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ORIGINAL ARTICLE

Limited awareness of the effective timing of HIV post-exposure prophylaxis among people with high-risk exposure to HIV

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Abstract

The effectiveness of post-exposure prophylaxis (PEP), a major strategy in the battle against HIV, depends on awareness of this modality and its proper timing among high-risk groups. While general awareness of PEP is improving, recently estimated to be 36–47% among men who have sex with men (MSM), PEP implementation remains disappointingly low and may be driven by limited awareness of effective PEP timing window. The level of detailed understanding of PEP timing and effectiveness among populations at risk has not been prospectively assessed to date. We prospectively evaluated, for the first time, actionable awareness regarding effective timing of PEP among a large cohort of individuals tested for HIV following unprotected sexual intercourse. Four hundred participants were assessed between December 2014 and February 2016. Overall awareness of the option of PEP was 60% and was significantly higher among male members of the LGBTQ community (75·5% as compared to 52·6% among heterosexual males) and those undergoing past HIV testing (67·1%). However, only 24% of individuals at risk were aware as to the proper timing of effective PEP treatment, thereby leading, in the majority of cases, to missing the window of opportunity for PEP treatment. This study highlights the lack of knowledge as to the specific requirements needed for effective PEP timing. Expanded advertising, better targeting of the heterosexual population, training of family physicians in the field of gender, sexuality, and LGBTQ medicine, may improve effective PEP availability, thereby reducing HIV transmission.

Keywords HIV · Post-exposure prophylaxis · Awareness

Introduction

From the start of the AIDS epidemic, key elements of its prevention strategies included the promotion of the use of condoms, screening for HIV infection among populations at risk, and sexual education. With the introduction of effective drug therapy for HIV, post-exposure prophylaxis (PEP), treatment as prevention (TaP), and pre-exposure prophylaxis (PrEP) became additional important prevention strategies.

PEP administration guidelines were published by the Center for Disease Control (CDC) in 2005 [1], although PEP was in use even earlier. PEP is recommended for HIV-negative persons approaching medical assistance within 72 h following exposure to an infected biological fluid from an HIV-positive person, in a context of occupational exposure, sexual intercourse, or IVDU. Major barriers for PEP use include the concern that it might promote high-risk sexual activity, lack of knowledge regarding PEP effect among healthy people, fear of developing viral resistance, side effects, high costs, safety concerns, compliance, and unawareness of PEP and the appropriate time window for PEP administration. In a 2011 survey among the MSM community in New York, Rodrigez et al. [2] reported a low general awareness rate of only 36%. Similar rates were noted by Mahata et al. [3] in 2006–2007. Liu et al. [4] studied 1819 HIV-uninfected homosexual and bisexual men in California in 2006 and found 47% awareness regarding the existence of PEP, with only 4% of participants reporting PEP usage. Walters et al. determined that PEP/PrEP awareness among 2483 participants from different risk groups in 2011–2013 in NYC and Long Island ranged from 13

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to 25%, with the highest rate of awareness (25%) reported in urban MSM [5]. More encouraging PEP awareness rates (64%) were reported by Dolezal [6] in MSM from Boston while only 16% were found in San Juan.

The main goal of this study was to study the awareness regarding effective timing of PEP administration for prevention of HIV following unprotected sexual intercourse among individuals tested for HIV in the Jerusalem Open Clinic (JOHOC). Secondary objectives included characterization of people approaching the anonymous HIV testing center; elucidation of the time lapse between an unprotected sexual episode and coming for medical assistance; and estimation of PEP effects on sexual habits in this context.

Methods

This prospective study included individuals older than 18 who arrived at JOHOC to perform an HIV test, following an episode of unprotected sexual intercourse from 28 December 2014 to 14 February 2016. The JOHOC, located in the city center, is the only clinic that provides both HIV anonymous testing and rapid HIV tests in the greater Jerusalem metropolitan area serving a population of one million inhabitants. In this region, HIV tests can also be performed at the AIDS Center of Hadassah-Hebrew University Medical Center (anonymously or non-anonymously), or non-anonymously at different local HMOs.

