Effectiveness of Taiwan Nationwide HBV Vaccination in Persons at Risk for HIV Infection

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Abstract

Background: Seroprevalence of hepatitis B virus (HBV) after implementation of universal neonatal HBV vaccination and catch-up vaccination programs remains rarely investigated among the adults who were born in the vaccination era (in or after 1986) and engaged in high-risk sexual behaviors.
Materials and Methods: Between 2006 and 2012, we determined HBV surface antigen ([HBsAg), anti-HBs, and HBV core antibody (anti-HBc), hepatitis C virus antibody (anti-HCV) and rapid plasma reagin titers among HIV-infected men who have sex with men (MSM) born during 1984-1985 (Group I: 244 persons) and those born in or after 1986 (Group II: 523), and HIV-uninfected MSM (Group III: 377) and heterosexuals (Group IV: 217) born in or after 1986. Prevalence and incidence of HBV infection were estimated and multivariate analysis was performed to identify factors associated with HBsAg positivity.
Results: Compared with Group I, Groups II-IV had a significantly lower prevalence of HBsAg positivity (7.8% vs 3.7%, 2.4%, and 3.2%, respectively); and the prevalence of anti-HBc positivity was also lower for Groups III and IV (30.3% vs. 19.6%, and 18.0%, respectively), but no difference was observed between Groups I and II (30.3% vs. 26.3%). In multivariate analysis, HBsAg positivity was significantly associated with syphilis (adjusted odds ratio, 2.990; 95% confidence interval, 1.502-5.953) and anti-HCV positivity (adjusted odds ratio, 3.402; 95% confidence interval, 1.091-10.614). In subjects of Group II with all-negative HBV markers at baseline, the incidence rate of HBsAg seroconversion was 0.486 episodes per 100 person-years; and for those who received combination antiretroviral therapy containing lamivudine and/or tenofovir, none developed HBsAg seroconversion during the follow-up.
Conclusions: Among the adults who were born in or after 1986 and engaged in high-risk sexual behaviors in Taiwan, neonatal HBV vaccination and catch-up vaccination programs conferred long-term protection against HBsAg seroconversion and HBsAg positivity was associated with syphilis and anti-HCV positivity.

Background

1. July 1984: Nationwide HBV vaccination program in Taiwan was initially implemented to Vaccinate newborns of HBsAg-positive mothers alone with administration of immunoglobulin to infants born to mothers who tested positive for HBV envelope antigen (HBeAg)
2. July 1986: extended to cover all newborns
3. July 1987 to 1990: catch-up HBV vaccination to susceptible preschool children, school children, teenagers, and then to adults
4. 1991 catch-up HBV vaccination: the vaccination records of school children aged 7 years were checked, and those children who were unvaccinated or incompletely vaccinated would be given.
5. In this study, we aimed to investigate whether neonatal HBV vaccination and catch-up vaccination could confer long-term protection against HBV infection among HIV-infected patients and adults at risk for HIV infection; to identify factors associated with HBV infection; and to estimate the incidence of HBV surface antigen (HBsAg) seroconversion among HIV-infected patients in Taiwan where the background prevalence of HBsAg positivity was estimated 13-25% among the unvaccinated adults.

Methods

1. Between 2006 and 2012, we determined HBV surface antigen ([HBsAg), anti-HBs, and HBV core antibody (anti-HBc), hepatitis C virus antibody (anti-HCV) and rapid plasma reagin titers of the following groups.
2. Group I (244 persons): HIV-infected men who have sex with men (MSM) born during 1984-1985
3. Group II (523): HIV-infected MSM born in or after 1986
4. Group III (377): HIV-uninfected MSM born in or after 1986
5. Group IV (217): HIV-uninfected heterosexuals born in or after 1986.
6. The diagnosis of syphilis was made on the basis of a titer of rapid plasma reagin (RPR) ≧1:4

Results

1. Table 1 shows the clinical characteristics of Group I-IV.
2. Table 2 shows the comparisons of study subjects with and without positive HBsAg in univariate analysis.
3. Table 3 shows multivariate analysis for factors associated with positive HBsAg.
4. Table 4 shows crude incidence and incidence rate of seroconversion for HBsAg, anti-HBs or anti-HBc, HBsAg carriage, vaccination serology, and natural HBV infection.

Table 1: Clinical characteristics of Group I-IV. Except for age, there were no differences among the Four groups in terms of CD4 and PVL.

