582

Effectiveness of HAV vaccination among HIV-positive patients during an acute hepatitis A outbreak

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Introduction

1. During June 2015 to January 2017, more than 1100 indigenous cases of acute HAV infections were reported in Taiwan, with more than half in patients being HIV-positive men who have sex with men (MSM).
2. Hepatitis A vaccination has been recommended for MSM.
3. The serological response to HAV vaccination is reduced in HIV-positive patients compared with HIV-negative persons.
4. This ongoing study aimed to evaluate the effectiveness and serologic response of HAV vaccination among HIV-positive patients in this outbreak setting.

Methods

1. Design: prospective cohort study, June 2015 to September 2016.
2. Study site: National Taiwan University Hospital
3. Included subjects: HIV-positive patients aged ≥20 years with negative baseline anti-HAV IgG since June 2015.
4. Excluded subjects: patients with previous HAV vaccination.
5. Intervention: 2 doses of HAV vaccines (HAVRIX® or VAQTA®, 0 and 6 months) were advised for all HIV-positive and HAV-seronegative patients.
6. Primary endpoints:
   (1) Serologic response 4 weeks after the last dose of HAV vaccination.
   (2) Acquisition of acute HAV infection during the follow-up.
6. Secondary endpoint:
   (1) Serologic response between the first and the last doses of vaccination.
   (2) Serologic response at week 48 of vaccination.
5. Generalized estimating equation (GEE) was used to determine the associations between the predictor variables and repeated measured serologic outcomes.

Results

1. 1627 HIV-positive patients tested negative for anti-HAV IgG at baseline (Fig 1).
   - 1534 patients had not previously received HAV vaccination.
   - 1224 patients (79.8%) had received the first dose of HAV vaccine (Table 1).
   - 798 patients (52.0%) had completed the 2-dose HAV vaccine series.
2. The overall seroconversion rate before the last dose of HAV vaccination was 39.7% (602/1517). The rate increased to 93.4% (424/454) and 94.6% (87/92) 4 weeks after the last dose and at week 48 of vaccination (Fig 2).
3. Six vaccinees and 58 non-vaccinees had incident acute HAV infections, resulting in vaccine effectiveness of 93.0% (Fig 3).
4. The independent factor associated with seroconversion 4 weeks after the last dose of HAV vaccination was higher CD4 count (Table 2).

Figure 1. Study flow diagram

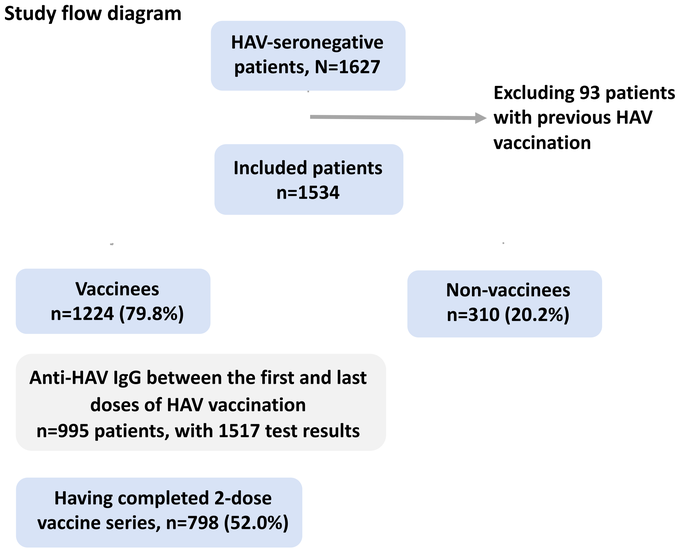

Table 1. Comparisons of the clinical characteristics between vaccinees and non-vaccinees

	Vaccinees (n=1224)	Non-vaccinees (N=310)	*p*
Age, median (IQR), years	34 (29-40)	35 (30-42)	0.030
Male, n (%)	1203 (98.3)	292 (94.2)	<0.001
Men who have sex with men, n (%)	1167 (95.3)	277 (89.4)	<0.001
HBsAg positivity, n (%)	121 (9.9)	25 (8.1)	0.329
Anti-HCV positivity, n (%)	83 (6.8)	35 (11.3)	0.008
Antiretroviral therapy use, n (%)	1171 (95.7)	282 (91.0)	0.001
Baseline CD4 count, median (IQR), cells/μL	568.5 (428-748)	560.5 (357-743)	0.097
Baseline PVL, median (IQR), $\log_{10}$ copies/mL	*UD (UD-UD)	UD (UD-1.41)	0.0001
Syphilis, n (%)	284 (23.2)	82 (26.5)	0.231