The JOHOC provides counseling by a qualified counselor. The participant is encouraged (but not obliged) to disclose the reason for HIV testing in order to perform risk assessment and to decide if further tests or physician counseling are also needed. Additional information regarding HIV, safe sexual habits, and proper use of a condom are provided. PEP is not included in routine counseling sessions, unless the participant asks about the treatment or is found to be eligible to receive the treatment, in which case, he is referred immediately to receive PEP at one of the city's emergency rooms or at the HIV clinic in Hadassah Medical Center.

During the study period, individuals who were identified by counselors as eligible were offered to participate in the study after the conclusion of the counseling session and then signed an informed consent. Individuals younger than 18 years of age, those arriving for an HIV test for reasons other than unprotected sexual intercourse, or those who discussed PEP during the counseling session were excluded from the study.

The study questionnaire (Sup. 1) included demographic data and independent variables such as gender identity, sexual preference, prior HIV tests, GP awareness of the participant's sexual preference, and time frame of HIV testing with regard to exposure. Dependent variables were qualitative dichotomous variables regarding the participant's awareness of PEP, and quantitative variables to evaluate the depth of knowledge about PEP procedure and its effective time window.

Ethics

The study was approved by the IRB committee of Hadassah-Hebrew University Medical Center (0438-14-HMO).

Statistical analysis

Sample size estimation was to ensure that the width of 95% CI would not exceed 10% for any percentage of awareness between 30 and 70%; thus, 400 participants were needed.

The association between two qualitative variables was tested using Fisher's exact test or chi-square test. Two-sample t test was used to compare quantitative variables between two independent groups with a normal distribution, while the Mann-Whitney non-parametric test was used when the distribution of values was skewed and not normal. ANOVA procedure was used to compare quantitative variables between three or more independent groups for normally distributed data and the non-parametric Kruskal-Wallis test was used for non-normally distributed data. A logistic regression model was used to study the simultaneous effects of several variables on a dependent dichotomous variable. All tests applied were two-tailed and a p value of 5% or less was considered as statistically significant.

Results

During the study period, 400 of the 877 people attending the JOHOC were found eligible and enrolled in the study.

Participants characteristics (Table 1)

The majority of participants were males, and 38% of participants were members of the LGBTQ community (lesbian, gay, bisexual, transgender, and queer), a higher proportion than the 10–20% estimation of the LGBTQ community among the general population (Table 1).

Two third of participants had previous unprotected sexual intercourse, and half reported recurrent prior unprotected episodes, ranging from two to five events per individual. No correlation was found between a past history of unprotected sexual intercourse or multiple unprotected sexual episodes and being a member of the LGBTQ community.

As compared to heterosexual participants, LGBTQ participants significantly shared less of the information regarding their sexual habits and preferences with their GPs, and performed more previous HIV tests, correlating with their higher visitation in JOHOC and among our study population.

Table 1 Participants' characteristics

Variable	Total		Hetero		LGBTQ		*p* value
	N	%	*N*	%	*N*	%	
Biological sex							
Total	400	100	248	100	152	100	
Male	266	66.5	135	54.5	131	86	
Female	134	33.5	113	45.5	21	14	
Age							
Total	398	100	247	100	151	100	
18–25	191	48	106	43	85	56.3	
26–35	170	42.7	107	43.3	63	41.7	
36–45	27	6.8	26	10.5	1	0.66	
46+	10	2	8	3.2	2	1.32	
Sexual preference							
Heterosexual	248	62					
Homosexual	103	25.8					
Bisexual	37	9.3					
Transgender	1	0.3					
Queer	11	2.8					
Physician awareness to sexual preferences	207	52	155	63.8	52	34.2	< 0.01^
First event of unprotected sexual intercourse							
Total	388	100	242	100	146	100	0.313^
Yes	134	34.5	79	32.6	55	37.7	
No	254	65.5	163	67.4	91	62.3	
Number of unprotected sexual intercourse							
Total	221	100	148	100	73	100	0.173^
1	16	7.2	11	7.4	5	6.8	
2–5	121	54.8	85	57.4	36	49.3	
6–10	27	12.2	13	8.8	14	19.2	
11+	57	25.8	39	26.4	18	24.7	
Prior HIV tests	246	61.5	137	55.2	109	71.7	< 0.01^

^ The Pearson chi-square

The median period of time between unprotected sex and the time of realization of possible exposure to HIV was 7 days. Additional 23 days, on average, was needed to decide to perform the HIV test, but participants attended the JOHOC only 30 days later (Table 4).

