

Non-occupational post-exposure prophylaxis for HIV

Background

This observational study was instigated in December 1998 to monitor the implementation of guidelines recommending PEP for HIV in the context of non-occupational exposure in Australia. Enrolment into the study ceased in May 2004, with final follow up completed by the end of 2004. Sixteen hundred and one participants were enrolled in the study, making it one of the largest observational studies of non-occupational post-exposure prophylaxis in the world.

The study aimed to examine the feasibility, safety and efficacy of non-occupational PEP, by monitoring the extent and appropriateness of non-occupational PEP utilization and its clinical outcomes in a population-based setting, where non-occupational PEP has been recommended and publicized since 1998. Final results from NSW participants are presented and discussed in this report.

Methods

Brief monitoring forms were completed, with the verbal consent of the patient, by the doctor prescribing PEP. They were administered at the time of prescription, at the four-week follow up visit, and at six months following exposure. People who elected not to take PEP despite fulfilling the criteria to receive it were also recruited.

Results

A total of 1096 participants from NSW were enrolled, and of these, 39 (3.6%) decided not to receive non-occupational PEP. Participants were overwhelmingly male (1045, 95%) and had a median age of 33 years. The great majority (986, 90%) had been previously tested for HIV and 165 (15.1%) reported previous PEP prescription.

Male homosexual contact was the most commonly reported exposure (944, 86.1%). Among these, the most commonly reported exposures were unprotected receptive (622, 65.9%) or insertive (285, 30.2%) anal intercourse. The source was known to be HIV positive in 292 participants with male homosexual exposure (30.9%). Heterosexual exposure was reported by 49 people (4.5%), 24 men and 25 women. The highest risk exposures were receptive vaginal intercourse in 22 (44.9%), receptive anal in 4 (8.2%) and insertive vaginal intercourse in 20 (40.8%). In men and women with heterosexual exposure, the source was known to be HIV positive in 8 (33.3%) and 11 (44%) of participants respectively.

Percutaneous exposure was reported by 88 participants (8.0%); 18 (20.5%) of these exposures involved sharing of injecting equipment, 60 (68.2%) were people who reported other types of needle stick injuries (NSI) and 10 (11.4%)

were other percutaneous exposures. A considerably higher proportion of injecting drug users (IDUs) (8, 44.4%) than people who sustained other percutaneous exposures (14, 20%) reported that their source was known to be HIV positive ($p = 0.03$). The other percutaneous exposures included a heterogeneous group, the majority presenting after assaults or physical altercations involving lacerations.

In total, 1017 participants (92.8%) were prescribed PEP within 72 hours of exposure and 575 (52.5%) were prescribed PEP within 24 hours of exposure. This information was missing for 29 participants (2.6%). The median time to receipt of PEP was 20.5 hours (IQR: 10-39h). Over half the prescriptions for PEP (647, 61.4%) were for three or more ARV drugs. PEP prescriptions are listed in Table 3.1. Prescription of three or more drugs was more likely when the source was reported to be HIV positive ($p < 0.0001$), and was similar among participants with receptive and insertive UAI exposures ($p = 0.99$).

Eight hundred and forty (76.6%) participants returned at least once for follow up at four or more weeks post-exposure and 369 (33.7%) returned for follow up and HIV testing at 24 or more weeks post-exposure. Of those 818 who returned for four week follow up and had elected to take PEP, 652 (79.7%) participants completed the initially prescribed regimen and 46 (5.6%) completed a modified regimen. Premature discontinuation of the initially prescribed regimen was reported by 82 (10.0%) participants. The most common reason for modification or discontinuation of the initially prescribed regimen was the incidence of side effects (90, 70.3%). Four (4.9%) stopped after ascertaining the source person was HIV negative. Six hundred and eighty-one (83.3%) reported full compliance to the prescribed regimen.

Side effects were reported by the majority of people (548, 67.0%) who returned for four week follow-up. A substantial number reported at least two side effects and the large majority rated side effects as mild or moderate. Of those for whom specific side effect data were available, the most common side effects included nausea in 357 (48.4%), diarrhoea in 247 (34.7%), headache in 125 (17.7%), and vomiting in 45 (6.4%). Being prescribed a combination of three or more drugs was associated with a greater incidence of side effects at any severity level ($p = 0.001$).

