccination informed consent was taken from each individual who was then screened for HBsAg, Anti-HBs and Anti-HBc (total) using commercial EIA kits viz. Auzyme, Ausab and Corzyme respectively from Abbott Laboratories, North Chicago, Illinois. Only individuals negative for all three of these HBV serum markers were given intramuscularly three doses of a plasma-derived HBV vaccine (Hepatitis B vaccine-KGCC) from Korea Green Cross Corporation on Day 0, 30, 180.

Two dosages of Hepatitis B Vaccine-KGCC were used: 10 mcg of HBV-KGCC for individuals below 10 years of age and 20 mcg HBV-KGCC for those aged 10 years and above.

Venous blood samples were collected for determination of Anti-HBs titres on Day 30, 180, 210 and 300 from 49 vaccinees who completed the three doses of Hepatitis B Vaccine-KGCC. Seroconversion was defined as a positive Anti-HBs response in which the Anti-HBs titre was equal to or greater than 10 International Units per litre (IU/L).

The Minitab Statistical Software Package was used to analyse the data. Geometrical mean (GM) was calculated using the formula

$$GM = 10^{\left[\frac{(\text{Log}Xi)}{n}\right]}$$

Results

Of the 150 individuals initially screened for inclusion into this study, 34 were considered unsuitable for Hepatitis B virus (HBV) vaccination. These consisted of individuals who were positive for Anti-HBs (n=25), for HBsAg (n=2) and for Anti-HBc (n=7).

Seventy-three individuals were vaccinated and were bled for Anti-HBs determination one month after the first dose of Korea Green Cross Plasma Vaccine.

Of the 73 individuals who were vaccinated, the first dose of vaccine led to 35 (47.95%) of them seroconverting, with Anti-HBs titre ranging from 3.5 to 125 IU/L.

Although all 73 individuals completed their three doses of vaccine only 49 volunteered for serial bleeding on Day 30, 180, 210, 300 and therefore only the titres of these 49 individuals were taken into account in this study (Tables I, II, III).

Discussion

The low cost plasma derived vaccine (HBV-KGCC) was found to be safe and immunogenic. All 49 vaccinees seroconverted even after the second dose, and

Table I
Sex distribution of the 49 vaccinees

Range of Age (Years)	Male (n)	Female (n)	Total (n)
< 10	8	6	14
≥ 10	17	18	35
Total	25	24	49

Table II
Racial composition of the 49 vaccinees

Race	Number
Malay	36
Indian	13
Chinese	0
Others	0
Total	49

Table III
Age distribution of 49 vaccinees

Range of Age (years)	Number
0 - 9	14
10 - 19	6
20 - 29	18
30 - 39	10
40 - 51	1
Total	49

after the third dose achieved levels of Anti-HBs ranging from 80 IU/L to 58,320 IU/L with a Geometric Mean Titre (GMT) of 7519.3. The Anti-HBs levels persisted 10 months post vaccination in all the 49 individuals (Fig. 1). No major side effects were reported except for local swelling and local pain occurring within 48 hours of vaccination (Table V).

We found that 10 mcg of the vaccine is highly immunogenic in individuals less than 10 years old with all of them seroconverting after the third dose with GMT of 8106 (Table IV, Fig. 2).

The response to 20 mcg of HBV-KGCC in individuals aged 10 years and above with GMT of 7297.4 after third dose (Table IV, Fig. 2) was also good.

Although 100% of the 49 vaccines seroconverted (Anti-HBs ≥10 IU/L) we noted that in adults (≥20 years) the Anti-HBs levels were lower than in the <10 years group. The 29 individuals aged ≥20 years had Anti-HBs titres ranging from 99.2 IU/L to 39680 IU/L

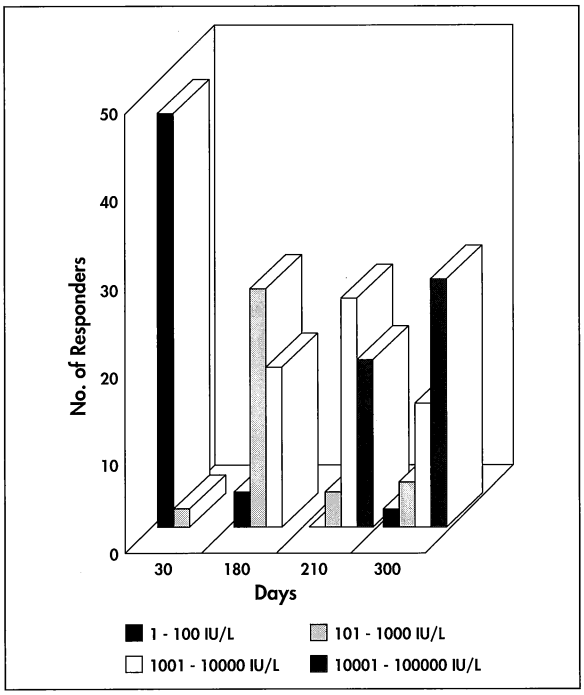

Fig. 1: Number of responders in relation to Anti-HBs (IU/L).

