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Antiretroviral prophylaxis for community exposure to the human immunodeficiency virus in Switzerland, 1997–2000

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Summary

Objective: To analyse the data from Swiss nationwide voluntary reporting on non-occupational HIV-postexposure prophylaxis (HIV-PEP) by prescribing physicians.

Methods: One hundred and seventy-six persons, who received antiretroviral prophylaxis for community exposure to HIV between December 1997 and March 2000, were included in this prospective cohort study with standardised data collection. Information on the source, the exposed person, type of exposure, treatment, and outcome was reported by physicians on a voluntary basis to three co-ordinating centers.

Results: HIV-PEP was prescribed predominantly following sexual exposure (69%). Needle injury was the second most common type of exposure (19% of all exposures), mostly occurring in a non-healthcare related "professional" setting (ie, housekeepers, concierges [caretakers], and policemen). Needle sharing accounted for only 4% of all cases of exposure. The HIV status of the source often remained unknown (56%). Most patients received a combination of three antiretroviral drugs (zidovudine/lamivudine/nelfinavir in 34.1%; zidovudine/lamivudine/indinavir in 22.8%; zidovudine/lamivudine/nevirapine in 18.6%; various triple combinations in 13.8%). Follow-up information was available for 86 patients. In this group 78 (91%) completed at least one week of prophylaxis. Side-effects were common (70.9%), particularly diarrhoea (29.6%) and nausea (20.9%). Two patients experienced severe side effects, nephrolithiasis with sepsis, and toxic hepatitis, respectively.

Conclusions: In most of the cases where HIV-PEP was prescribed the indication was questionable, with the HIV status of the source unknown. The role of HIV-PEP as part of HIV prevention programs should be well defined in view of the cost and potential for causing severe side-effects.

Key words: HIV-postexposure prophylaxis; prevention strategy; surveillance; antiretroviral drugs; toxicity

Introduction

Combinations of antiretroviral drugs are used to reduce the risk of HIV infection after HIV exposure of healthcare workers, particularly after needle-stick injury. Such prophylaxis is increasingly prescribed in cases of non-healthcare related exposure [1, 2], partly because the risk for HIV infection after exposure through sexual contact is similar to the risk after needle-stick injury. The estimated risk is highest following receptive anal intercourse (0.008 to 0.032), unprotected receptive vaginal intercourse (0.0005 to 0.0015), and penetrative vaginal intercourse (0.0003 to 0.0009) [3, 4].

In December 1997 the Federal Office of Public Health of Switzerland published guidelines that recommended prophylaxis with antiretroviral drugs for sexual exposure and needle sharing [5]. A voluntary reporting form accompanied the guidelines. The use of antiretroviral drugs was supported in case of unprotected vaginal or anal sexual intercourse, oral sexual intercourse with ejaculation, or intravenous drug use with contaminated drug injection equipment, provided that the source of exposure was known to be HIV infected. The proposed prophylactic regimen was a combination of a protease inhibitor (indinavir or nelfinavir) with zidovudine and lamivudine.

In this article, we report on 176 persons who were prescribed HIV-postexposure prophylaxis (HIV-PEP) between December 1997 and March 2000. We examined the setting of exposure, prophylaxis prescribed and extent to which source HIV status was known.

Methods

Physicians were asked to report detailed information about non-occupational HIV-PEP prescription by completing the questionnaire published with the official guidelines. This questionnaire was standardised and derived from a similar form designed for healthcare related professional postexposure prophylaxis [6]. German, French, or Italian versions of the form were used.

The following information was collected on the source of exposure (HIV status, suspected mode of HIV-infection, stage of HIV disease, current treatment), the exposed person (age, gender, profession), the exposure itself (timing, type of sexual exposure, type of injury, needle exchange), and treatment (regimen, side-effects). This was a passive surveillance system which also required physicians to provide follow-up HIV serology at 3, 6 and 9 months after exposure.

Forms were sent to one of the three co-ordinating centres (Zurich, Lausanne, and Lugano). Reports were validated by one of the study investigators and data were entered in an MS-Access 1997 database® (Microsoft Corporation). Statistical analysis was conducted with SPSS® version 10 (SPSS Inc., Chicago, Illinois).

Results

The characteristics of 176 reportedly exposed persons between December 1997 and March 2000 are described in table 1. Most patients were male (62%) and relatively young (median age: 30 years).

Table 1

Characteristics of patients prescribed HIV-postexposure prophylaxis in Switzerland, 1997–2000 (N = 176).

Characteristic		N	(%)
Gender	Male	110	(62)
	Female	61	(35)
	Unknown	5	(3)
Median age [range]		30	[9–71]
Language region	German (Italian = 7)	52	(30)
	French	124	(70)
Year of reporting	1997*	6	(3)
	1998	80	(46)
	1999	72	(41)
	2000**	18	(10)

* Reporting started in December 1997
** Up to March 2000

Table 2

Mode of exposure of patients prescribed HIV-postexposure prophylaxis in Switzerland, 1997–2000.