PEP awareness (Tables 2 and 3)

Two hundred and forty of our participants (60.0%) reported that they were aware of PEP following unprotected sexual intercourse. Similar rates of participants were aware of PEP following occupational exposure and following a sexual assault (62,·4%, and 63%, respectively, data not shown).

Only 40% of those who reported being aware of PEP (24% of total participants) were aware that the time window for an effective PEP is 72 h. 38.3%, 12.1%, and 9.2% thought that PEP should be administered within the first 24 h, 1 week, or more than 1 week after exposure, respectively.

A significant correlation (Table 3) was found between awareness of PEP and male sex, belonging to the LGBTQ community, and prior HIV testing. In contrast to the concern that PEP may promote high-risk sexual behavior, our results indicate that only 13.5% of participants, heterosexual and

Table 2 PEP awareness and knowledge of PEP time frame

	Awareness of PEP		No awareness of PEP		*p* value
	N	%	*N*	%	
Total	240	100	160	100	*p* < 0.01*
Up to 24 h	93	38.3	89	55.6	
Up to 72 h	96	40	28	17.5	
Up to 1 week	29	12.1	9	5.6	
Up to 1 month	12	5.0	18	11.3	
Over 1 month	10	4.2	10	10	

*The Pearson chi-square

Table 3 Correlation between different variables and awareness to PEP

	Awareness of PEP		No awareness of PEP		*p* value
	N	%	*N*	%	
All participants	240	60	160	40	
Age					
18–25	111	58.1	80	41.9	$p = 0.292$*
26–35	106	62.4	49	37.6	
36–45	13	48.1	14	51.9	
46+	8	80	2	20	
Physician awareness of sexual preference					
Yes	125	60.4	82	39.6%	0.919*
No	114	59.7	77	40.3%	
Biological gender					
Male	170	63.9	96	36.1%	0.025*
Female	70	52.2	64	47.8%	
Sexual preference					
Heterosexual	125	50.5	123	49.6%	< 0.01*
Homosexual	79	76.7	24	23.3%	
Bisexual	26	70.3	11	29.7%	
Transgender	1	100	0	0%	
Queer	9	81.8	2	18.2%	
Prior HIV test	165	67.1	81	32.9%	< 0.01*

*The Pearson chi-square

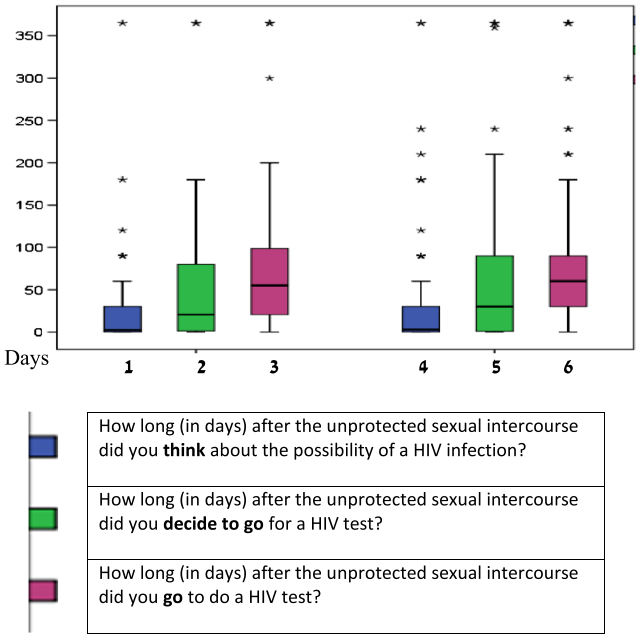

Fig. 1 Describing the time frames following an unprotected sexual intercourse, showing only those who claimed being aware of PEP. Columns 1–3 describe those who are aware of the treatments condition, and columns 4–6 describe those who are not aware of the treatments condition

LGBTQ alike, declared that PEP availability would change their sexual habits (Table 4, Fig. 1).

