1025

Prophylactic effect of PrEP against HBV infection among MSM

Daisuke Mizushima[1], Misao Takano[1], Haruka Uemura[1], Yasuaki Yanagawa[1], Takahiro Aoki[1], Koji Watanabe[1], Hiroyuki Gatanaga[1], Yoshimi Kikuchi[1], and Shinichi Oka[1]
[1]National Center for Global Health and Medicine, AIDS Clinical Center, Tokyo, Japan

BACKGROUND

Universal HBV vaccination had not been available in Japan until 2016 and men who have sex with men (MSM) are still vulnerable to hepatitis B virus (HBV) infection. Previous studies identified tenofovir disoproxil fumarate (TDF)'s prophylactic effect against HBV infection among HIV-infected patients.

Clin Infect Dis. 2013 Jun;56(12):1812-9.

Thus, we evaluated incidence of HBV infection and prophylactic effect of pre-exposure prophylaxis (PrEP) with TDF/emtricitabine (FTC) against HBV infection among a non HIV-infected MSM cohort, sexual health clinic (SHC) in Tokyo.

METHODS

MSM cohort (SHC):
MSM over 16 years old were included in SHC cohort. Participants were examined for HIV infection, syphilis (quantitative RPR/TPHA), pharyngeal and rectal *Chlamydia trachomatis* and *Neisseria gonorrhoeae infections,* and HBs antigen/antibody and HBc antibody, HCV antibody and HAV IgG antibody every 3 months there.

Entry criteria of this study were as follows:
HBc antibody negative (< 1.0 S/CO CLIA method) and HIV negative at the study enrollment.

Follow-up period
The participants were followed between January 2018 and September 2019 and incidence rate of HBV infection were evaluated. Participants who acquired HBV infection or HIV infection were censored.

Definition:
The definition of HBV infection was positive conversion of HBc antibody or HBs antigen during follow-up period. Use of vaccination of HBV were defined as self-report of their experience of HBV vaccination or HBs antibody >= 10 mIU/ml (CLIA method). TDF/FTC for PrEP were provided for free via an official program of daily PrEP or purchased via internet for its generic drug at their own expense.

Statistics:
The cox proportional hazards regression analysis was used to evaluate prophylactic effect of PrEP against HBV infection and other factors including HBV vaccination. Factors with statistically significance ($p<0.05$) and the use of HBV vaccination as a known preventive factor against HBV infection were entered into multivariate analysis.

Table 2. Results of uni- and multivariate analysis to estimate prophylactic effect of PrEP and other factors against HBV infection

	Univariate analysis			Multivariate analysis		
	Hazard ratio	95% confidence interval	p value	Hazard ratio	95% confidence interval	p value
Age, years	0.987	0.931-1.046	0.650			
PrEP use	0.114	0.015-0.873	0.037	0.123	0.016-0.948	0.044
HBV vaccination	0.505	0.161-1.588	0.242	0.627	0.198-1.981	0.426
HIRI-MSM score[1]	1.038	0.965-1.116	0.320			
CT and/or NG[2]	2.744	0.976-7.713	0.056			
Previous syphilis	2.259	0.873-7.501	0.087			
Active syphilis	1.629	0.214-12.415	0.638			

1. HIRI-MSM score; HIV incidence Risk score for men who have sex with men 2. CT; *Chlamydia Trachomatis*, NG; *Neisseria Gonorrhoeae*

Figure 2. Preventive effect of PrEP against HBV infection by Kaplan-Meier

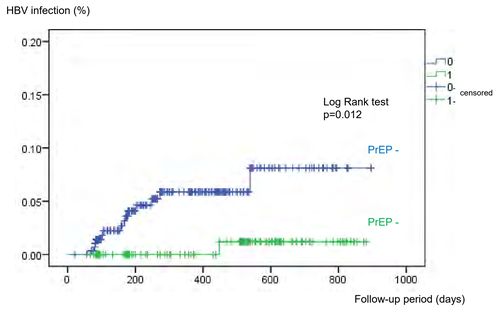
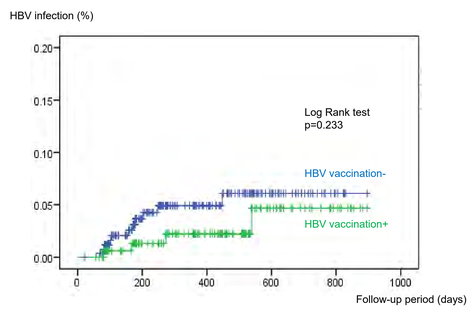


