Limited effectiveness of high-dose flu vaccine in augmenting influenza A responses in older people with HIV

0481

Jonah Kupritz[1], Sheldon Davis[1], Prabhsimran Singh[1], TianHao Liu[1], Daniel Diaz-Pachon[1], Allan Rodriguez[1], Scott Boyd[2], Rajendra Pahwa[1], **Suresh Pallikkuth[1], and Savita Pahwa[1]**
[1]University of Miami Miller School of Medicine, Miami, FL, USA, [2]Stanford University, Palo Alto, CA, USA

BACKGROUND

- Aging impairs antibody responses to influenza (flu) vaccination, with greater impairment in people with HIV (PWH) than in people without HIV (PWoH).
- High-dose (HD) vaccine, containing 4x more antigen than standard-dose (SD), is recommended for people aged ≥65 years but has not been studied in older PWH.
- To address these knowledge gaps and inform better protection of PWH, we conducted a first-of-its-kind, paired-format study of SD and HD flu vaccine responses in young and old virally suppressed PWH and PWoH.
- A total of *N*=235 participants received SD vaccine. The following year, *N*=107 participants (YPWoH, *N*=18; YPWH, *N*=15; OPWoH, *N*=37; OPWH, *N*=37) returned for HD flu vaccination (Fig. 1).
- To our knowledge, this is the first study to directly examine the relative benefit of HD versus SD vaccination in older people with HIV who received SD and HD in consecutive flu seasons.

METHODS

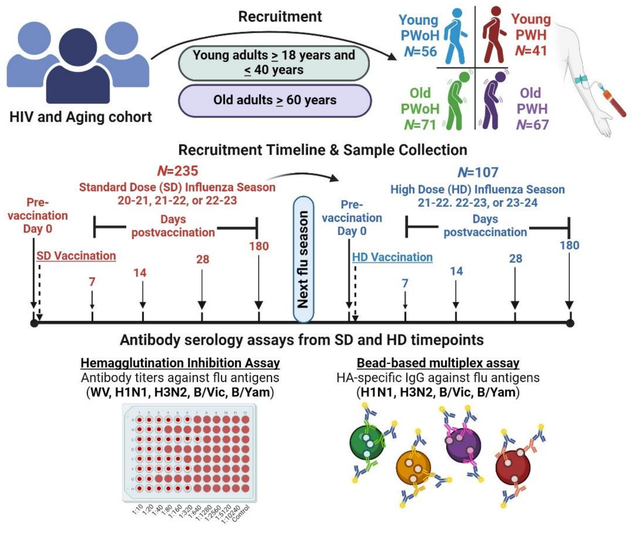


Fig 1: Overview of the study design. A total of *N*=235 young (Y, ≤40 years) and old (O, ≥65 years) participants were recruited into the HIV and Aging study and received SD influenza vaccine. Participants with HIV were virally suppressed on antiretroviral therapy. The following season, *N*=107 participants returned to receive HD vaccine. Hemagglutinin (HA) inhibition (HAI) titers and HA IgG were measured in serum samples at 0-, 7-, 14-, 28-, and 180- days postvaccination to assess responses to flu vaccination.

Our data underline the benefit of annual flu vaccination while highlighting the limitations of unadjuvanted high dose vaccine in further augmenting influenza A responses among older PWH

RESULTS

- SD and HD vaccine both elicited robust responses to flu antigens at 28 dpv, across all groups.
- Compared to YPWoH, A/H1N1-specific HAI and HA IgG were lower among older participants with HIV following SD and HD flu vaccination (Fig. 2a).
- Serological responses sharply waned after 28 dpv across all groups, largely returning to baseline levels by 180 dpv (not shown).
- Multivariate analyses revealed that HD vaccination improved B/Victoria HA-specific IgG levels among OPWoH and OPWH at 28 dpv. Improved A/H3N2 HA-specific IgG levels were observed among the combined cohort of PWoH, but not PWH, following HD vaccination (Table 1).
- Durability of A/H3N2 HA-specific IgG was greater after HD vaccination among OPWoH, but not among OPWH (Figs. 2b & 3). A/H1N1 responses were not improved among either group (Table 1).