Exposure		N	(%)
Sexual		*122*	*(69%)*
Heterosexual		85	(48%)
	Unprotected sex		(29%)
	Condom rupture/slippage		(71%)
Homosexual		28	(16%)
	Unprotected sex		(56%)
	Condom rupture/slippage		(44%)
Rape		9	(5%)
Non-sexual		*54*	*(31%)*
Needle injury		34	(19%)
	"Professional"*		(57%)
	Infants		(10%)
	Others		(33%)
Needle sharing		7	(4%)
Other		13	(8%)

* Occupational but not healthcare related (housekeepers, concierges [caretakers], policemen)

The majority of reports came from the French speaking part of Switzerland (70%). HIV-PEP was prescribed mostly following sexual exposure (69%), including rape, and more frequently among heterosexual partners (table 2). Condom rupture was the main cause of exposure among heterosexuals (71% in this group), whereas unprotected sex was most common among homosexual males (56% in this group). Nine persons (2 males and 7 females) were treated after they were raped. Needle injury was the second most common type of exposure (19% of all exposures). More than half of the needle injuries (57%) occurred in a non-healthcare related occupational setting, ie, in persons who were at work when they were injured (housekeepers, caretakers, policemen). Needle sharing represented a small proportion (4%) of all exposures. The average time interval between exposure and prescription of HIV-PEP was 25.2 hours (± 2.9 hours; median: 18 hours; range: 45 minutes –168 hours).

The HIV status of the source was only known for 78 (44%) of the exposed persons (table 3). This proportion was lower among persons who sustained a needle injury (26%) and victims of rape (26%). Among 71 source-persons known to be HIV-positive, 12 (17%) were related to exposure via homosexual sex, 10 (14%) IVDU with needle sharing, and 43 (60%) heterosexual sex. Among 38 source-persons with known CDC stage, 25 (66%) were in CDC stage A, 6 (16%) in stage B, and 7 (18%) in stage C. Information of CD4 cell counts was available for 38 patients and information of viraemia for 40. Median CD4 counts were 410 cells per mm^3 (range: 30–1453) and 19 (47%) patients had a viral load below 400 copies/mL (range: <400–750,000). Information about the treatment of the source of exposure was available for 28 persons. All but 9 (on zidovudine plus lamivudine or in one case zidovudine plus didanosine) were receiving highly active antiretroviral therapy, con-

Table 3

Knowledge of the source status and type of exposure of patients prescribed non-professional HIV-postexposure prophylaxis in Switzerland, 1997–2000.

	HIV status of source		
	positive (n = 71) (40%)	**negative (n = 7)** (4%)	**unknown (n = 98)** (56%)
Year			
1997 (6)	50%	0%	50%
1998 (80)	31%	6%	63%
1999 (72)	49%	3%	48%
2000 (17)	47%	0%	53%
Gender of exposed person			
Male	35%	2%	63%
Female	49%	8%	43%
Unknown	50%	0%	50%
Exposure			
Heterosexual sex	50%	2%	48%
Homosexual sex	43%	0%	57%
Rape	13%	13%	74%
Needle injury	17%	9%	74%
Needle exchange	57%	0%	43%
Language region			
German / Italian	39%	4%	57%
French	41%	4%	55%

sisting of at least two nucleoside reverse transcriptase inhibitors and a protease inhibitor or a non-nucleoside reverse transcriptase analogue.

Data on regimens prescribed as HIV-PEP were reported for 167 (95%) of the exposed persons. Most patients received zidovudine/lamivudine (AZT/3TC: 8, 4.8%), or AZT/3TC in combination with nelfinavir (NFV: 57, 34.1%), indinavir (IDV: 38, 22.8%), or nevirapine (NEV: 31, 18.6%). Twenty-three patients (13.8%) received other triple combinations and one patient (0.6%) AZT combined with didanosine. For 9 patients no detailed information was available on the prescribed drugs. Four patients stopped their treatment when information, indicating that the source of exposure was HIV-negative, became available. Detailed follow-up information on treatment tolerance was only available for 86 patients. In this group, 78 patients (91%) completed at least one week of treatment. The most common side-effects were diarrhoea (30%) and nausea (21%); 71% of patients experienced at least one type of side-effect (table 4). Tolerance of the two regimens most often prescribed (AZT/3TC/NFV and AZT/3TC/IDV) was relatively similar with diarrhoea more common with AZT/3TC/NFV and nausea with AZT/3TC/IDV. Two patients presented severe side-effects. Nephrolithiasis occurred in a 70-year-old caretaker exposed through needle-stick injury of unknown HIV status while working. She had received AZT/3TC/IDV. She developed pyonephritis, as a result of ureteral obstruction, requiring hospitalisation and surgery. A 31-year-old laboratory technician, with sexual exposure and condom rupture, received AZT/3TC/NFV and developed toxic hepatitis. The HIV status of the source was not known.

