Prescription and tolerance of HIV post-exposure prophylaxis in France

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Background

In 1998, French recommendations for post-exposure prophylaxis (PEP) for occupational exposures in health care workers (HCW) were extended to include sexual exposures (SE), syringe sharing drug users (IDU) and other exposures (OE) (e.g. injuries with discarded syringes, human bites). A 3 antiretroviral (ARV) combination was recommended for 4 weeks.

In April 2003, recommendations were revised downwards (particularly for exposures to a source with HIV status unknown) and were updated regarding the 3-drug or 4-drug combination used: 2 nucleoside reverse transcriptase inhibitors (NRTI) were recommended in association with nelfinavir or ritonavir/lopinavir combination while abacavir, stavudine/didanosine combination, non nucleoside reverse transcriptase inhibitors and indinavir were contraindicated.

From January 2000 to December 2003, a hospital-based voluntary surveillance monitored the characteristics of exposed persons and exposures, ARV drug use, tolerance of PEP and follow-up HIV testing.

Methods

Persons seeking advice on PEP in the first week following exposure to an HIV (+) source or a source of unknown status were included after giving consent.

Data were collected on 3 anonymous standardised forms (inclusion, 1 and 6 months follow-up).

In order to study the trends in prescriptions (in particular, the impact of the April 2003 recommendations) and the tolerance of PEP, data were analysed according to six 8-month periods: from January-August 2000 (period 1) to May-December 2003 after recommendation update (period 6).

Results

1. Characteristics of exposed persons and exposures

By December 2003, 14 273 persons were reported to have sought advice on PEP: 55.1% after SE, 30.7% in HCW, 13.8% after OE and 0.4% in IDU.

Exposure		Sexual	HCW	Other	IDU
	N	7 869	4 376	1 967	61
Sex	male	67%	27%	70%	59%
	female	33%	73%	30%	41%
Median age [IQR]		29 [24;36]	34 [27;44]	32 [25;42]	31 [27;38]
Median time between exposure and advice [IQR]		16h [8;33]	2h [1;7]	4h [2;19]	24h [9;52]
HIV status of source*	unknown	77%	71%	89%	51%
	positive	23%	29%	11%	49%
Severity of exposure	low[1]	12%	54%	89%	11%
	intermediate[2]	46%	33%	9%	41%
	high[3]	42%	13%	2%	48%

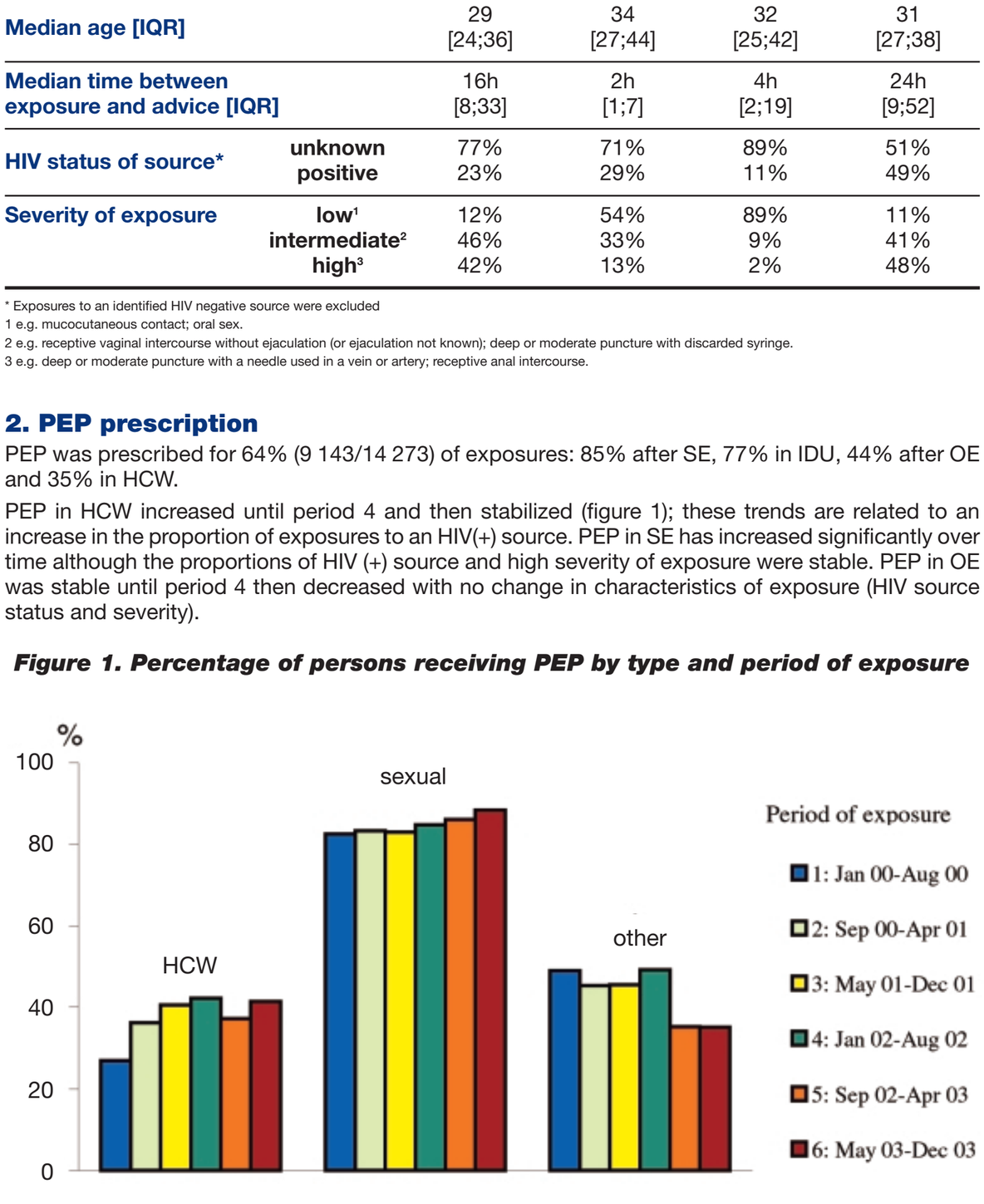
* Exposures to an identified HIV negative source were excluded
1 e.g. mucocutaneous contact; oral sex.
2 e.g. receptive vaginal intercourse without ejaculation (or ejaculation not known); deep or moderate puncture with discarded syringe.
3 e.g. deep or moderate puncture with a needle used in a vein or artery; receptive anal intercourse.