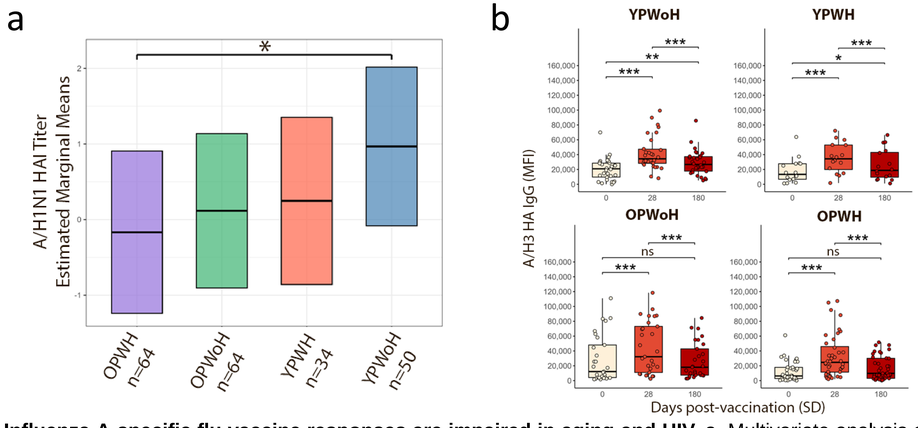


Fig. 2: Influenza A-specific flu vaccine responses are impaired in aging and HIV. a. Multivariate analysis of A/H1N1 HAI titer at 28 days post-standard-dose flu vaccination (dpv) across the four groups, controlling for baseline responses, vaccination history, and demographic data. **b.** A/H3N2 (A/H3) HA-specific IgG at 0, 28, and 180 dpv in young people without HIV (YPWoH, N=30), young people with HIV (YPWH, N=16), old people without HIV (OPWoH, N=29), and old people with HIV (OPWH, N=40); Wilcoxon signed-rank test, FDR-adjusted. *=P<0.05, **=P<0.01, ***=P<0.001, ns=not significant.

CONCLUSIONS

- OPWH had lower A/H1N1-specific HAI responses at 28 days post-SD flu vaccination, compared to YPWoH.
- Influenza B responses were improved in OPWoH and OPWH after HD vaccination, while improved influenza A-specific responses were only observed among OPWoH.
- Our data highlight the need for optimal timing of vaccination to ensure protection throughout the flu season, and suggest that alternative strategies, such as recombinant or adjuvated vaccines, may be necessary to augment influenza A-specific immunity among OPWH.

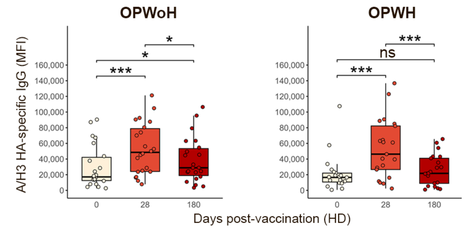


Fig. 3: Durability of A/H3 specific IgG responses after HD flu vaccination. A/H3 HA-specific IgG (MFI) at 0, 28, and 180 dpv in old people without HIV (OPWoH, N=22), and old people with HIV (OPWH, N=21); Wilcoxon signed-rank test: *=P<0.05, **=P<0.01, ***=P<0.001.

	Group (*N*)	HAI titer	*P* value	HA-specific IgG	*P* value
A/H1N1	YPWoH (14)	=	0·7	=	0·6
	YPWH (14)	=	0·6	=	0·2
	OPWoH (34)	=	0·4	=	0·2
	OPWH (30)	=	0·5	=	>0·9
	Old (64)	=	>0·9	=	0·7
	Young (28)	=	>0·9	=	0·8
	PWH (44)	=	0·8	=	0·4
	PWoH (48)	=	0·9	=	0·4
A/H3N2	YPWoH (14)	-	-	=	0·7
	YPWH (14)	-	-	=	0·10
	OPWoH (34)	-	-	=	0·080
	OPWH (30)	-	-	=	0·15
	Old (64)	-	-	=	0·3
	Young (28)	-	-	=	0·2
	PWH (44)	-	-	=	0·2
	PWoH (48)	-	-	↑	**0·047**
B/Victoria	YPWoH (14)	=	0·8	=	0·12
	YPWH (14)	↑	**0·036**	=	0·5
	OPWoH (34)	↑	**0·005**	↑	**0·027**
	OPWH (30)	=	0·5	↑	**0·014**
	Old (64)	=	0·3	=	0·2
	Young (28)	=	0·6	=	0·7
	PWH (44)	=	0·4	=	0·079
	PWoH (48)	=	0·7	=	0·3
B/Yamagata	YPWoH (14)	=	0·5	=	0·3
	YPWH (14)	=	0·6	=	0·2
	OPWoH (34)	=	0·6	=	0·2
	OPWH (30)	=	0·7	=	0·4
	Old (64)	=	>0·9	=	0·6
	Young (28)	=	0·13	=	0·7
	PWH (44)	=	0·6	=	0·6
	PWoH (48)	=	0·2	=	0·3

Table 1: Summary of changes to HAI titer and HA-specific IgG at 28 dpv for HD vs. SD flu vaccination, from a multivariate analysis controlling for baseline responses, vaccination history, and demographic data. =no difference, ↑increased, -not assessed.

ADDITIONAL KEY INFORMATION

The study was approved by the IRB at University of Miami (IRB #20200752). This project was supported by a NIH grant (R01AG068110) to Savita Pahwa and Suresh Pallikkuth, the University of Miami Microbiology and Immunology Department, and the Immunology Core of the Miami CFAR (P30AI073961).