RESEARCH PAPER

When effective post-exposure prophylaxis of HIV infection fails – data from clinical practice

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Abstract

Human immunodeficiency virus (HIV) prophylaxis with antiretroviral treatment after sexual exposure (sPEP) is an effective and safe approach; however, its influence on future exposures and, consequently, future HIV status remains under-investigated. We have evaluated the medical records of persons who received antiretroviral drugs (ARVs) as sPEP in the years 2009-2013. Cox proportional hazard models were used to identify predictors of having sexual exposure after finalising sPEP with HIV-negative status. In total 98 persons received sPEP: 37 (38%) after unprotected men who have sex with men (MSM) intercourse, 38 (39%) after sexual assault, and 23 (23%) after unprotected vaginal intercourse. In 40 (41%) cases the partner was HIV positive. Twelve persons (12%) repeated the same pattern of exposure; median time to next exposure was 1.55 (IQR 0.78-2.43) months. In multivariate Cox models older age was increasing, and heterosexual orientation decreasing the risk of having another exposure (HR = 1.06 [95% CI: 1.00-1.12; p = 0.033] and HR = 0.14 [95% CI: 0.02-1.06; p = 0.057], respectively). There were no HIV infections after completing sPEP, but three (3%) persons had occasional sexual contact afterwards, resulting in HIV infection. Median time from last negative exposure to HIV infection was 1.85 (IQR 1.79-2.43) months.

In a considerable proportion of persons sPEP had no effect on behavioural patterns, mostly in those having occasional sexual contact. The risk of having another sexual exposure was higher with age and for MSM patients. For this group of persons pre-exposure prophylaxis may be a more viable method of HIV infection prophylaxis.

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Key words: HIV, transmission, prophylaxis, PEP, PreP.

Introduction

Post-exposure prophylaxis (PEP) is a well-recognised and routinely used approach in both occupational and non-occupational exposures to human immunodeficiency virus (HIV) infection.

There is a large body of evidence showing high infectiousness for various modes of sexual transmission and providing some evidence for the utilisation of antiretroviral treatment after sexual exposure (sPEP). Despite the fact that sPEP is still an underutilised prevention strategy. There is a strong need for educating and increasing awareness about such methods of HIV prevention, especially among persons or populations with high-risk behaviours.

If properly addressed sPEP should theoretically improve knowledge and interest in other prevention methods available for persons at increased risk of HIV acquisition. In a recent study three quarters of sPEP users expressed interest in pre-exposure prophylaxis with antiretrovirals (PreP). How-

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Table 1. Comparison of baseline characteristics for patients having and not having repeated exposure after post sexual-exposure prophylaxis (sPEP) care

Characteristic	Repeated exposure, *n* = 12	No repeated exposure, *n* = 86	*p* value
Gender (male), *n* (%)	9 (75.0)	43 (50.0)	0.10
Age in years, median (IQR)	33.9 (28.6-39.3)	28.0 (23.2-35.4)	0.27
Sexual orientation MSM, *n* (%)	7 (58.3)	30 (34.9)	0.12
Source HIV positive, *n* (%)	3 (27.3)	28 (32.6)	0.72
NDL, *n* (%)	3 (25.0)	35 (40.7)	0.29
Type of exposure, *n* (%)			
MSM anal sex	7 (58.3)	25 (29.1)	0.06
MSM oral sex	0 (0.0)	5 (5.8)	
Vaginal sex	4 (33.3)	19 (22.1)	
Sexual assault	1 (8.3)	37 (43.0)	

MSM – men who have sex with men

ever, the use of both interventions in different risk groups and in clinical settings needs to be further discussed. For example their utilisation in serodiscordant couples, where an HIV-positive partner is on effective antiretroviral treatment, needs to be re-evaluated.

The use of antiretroviral treatment in HIV uninfected individuals is generally considered as a safe method, both for older and newer agents . Although most observed adverse drug reactions are mild and of reversible nature, their occurrence is much higher in HIV-negative than HIV-positive persons . This can lead to poorer adherence to treatment and decrease the net benefit from such prevention methods.

Another concern is the effect of sPEP on sexual risk perception and future sexual behaviours. Studies investigating this vital problem showed inconsistent results, which reflects the difference in both design and target population. Studies report sPEP users to be more likely to present high-risk behaviours, but whether sPEP has a preventive influence towards such behaviours remains uncertain.

The influence of sPEP on future exposures and, in consequence, future HIV status, especially in the clinical setting, remains under-investigated. Therefore, we have evaluated medical records of persons who received sPEP in an HIV Outpatient Clinic in Warsaw in the past five years.

Material and methods

Medical records of persons consulted at the HIV Outpatient Clinic of the Hospital for Infectious Diseases in Warsaw after unprotected sexual intercourse were reviewed. Only patients who received antiretroviral therapy as HIV prophylaxis for sexual exposure were included into the study. Five consecutive years (2009-2013) were reviewed.

The routine consultation after exposure to HIV infection including counselling and individual risk assessment was performed by an infectious disease specialist working in the clinic. It was followed by a decision on prescribing and the choice of antiretroviral drugs. Testing for HIV infection was performed at baseline, six weeks, and three months. At each visit the patient was advised on safe sex methods and given an opportunity to discuss any doubts on the risk of acquiring HIV.

For the study, indications for starting nPEP were grouped as following: men who have sex with men (MSM) oral intercourse, MSM anal intercourse, heterosexual vaginal intercourse, and sexual assault (irrespective of sexual orientation). Information on adverse drug reactions was evaluated as part of another project but was available for this analysis .