Among participants who were aware of the correct effective time frame for PEP (40%) versus those aware of PEP but not of its effective window (60%), there was no difference in the time to consideration of an HIV test, time to decision to be tested for HIV, or time to the actual performance of an HIV test. These findings suggest that prior knowledge of the correct timing of PEP did not affect the cognitive and physical process leading to a voluntary HIV test following a potential exposure. In contrast, participants not aware of PEP featured a longer period from exposure to a decision to perform HIV test.

Table 4 Reaching out for PEP

		All participants ($n = 271$)	Not aware of PEP ($n = 109$)	Aware of PEP ($n = 162$)		*p* value$		*p* value*
				Total (aware of PEP) (162)	Aware of correct time frame ($n = 64$)	Not aware of correct time frame ($n = 98$)		
Time from intercourse to realizing potential HIV exposure (days)	Mean	46.7	59	38.1	37.3	38.5	0.465	0.671
	Std. deviation	132.8	182	84.1	102	69.9		
	Median	7	7	3	2.5	3		
Time from intercourse to decision to test for HIV (days)	Mean	121.2	144.8	104.25	135	84.2	0.015	0.754
	Std. Deviation	336.2	403	278.5	385	177		
	Median	30	30	21	20.5	30		
Time from intercourse to performance of test for HIV (days)	Mean	153.15	174.5	137	177.2	110. 5	0.163	0.856
	Std. Deviation	341.4	407	284.2	388	183		
	Median	60	90	60	55	60		

$ *p* value by the Mann-Whitney test comparing the action time (realizing potential exposure to HIV, deciding to test for HIV and actual performance of HIV test) between participants that were aware of PEP and participants that were not aware of PEP. **p* valve by the Mann-Whitney test comparing in the group that was aware of PEP (total 162) the action time (realizing potential exposure to HIV, deciding to test for HIV and actual performance of HIV test) between participants that were aware of the correct timing of Pep ($N = 64$) and the ones that were not ($N = 98$)

Discussion

PEP is a pivotal strategy in HIV prevention, but necessitates post-exposure awareness of this medical option and its effective timeline for administration. Our study revealed a 60% awareness rate of the PEP option among people who approached the JOHOC to perform an HIV test following unprotected sexual intercourse, a significantly higher awareness of PEP than has previously been reported in most studies [2–5], similar only to the awareness in MSM in Boston reported by Dolezal [6]. The awareness rate was even higher among participants belonging to the LGBTQ community (75.5%) and may be due to the improvement in communication and the high impact of social media PEP advertisement achieved since the publication of previous surveys.

This high rate of PEP awareness was in stark contrast to the actual rate of PEP performance in our at-risk population, suggesting that a second barrier to effective PEP implementation may include a lack of detailed knowledge of the timing in which PEP exerts an effective protection against HIV infection. Both the assumption that PEP may be useful only within 24 h after exposure and the erroneous notion that it is effective even after 72 h post-exposure undermine PEP seeking and its successful application. Indeed, only 24% of the study participants were aware of the 72-h time frame necessary for the treatment to be effective. Importantly, even the knowledgeable minority considered the treatment option only 2.5 days after the unprotected intercourse episode, very close to the end of the effective PEP time window period. The dire result is that the majority of the population at risk mostly missed the "window of opportunity" as they approached the testing center only 55 days in average after their unprotected sexual contact.