No HIV infection has been notified among this group of reportedly HIV-exposed persons.

Table 4

Side-effects and treatment follow-up of drug regimens prescribed as HIV-postexposure prophylaxis in Switzerland, 1997–2000, among 86 patients with available information.

Regimen	**AZT/3TC/NFV**	**AZT/3TC/IDV**	**AZT/3TC/NEV**	**Other triple combinations**	**AZT/3TC(DDI)**	**Total**
N (%)	**30 (34.9)**	**24 (27.9)**	**16 (18.6)**	**11 (12.8)**	**5 (5.8)**	**86**
Side-effect						
Diarrhoea	46.7%	25.0%	37.5%	45.5%	0%	29.6%
Nausea	23.3%	37.5%	12.5%	0%	0%	20.9%
Fatigue	20.0%	20.8%	25.0%	18.2%	0%	16.9%
Vomiting	13.3%	12.5%	6.3%	0%	20.0%	10.5%
Headache	3.3%	4.2%	6.3%	9.1%	0%	4.7%
Others*	16.5%	45.8%	25.0%	36.4%	0%	27.9%
Any side-effect	70.0%	79.2%	75.0%	72.7%	20.0%	70.9%
Treatment follow-up						
Modification	0%	25.0%	6.3%	27.3%	0%	11.6%
Interruption**	6.7%	8.3%	6.3%	27.3%	0%	9.3%

* Skin rash, anorexia, insomnia, abdominal pain.

** Due to severe side-effects in two patients: (1) Nephrolithiasis: 70-year-old caretaker with needle-stick injury while working. Unknown HIV status of source. Received AZT/3TC/IDV. Required hospitalisation and surgery. (2) Toxic hepatitis: 31-year-old laboratory technologist. Sexual exposure with condom rupture. HIV status of source unknown. Received AZT/3TC/NFV.

AZT = zidovudine; 3TC = lamivudine; NFV = nelfinavir; IDV = indinavir; NEV = nevirapine; DDI = didanosine

Discussion

We found that outside the healthcare setting HIV-postexposure prophylaxis (HIV-PEP) was prescribed in 122 out of 176 reported cases (69%) after suspected sexual exposure to HIV. The observation that HIV status of the source was most often unknown demonstrates that reported prescriptions often did not comply with official guidelines. This finding may be an indication that either physicians were not aware of these recommendations or, alternatively that, although these recommendations were epidemiologically sound, they were not acceptable or applicable. In practice, the physician's decision must take into account the patient's anxiety and demands.

Nine persons were prescribed HIV-PEP after they were raped, although a positive HIV-serology of the source was known in only one case. In victims of sexual assault there are often associated factors which increase the risk of HIV transmission, particularly trauma, laceration, and bleeding [7]. However, there have been only a few documented cases of HIV transmission following rape [8]. A careful evaluation and counselling of the rape victim, including consideration of the risk-benefit of HIV-PEP is recommended [9]. The detection of semen anti-HIV antibodies within the cervicovaginal secretions from a rape victim has been reported [10], but the predictive value of this analysis is unknown.

Needle-stick injuries caused 19% of exposures leading to a HIV-PEP prescription. Although they occurred outside the healthcare setting, most (57%) of these exposures involved housekeepers, caretakers, and policemen in the context of professional activity. This emphasises the need for better education of prescribing physicians and professionals about the very low risk of transmission associated with these exposures. In addition, better protective measures against the risk of needle-stick injuries, eg, gloves and the use of disposal facilities should be recommended. Notably, HIV transmission by means of a needle-stick injury outside the healthcare setting has not been reported. Despite the emphasis of the Swiss guidelines on the low risk of HIV transmission associated with needle-stick injuries outside the health-care setting, antiretroviral drugs were often prescribed, an indication of the discrepancy between objective and subjective risk perception.

Postexposure prophylaxis with antiretroviral drugs should be initiated as soon as possible but not later than 72 hours, as it has been recommended for occupational exposures [11]. In our study, the average time interval between exposure and prescription of HIV-PEP was 25.2 hours, with extremes of 45 minutes to 168 hours. Since some of the studies in animal models suggested no benefit from PEP if started later than 24–36 hours after HIV exposure [12, 13], there is a need to optimise the care of the exposed person to initiate the antiretroviral prophylaxis as soon as possible.