No HIV seroconversions related to treatment failure were observed. Overall, there were eight new HIV diagnoses, but five of these were people who were diagnosed HIV positive at baseline. One participant seroconverted three months after being prescribed zidovudine, lamivudine and nelfinavir, but he was poorly compliant and reported ongoing risk behaviours. One participant seroconverted 311 days after initiation of zidovudine, lamivudine and nelfinavir and

another seroconverted 110 days after initiation of stavudine didanosine and lamivudine. Both had completed the prescribed regimen but were believed by the prescribing doctors to have had other risk episodes after completion of PEP.

Over the 6 years of the study, the proportion of NSW study participants reporting a known HIV positive source declined significantly ($p < 0.0001$). An increase in PEP prescriptions containing two drugs was observed over the study period, increasing from 25% in 1999 to 85% in 2004 ($p < 0.0001$). The prescription of nevirapine declined markedly from 2001, from 35.9% of prescriptions in 2000 to no prescriptions in 2004. Prescription of tenofovir became common over the study period, with no prescriptions containing tenofovir until 2002 increasing to 61.2% of prescriptions in 2003 and 53.2% of prescriptions in 2004 (Figure 3.1). Reports of any side effects became significantly less frequent over the study period ($p < 0.0001$).

Discussion

In most respects, prescription of PEP in NSW reflected the national and state guidelines, with most prescriptions of PEP administered for high-risk exposures. The median time to prescription of PEP during the study was less than one day, and the vast majority of prescriptions were within the recommended 72 hours. Three drugs were prescribed for the majority of exposures in the study on the whole. However, over the study period there was a trend towards prescription of two drugs, with a dramatic increase in two drug prescriptions in 2004. Nevirapine has not been prescribed to study participants since 2002 and prescription of tenofovir has become increasingly frequent in NSW, with over half of PEP prescriptions in 2004 containing tenofovir. No definite cases of HIV seroconversion due to PEP failure were observed during the study period.

Figure 3.1: The proportion of prescriptions containing 3 or more drugs, nevirapine, and tenofovir

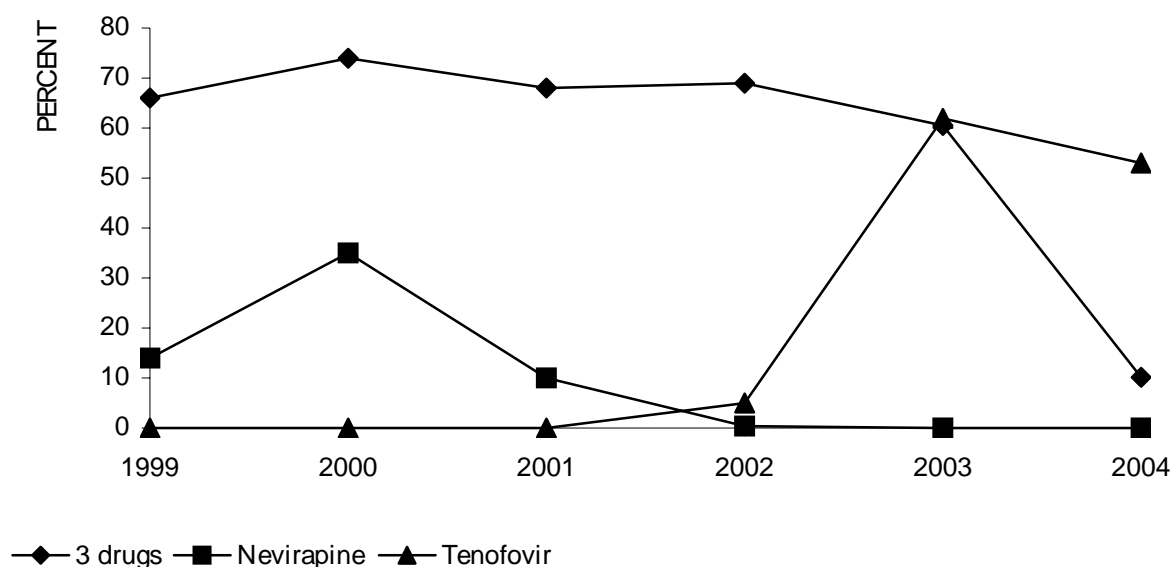


Table 3.1: PEP drug combinations, 1999 - 2004

Drug combination	N	(%)
Lamivudine, zidovudine and nelfinavir	321	30.5
Lamivudine and zidovudine	257	24.5
Lamivudine, stavudine and tenofovir	159	15.1
Lamivudine and tenofovir	81	7.7
Lamivudine, zidovudine and nevirapine	46	4.4
Lamivudine, and stavudine	38	3.6
Lamivudine, zidovudine and indinavir	23	2.2
Lamivudine, stavudine and nevirapine	20	1.9
Others	106	10.1
Total	1051	100