***UD, undetectable**

Figure 2. Seroconversion rates after the first dose of hepatitis A vaccination

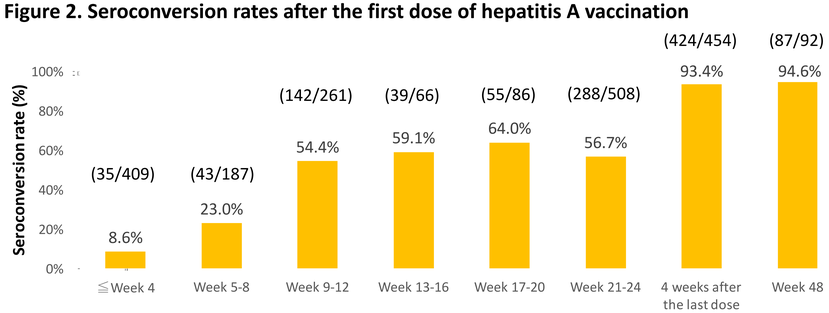

Figure 3. Kaplan-Meier estimates of the cumulative percentage of acute HAV infections

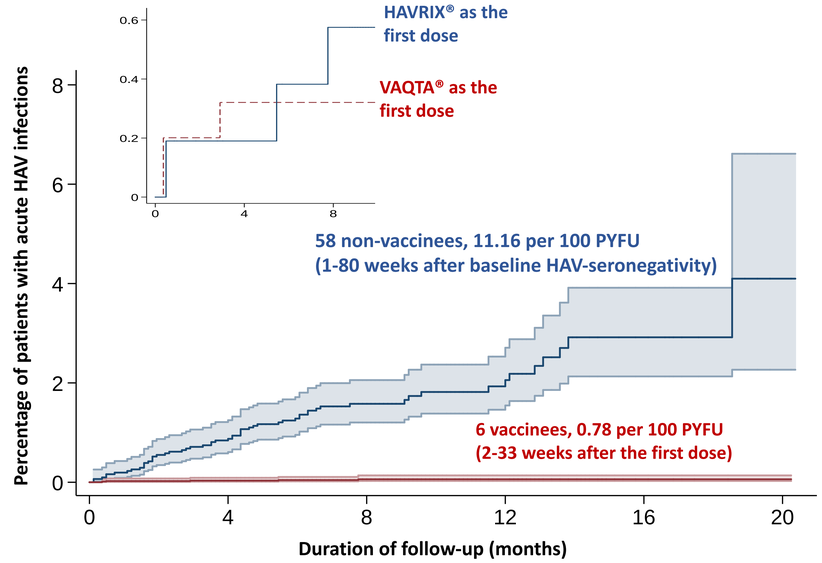

Table 2. Factors associated with HAV seroconversion (A) at 4 weeks after the last dose of HAV vaccination; and (B) between the first and the last doses of HAV vaccination

Multivariable analysis	(A) Adjusted OR (95% CI)	(B) Adjusted OR (95% CI)
Age, per 1-year increase	0.97 (0.91-1.03)	0.98 (0.96-1.00)
Men who have sex with men	-	1.40 (0.60-3.26)
Weight, per 1-kg increase	0.99 (0.95-1.04)	1.00 (0.99-1.02)
Smoking	1.27 (0.41-3.86)	1.21 (0.88-1.65)
HBsAg positivity	0.48 (0.16-1.39)	0.71 (0.45-1.13)
Anti-HCV positivity	0.33 (0.07-1.49)	1.31 (0.69-2.49)
Nadir CD4, per 10-cell/μL increase	1.01 (0.97-1.05)	1.00 (1.00-1.01)
Updated CD4 count, per 10-cell/μL increase	1.04 (1.01-1.07)	1.00 (1.00-1.01)
Updated PVL, per 1-$\log_{10}$ copies/mL increase	1.03 (0.49-2.14)	0.92 (0.78-1.08)
First dose of HAV vaccine, VAQTA® vs. HAVRIX®	0.84 (0.24-2.85)	4.44 (3.16-6.23)
Time to anti-HAV IgG testing, per 1-week increase	1.03 (0.91-1.16)	1.12 (1.11-1.14)

Conclusions

Despite the delayed serologic response to HAV vaccination in HIV-positive MSM, the risk of acute HAV infection was significantly reduced by HAV vaccination during the outbreak setting. Higher CD4 counts were associated with better serologic response to 2-dose HAV vaccination.