	Group I: HIV-infected MSM, 1984-1985	Group II: HIV-infected MSM, 1986	Group III: HIV-uninfected MSM, 1986	Group IV: HIV-uninfected heterosexuals, 1986	*P*[a] value	*P*[b] value	*P*[c] value
Case no.	244	523	377	217	NA	NA	NA
Age, mean (SD), year	28.5 (0.5)	24.8 (1.9)	25.6 (1.4)	25.4 (1.6)	<0.001	<0.001	<0.001
HIV infection							
CD4 count, mean (SD), cells/μL	370.4 (215.8)	401.9 (276.5)	NA	NA	NA	0.197	NA
CD4<200 cells/μL, % (n)	21.7 (39/180)	16.7 (46/275)	NA	NA	NA	0.186	NA
PVL, mean (SD), log_{10} copies/mL	4.31 (1.28)	4.43 (1.11)	NA	NA	NA	0.303	NA
PVL <200	12.4 (22/177)	6.1 (7/114)	NA	NA	NA	0.080	NA

Table 2: Comparisons of study subjects with and without positive HBsAg in univariate analysis. HIV Infections, born during 1984-1985, syphilis, and positive anti-HCV were factors associated with Positive HBsAg.

	Positive HBsAg	Negative HBsAg	*P* value
Patient no.	53 (4.0%)	1280 (96.0%)	
Age, mean (SD), years	26.8 (1.8)	25.7 (2.0)	<0.001
MSM, % (n)	84.8 (39/46)	82.5 (993/1203)	0.694
HIV infection	69.8 (37)	54.8 (702)	0.032
Born during 1984-1985	34.0 (18/53)	16.7 (214/1280)	0.001
Born in or after 1986	66.0 (35/53)	83.3 (1066/1280)	0.001
RPR titer >4	31.9 (15/47)	11.1 (128/1148)	<0.001
Positive anti-HCV	7.5 (4/53)	2.2 (28/1271)	0.03

5. Figure 1 shows the comparisons of the proportions of persons with positive HBsAg (HBsAg), all-negative HBV markers (All-negative), vaccination serology (Vaccination), and positive anti-HBc (anti-HBc) among Group I-IV.
6. Figure 2 shows the comparisons of syphilis (RPR≧4) and anti-HCV positivity among Group I-IV.

Table 3: Multivariate analysis for factors associated with positive HBsAg. Being born in or after 1986 protects positive HBsAg while syphilis and positive anti-HCV were associated with positive HBsAg.

Variables	Reference	Odds ratio	95% confidence interval	*P* value
HIV infection	No HIV infection	1.169	0.531-2.577	0.698
Born in or after 1986	Born during 1984-1985	0.421	0.208-0.854	0.017
RPR>4	RPR <4	2.990	1.502-5.953	0.002
Positive anti-HCV	Negative anti-HCV	3.402	1.091-10.614	0.035

Table 4: Crude incidence and incidence rate of seroconversion for HBsAg, anti-HBs or anti-HBc, HBsAg carriage, vaccination serology, and natural HBV infection.

	Crude incidence	Incidence rate (episodes per 100 person-years of follow-up)
ll-negative HBV markers at baseline =64), % (n)		
HBsAg seroconversion	1.6 (1/64)	0.486
Anti-HBs seroconversion	28.1 (18/64)	9.897
Anti-HBc seroconversion	10.9 (7/64)	3.576
Vaccine-type serology	21.9 (21/64)	7.406
Natural HBV infections	10.9 (7/64)	3.578
eceiving anti-HBV agents (n=37), % (n)		
HBsAg seroconversion	0 (0/37)	0
Anti-HBs seroconversion	18.9 (7/37)	14.788
Anti-HBc seroconversion	8.1 (3/37)	6.338
Vaccine-type serology	13.5 (5/37)	10.563
Natural HBV infection	8.1 (3/37)	6.338

Conclusion

Among the adults who were born in or after 1986 and engaged in high-risk sexual behaviors in Taiwan, neonatal HBV vaccination and catch-up vaccination programs conferred long-term protection against HBsAg seroconversion and HBsAg positivity was associated with syphilis and anti-HCV positivity.

Figure 1: Comparisons of the proportions of persons with positive HBsAg (HBsAg), all-negative HBV markers (All-negative), vaccination serology (Vaccination), and positive anti-HBc (anti-HBc) among Group I-IV. Compared with Group II, Group I had higher rate of positive HBs, all negative, vaccine serology, but similar positive anti-HBc.

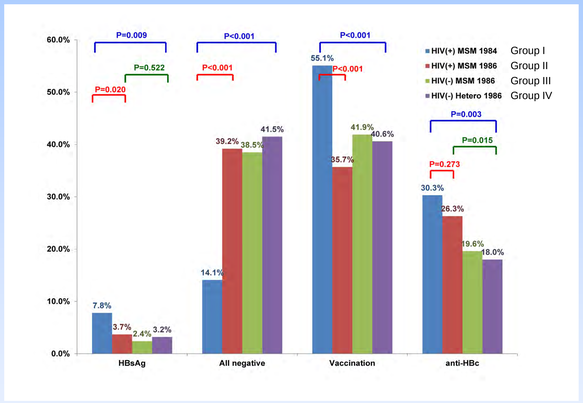


Figure 2: Comparisons of syphilis (RPR≧4) and anti-HCV positivity among Group I-IV. Group I and II had higher rates of syphilis and positive anti-HCV.