Almost half (47%) the source patients with known HIV infection had an undetectable viral load. Although this situation is likely to be associated with a lower transmission risk [14], prophylaxis with antiretroviral drugs was uniformly prescribed. The vast majority of treated persons received a combination of two nucleoside reverse transcriptase inhibitors and a protease inhibitor. However, the wide spectrum of antiretroviral drugs available is reflected in the variety of treatment combinations. Individualisation of the treatment may be justified when the source-patient has been receiving treatment for some time and resistance to one or more drugs is suspected. Some experts favour a prophylaxis with two nucleoside reverse transcriptase inhibitors, eg, zidovudine and lamivudine, in the majority of situations of non-occupational HIV exposures [4]. In our experience, although the numbers are small, this was better tolerated than more complex regimens. Addition of a protease inhibitor would be considered if the source patient has advanced HIV disease, or is known to have a plasma viral load >50,000 RNA copies/ml, or if the source patient has been previously treated with zidovudine, lamivudine, or both.

A variety of side-effects of the antiretroviral therapy were reported in 71% of patients who had available follow-up information on treatment. Gastrointestinal symptoms (ie, diarrhoea, nausea, and vomiting), headache, and fatigue were the most common side-effects. Intolerance of antiretroviral drugs led to premature discontinuation of treatment or treatment modification in 21% of cases. Of greater concern, is the observation of two severe adverse events related to the antiretroviral drugs, ie, nephrolithiasis complicated by pyonephritis and severe toxic hepatitis. These cases underscore the importance of a careful evaluation of the potential danger of antiretroviral prophylaxis. In addition, we have recently observed Stevens-Johnson syndrome in a young physician exposed to HIV through needle-stick injury, 12 days after starting prophylaxis with nevirapine, zidovudine and lamivudine (unpublished observation).

Because reporting of HIV-PEP prescription was voluntary, it is likely that the reported cases represent only a fraction of the total number of non-occupational HIV exposures in Switzerland. Under-reporting seems even more probable in the German speaking part of Switzerland. Only one third of the reports came from this part of the country where about 65% of the HIV-infected population lives.

HIV-PEP prescription should be restricted to situations where the risk of HIV transmission is well documented and clearly outweighs the risk of severe side-effects [15]. Although, in certain circumstances, the use of antiretroviral prophylaxis is beneficial, HIV-PEP is expensive and potentially

harmful, as demonstrated by our two observations of severe side-effects. By using a cost-benefit analysis, Pinkerton and collaborators recommended restricting HIV-PEP following suspected sexual exposure to regular partners of infected persons, to patients reporting unprotected receptive anal intercourse, and possibly to situations where the probability of the partner's infection is very high or where the transmission would be unusually effective, ie, the patient or partner has genital ulcers or the sex was traumatic [16]. However, other authors sustain a more permissive view by recommending antiretrovirals also in the situation of penetrative vaginal or anal intercourse with a partner who is or is likely to be HIV infected, and also offering HIV-PEP in the case of receptive fellatio with ejaculation [4].

The use of a rapid HIV test of the source patient can lower unnecessary intake of antiretroviral drugs by exposed healthcare workers [17, 18]. Therefore, the feasibility of rapid HIV testing in the context of non-occupational exposure merits further attention.

Along with public health messages that emphasise safer sex, HIV-PEP can play a role as "salvage preventive strategy", when primary prevention has failed. Better information aimed at training physicians about the indications, the risks, and merits of HIV-PEP, as well as careful documentation of prescriptions via a national HIV-PEP registry are indispensable if we are to improve our use of this important prevention tool.

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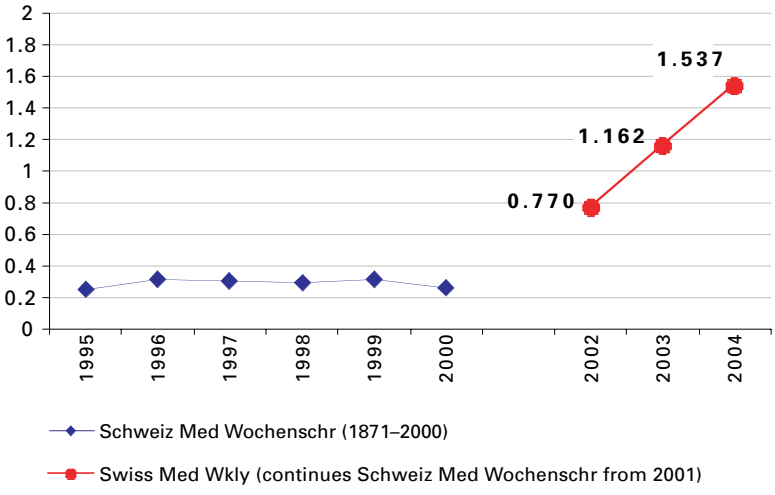

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