Figure 3. Preventive effect of HBV Vaccination against HBV infection by Kaplan-Meier



RESULTS

- 827 MSM were included in the cohort as of September 2019. Of 827 MSM, 25 and 211 MSM were excluded from the study due to HIV infection and HBc antibody positivity at the enrollment, respectively. 591 (148 were PrEP+ and 443 were PrEP-) were followed every 3 months with 419.8 person-years [mean age (SD), 34.5 years (9.3)]. The incidence rate of HBV infection was 3.57 cases per 100 person-years (15 HBV infections, one in the PrEP+ group and 14 in the PrEP- group, Log Rank test p=0.012,). The table 2 identified the preventive and risk factors estimated by the cox hazard analysis which showed significant prophylactic effect of PrEP against HBV infection.

Figure 1. Flow chart of MSM with and without PrEP

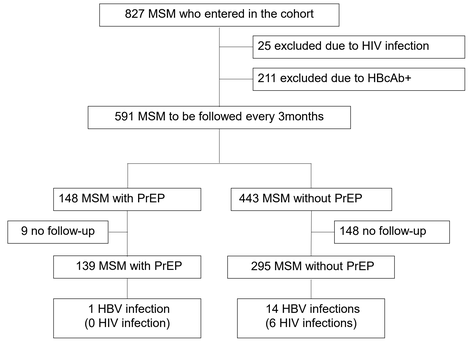


Table 1. Baseline characteristics of MSM with and without PrEP

	MSM with PrEP（n=139）	MSM without PrEP（n=295）	All（n=434）
Age, years	36.7±8.67	33.4±9.37	34.5±9.27
HIRI-MSM score[1]	13.4±7.57	13.2±7.48	13.3±7.50
Self-reported HBV vaccination	71（52.6%）	97（32.9%）	168（38.7%）
HBs antibody > 10 ml/U	60（43.2%）	77（26.1%）	137（31.6%）
CT and/or NG[2]	52（37.4%）	93（31.5%）	145（33.4%）
HCV Ab positive	1（0.7%）	0（0%）	1（0.2%）
Previous syphilis	27（19.4%）	49（16.6%）	76（17.5%）
Active syphilis	9（6.5%）	14（4.7%）	23（5.3%）

CONCLUSIONS

- PrEP has strong prophylactic effect against HBV infection and is a good indication especially for non-responders to HBV vaccination.

ADDITIONAL KEY INFORMATION

Limitation: This study retrospectively reviewed the cohort data. As a result, timing of PrEP or HBV vaccination initiation was not unified in the analysis. Furthermore, self-reported information on their HBV vaccination could be imprecise which attributes to scarce preventive effect of HBV vaccination.

Other key information: All the cases of HBV infection who had HBV vaccination were asymptomatic, which is also a beneficial effect of HBV vaccination.

Author Contact Information
Daisuke Mizushima, email:dmizushi@acc.ncgm.go.jp

Acknowledgements
Special thanks to Ms. Kazuko Tanaka, Ms. Mikiko Ogata. MSM cohort, SHC is partially sponsored by VIIV Healthcare for an Investigator Sponsored Study (ISS).

Table 3. Characteristics of 15 cases with HBV infection

age	PrEP	Self-reported HBV Vaccination	HBs Ab > 10 ml/U	HIRI MSM score	symptom
38	-	+	+	15	-
42	-	-	−	6	+
26	-	-	−	18	-
50	-	+	+	10	-
37	-	+	+	22	-
22	+	-	−	25	+
49	-	-	−	10	-
39	-	+	−	19	-
30	-	-	−	5	-
19	-	-	−	25	+
27	-	-	−	8	+
35	-	-	−	15	+
30	-	-	−	15	+
31	-	-	−	19	+
29	-	-	−	15	+