The lower awareness of PEP in the heterosexual participants especially women in the light of the increase in the rate of newly acquired infections in Israel [7] related to heterosexual contacts, call for further action. The majority of the HIV awareness campaigns in the social media in Israel in the past 10 years target the MSM population, while not a single campaign was designated for the heterosexual community. Additionally, pre-exposure prophylaxis (PrEP) is distributed in Israel mainly to high-risk MSM. Thus, it seems that the heterosexual community is being neglected while planning the various prevention strategies. A better understanding of risk factors for HIV acquisition in this population are needed and PEP should be re-considered according to the findings of this study.

Our results also indicate that the dialog between MSM patients and their family physicians regarding sexually transmitted diseases (STIs) and sexual health is lacking and impaired, thereby potentially adversely impacting other critical components of a comprehensive treatment strategy to these patients such as vaccinations and STI screening. We speculate that integration of HIV testing with professional counseling in anonymous HIV testing centers, like the JOHOC and the Israeli AIDS Task Force, may complement the HMO system, resulting in a significant positive impact on public health.

Our study's limitations include non-inclusion of those directly referred to receive PEP at the emergency room and a potential population behavior bias stemming from the relatively conservative LGBTQ population behavioral patterns in the Jerusalem area, as compared to the more secular Tel Aviv metropolitan area.

In conclusion, our work is the first study evaluating not only the awareness of PEP among target populations, but also the awareness of the important details of its effective time period. We note a modestly high (60%) awareness of PEP, with even higher awareness noted among the LGBTQ and male communities. However, we highlight a marked lack of knowledge regarding the correct time frame for PEP administration that greatly undermines the effectiveness of the approach after a suspected exposure. These results call for a modification of knowledge dissemination regarding PEP, especially in populations at risk but also heterosexual and female populations, in an aim to not only to improve general PEP awareness but also to enhance knowledge about its effectiveness specificities. Future studies will assess whether this change in policy resulted in increased compliance to PEP among the at-risk population.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval The study was approved by the IRB committee of Hadassah-Hebrew University Medical Center.

Informed consent Informed consent was obtained from all individual participants included in the study.

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References

1. Smith DK, Grohskopf LA, Black RJ, Auerbach JD, Veronese F, Struble KA et al (2005) Antiretroviral postexposure prophylaxis after sexual, injection-drug use, or other nonoccupational exposure to HIV in the United States: recommendations from the U.S. Department of Health and Human Services. MMWR Recomm Rep 54:1–20
2. Rodriguez AE, Castel AD, Parish CL, Willis S, Feaster DJ, Kharfen M et al (2013) HIV medical providers' perceptions of the use of antiretroviral therapy as nonoccupational postexposure prophylaxis in 2 major metropolitan areas. J Acquir Immune Defic Syndr 64(Suppl 1):S68–S79
3. Mehta SA, Silvera R, Bernstein K, Holzman RS, Aberg JA, Daskalakis DC (2011) Awareness of post-exposure HIV prophylaxis

in high-risk men who have sex with men in New York City. Sex Transm Infect 87:344–348
4. Liu AY, Kittredge PV, Vittinghoff E, Raymond HF, Ahrens K, Matheson T et al (2008) Limited knowledge and use of HIV post- and pre-exposure prophylaxis among gay and bisexual men. J Acquir Immune Defic Syndr 47:241–247
5. Walters SM, Rivera AV, Starbuck L, Reilly KH, Boldon N, Anderson BJ et al (2017) Differences in awareness of pre-exposure prophylaxis and post-exposure prophylaxis among groups at-risk for HIV in New York State: New York City and Long Island, NY, 2011–2013. J Acquir Immune Defic Syndr 75(Suppl 3):S383–S391
6. Dolezal C, Frasca T, Giguere R, Ibitoye M, Cranston RD, Febo I, et al. Awareness of post-exposure prophylaxis (PEP) and pre-exposure prophylaxis (PrEP) is low but interest is high among men engaging in condomless anal sex with men in Boston, Pittsburgh, and San Juan. AIDS
7. HIV/AIDS in Israel: Periodic Epidemiological Report 1981–2016. In; 2017. https://www.health.gov.il/PublicationsFiles/AIDS_PeriodicReport2017e.pdf. Accessed 01 June 2018