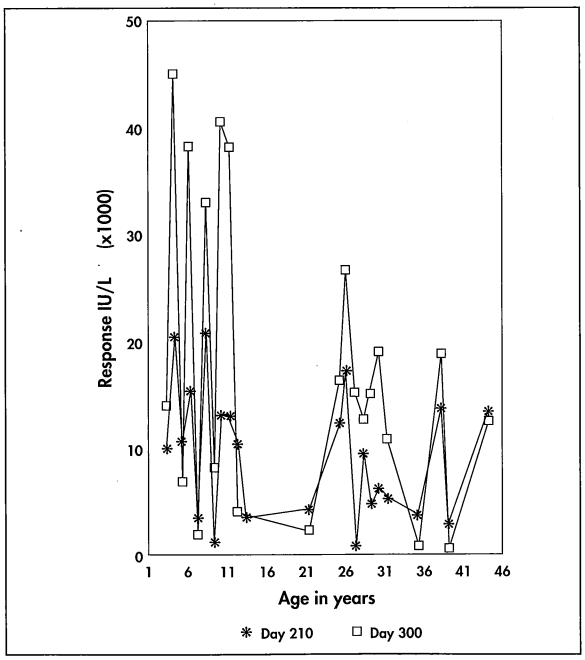

Fig. 2: Antibody response against average age of vaccinees after completion of 3 doses of HBV vaccine.

Table IV
Response to Hepatitis B Vaccine-KGCC on day 30, 180, 210, 300

	Day 30 (second dose)	Day 180 (third dose)	Day 210	Day 300	Total
Number of vaccinees n=14					
Number of responders aged <10 years	7	14	14	14	14
%	50.00	100	100	100	
GMT (IU/L)	3	397.556	7,042.15	8,106.0	
Number of vaccinees n=35					
Number of responders aged ≥ 10 years	14	35	35	35	35
%	40	100	100	100	
GMT (IU/L)	2.89	499.68	6,478.2	7,297.36	
Total GMT (IU/L)	–	–	–	7,519.3	49

Table V
Side effects following first, second and third dose of Hepatitis B Vaccine-KGCC in 49 vaccinees

Side effects	Post first dose		Post second dose		Post third dose		Total
	n	%	n	%	n	%	n
Local swelling	3	6.12	2	4.08	0	0	5
Fever	1	2.04	1	2.04	0	0	2
Local pain	0	0	5	10.20	0	0	5
Giddiness	4	8.16	3	6.12	2	4.08	9
Body rash	0	0	0	0	0	0	0
Total	8	–	11	–	2	–	21

(GMT 6511 IU/L). Thus although increasing age was associated with lower antibody levels, the titres were above 99.2 IU/L. The 14 individuals aged <10 years had Anti-HBs titres up to 58320 IU/L (GMT 8106 IU/L).

The Anti-HBs response was compared for differences in the male (n=25) and female (n=24) vaccinees. There was no significant difference in immune response following primary vaccination between the sexes (GMT in male 7912.8 IU/L; female 6851.7 IU/L).

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References

1. Recommendations of the Immunisation Practices Advisory Committee (ACIP). Morbidity and Mortality Week Report 1985;34 : 313-35.

2. Beasley RP, Lin CC, Hwang LY, Chien CS. Hepatocellular carcinoma and hepatitis B virus: A prospective study of 22,707 men in Taiwan. Lancet 1981;2 : 1129-32.

3. Tan DSK, Zaini R, Fang R, Collett D, Ooi BG. Hepatitis B markers in non-icteric medical patients in Malaysia. Southeast Asian J Trop Med Pub Hlth 1986;17(2) : 214-8.

4. Ton SH, Lopez CY, Ramli N. Assessment of infectiousness of male Malaysian blood donors. Vox Sang 1983;45 : 389-91.

5. Mangalam S, Tan DSK, Vijayamalar B, Collett D, Fang R. Markers of hepatitis B virus infection in asymptomatic drug abusers in Malaysia. Southeast Asian J Trop Med Pub Hlth 1986;17(2) : 209-13.

6. Rajakumar MK, Ton SH, Lim KF, Oorloff KH. Hepatitis B markers in heterosexuals involved in promiscuous sexual activity. Med J Malaysia 1984;39 : 65-7.

7. Ton SH, Lopez CS, Cheong KS, Noriah R. Infectiousness with respect to HBV of medical staff and patients in the general hospital Kuala Lumpur. Singapore Med J 1984;25(4) : 244-6.

8. Blumberg BS, Gertsley BJS, Hungerford DA, London WT, Sutnick AI. A serum antigen (Australian antigen) in Down's syndrome, leukaemia and hepatitis. Ann Intern Med 1967;66 : 924.