In statistical analyses χ^2 and Kruskal-Wallis tests were used for group comparisons. Cox proportional hazard models were used to identify predictors of having sexual exposure after finalising sPEP. Variables tested in univariate analyses were age, gender, sexual orientation, HIV status of sexual partner, and adverse reaction to any medication used in sPEP. A multivariable model included all listed variables. A confidence interval (CI) of 95% was accepted. All analyses were performer using SAS version 9.3 (SAS Institute, Cary, NC).

Results

In total 98 persons received sPEP, 37 (38%) MSM after unprotected intercourse, 38 (39%) MSM after sexual assault, and 23 (23%) heterosexual persons after unprotected vaginal intercourse. In 40 (41%) cases the sexual partner was known to be HIV positive.

Twelve persons (12%) repeated the same pattern of sexual exposure, five through vaginal and seven through MSM anal intercourse. Eight exposures were with an occasional partner (two with an HIV-positive partner), four in serodiscordant couples. Median time from the first to next sex-

Table 2. Cox proportional hazard models for the risk of having next sexual exposure

Factor	Univariate			Multivariate		
	Hazard ratio	95% CI	*p* value	Hazard ratio	95% CI	*p* value
Gender						
Female	1.00	–	–	1.00	–	–
Male	2.18	0.59-8.14	0.244	0.74	0.11-4.88	0.755
Age						
Per 1 year older	1.04	0.99-1.09	0.116	1.06	1.00-1.12	0.033
Per 10 years older	1.46	0.91-2.35	0.116	1.84	1.05-3.22	0.033
Adverse reaction to any medication used in sPEP						
No	1.00	–	–	1.00	–	–
Yes	0.63	0.17-2.33	0.484	0.50	0.12-2.00	0.327
Sexual orientation						
MSM	1.00	–	–	1.00	–	–
Heterosexual	0.40	0.12-1.26	0.118	0.14	0.02-1.06	0.057
Sexual partner HIV status						
Unknown	1.00	–	–	1.00	–	–
HIV (+)	0.838	0.22-3.17	0.794	0.33	0.07-1.61	0.170

sPEP – post sexual-exposure prophylaxis, HIV – human immunodeficiency virus, MSM – men who have sex with men

ual exposure consulted in the clinic was 1.55 (interquartile range, IQR: 0.78-2.43) months. Six persons (6%) received sPEP again.

In general, persons reporting repeated exposure were more likely to be older, male, and MSM. Persons having MSM anal sex and vaginal sex were more likely to repeat the exposure. However, none of these differences reached statistical significance (Table 1).

In the multivariate Cox model older age was increasing, and heterosexual orientation decreasing the risk of having another sexual exposure (HR = 1.06 [95% CI: 1.00-1.12; $p = 0.033$] and HR = 0.14 [95% CI: 0.02-1.06; $p = 0.057$], respectively) (Table 2).

There were no HIV infections after completing sPEP, but three (3%) persons had occasional sexual contact afterwards resulting in HIV infection. Median time from last negative exposure until HIV infection was 1.85 (IQR 1.79-2.43) months.

Discussion

In one out of ten persons sPEP had no effect on behavioural patterns, mostly in those having occasional contact. The risk of having another sexual exposure was higher with age and for MSM patients. For this group of persons pre-exposure prophylaxis may be a more viable method of HIV infection prophylaxis.

Numerous studies have reported an increase in the number of sexual exposures to HIV in recent years, mostly through high-risk behaviours and unprotected sexual intercourse, especially among MSM. A recent molecular phylogenetic analysis by Drescher *et al.* showed that treatment naïve HIV-positive MSM are the main group transmitting HIV in the British Columbian population . In fact, MSM sexual contact is the main mode of transmission in high-income countries. In Poland MSM remains an increasing and recently dominating group of newly diagnosed HIV persons. Also, in our work MSM were associated with higher risk of repeated sexual exposure, and the only HIV infections that were reported in our study occurred as a result of MSM sexual intercourse.

As of today many different approaches have been proposed in response to the observed situation. These include better testing strategies, increased linkage to care, offering antiretroviral treatment to HIV-positive patients for transmission risk reduction, and using antiretrovirals in the HIV-negative population as sPEP or PreP. Although effective in clinical studies, none of these methods was proven to work in clinical settings as a single intervention. Therefore, combination prevention strategy that includes all elements, as well as STI treatment and structural behavioural interventions, seems to be the only feasible approach. Moreover, any planned intervention needs to be re-evaluated in real-life settings. There are far more factors associated with sexual behaviours: pattern of illicit drug or legal highs use, program availability, cultural diversity, and many others. In this light, any experience in addressing the risk of HIV exposure in clinical practice is a vital addition to strategy planning.

There are some limitations to our work, which need to be mentioned. First of all, the retrospective nature of this work should be considered while interpreting the results. The number of HIV infections could be underestimated, but all persons diagnosed with HIV in the central region of Po-

land are referred and registered in the Warsaw Outpatient Clinic. Their earlier records from sPEP counselling are included in both electronic and paper documentation. Finally, because we had no access to the information on HIV-positive partner treatment, we were not able to describe the protective effect of sPEP separately from these vital factors.

An important limitation for sPEP is the fact that it can only be prescribed in clinical centres with specialists experienced in HIV treatment. On the other hand, in most European countries it is available free of charge, unlike PreP.

Post-exposure prophylaxis is an emergency medical assistance and as such will always have its place in any prevention program.

Conflict of interest

The author's declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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