2. PEP prescription

PEP was prescribed for 64% (9 143/14 273) of exposures: 85% after SE, 77% in IDU, 44% after OE and 35% in HCW.

PEP in HCW increased until period 4 and then stabilized (figure 1); these trends are related to an increase in the proportion of exposures to an HIV(+) source. PEP in SE has increased significantly over time although the proportions of HIV (+) source and high severity of exposure were stable. PEP in OE was stable until period 4 then decreased with no change in characteristics of exposure (HIV source status and severity).

Figure 1. Percentage of persons receiving PEP by type and period of exposure



The 3-drug regimen with nelfinavir was the most frequent in all the periods. The 4-drug regimen with ritonavir/lopinavir increased over time, especially in the last period (tables 1 and 2).

Table 1. Prescription of PEP by regimen and period of exposure

Period of exposure	1 01/2000 08/2000	2 09/2000 04/2001	3 05/2001 12/2001	4 01/2002 08/2002	5 09/2002 04/2003	6 05/2003 12/2003
N of exposures*	2 873	2 232	2 247	2 183	2 184	2 082
n of PEP (% of PEP)	1 533 (53)	1 354 (61)	1 480 (66)	1 515 (69)	1 506 (69)	1 508 (72)
Regimen	%	%	%	%	%	%
2-drug	15	12	9	10	7	3
3-drug with indinavir	24	14	6	4	2	1
3-drug with nelfinavir	50	53	64	66	70	66
3-drug with NNRTI	4	8	6	4	3	2
3-drug with 3 NRTI	3	6	8	7	6	1
4-drug with 2 PI°	2	6	6	8	10	24
Other/unknown	2	1	1	1	2	3

NNRTI: non nucleoside reverse transcriptase inhibitor
NRTI: nucleoside reverse transcriptase inhibitor
* military hospitals excluded because of irregular participation
° ritonavir used as a booster of another protease inhibitor (PI)

Table 2. Prescription of PEP by main antiretroviral and period of exposure

Period of exposure	1	2	3	4	5	6
n of PEP	1 533	1 354	1 480	1 515	1 506	1 508
	%	%	%	%	%	%
DDI/D4T	10	11	10	6	4	1
IDV	26	20	9	8	4	2
NVP*	3	7	5	4	2	2
RTV/LPV	0	0	2	4	9	23
TDF	0	0	0	1	3	4

*most often short nevirapine regimen (3-4 days)

3. PEP tolerance

One-month follow-up data were available for 42% of treated persons (3 863/9 143): from 48% after OE to 34% after IDU.

Overall, PEP was completed in 87% (3 360/3 863). Adverse symptoms interrupting daily activities were observed in 10%, and biological abnormalities in 6%, but proportions varied according to the regimen used (table 3).

Table 3. Side effects and interruption of PEP by regimen

Regimen	N	Adverse symptoms* %	Biological abnormalities %	Premature interruption° %
2-drug	422	5	3	13
3-drug with indinavir	336	18	11	20
3-drug with nelfinavir	2 159	10	6	12
3-drug with NNRTI	232	7	2	11
3-drug with 3 NRTI	263	5	3	7
4-drug with 2 PI	398	16	5	16
Other	53	16	4	8
Total	**3 863**	**10**	**6**	**13**

*adverse symptoms interrupting daily activities
° whatever the reason (including side effects)

Conclusion

These data suggest a real impact of the PEP recommendations on the use of ARV regimen. However, adverse symptoms interrupting daily activities and premature interruption are frequent with the prescription of a 4-drug regimen with ritonavir and another protease inhibitor. The choice of this combination should be considered carefully.

Rate of prescription remained high for sexual exposures even though the HIV status of the source was often unknown. Recommendations could be further restricted to help clinicians to say "no PEP".