Tolerability of Postexposure Prophylaxis with Zidovudine, Lamivudine, and Nelfinavir for Human Immunodeficiency Virus Infection

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Tolerability of the combination of zidovudine, lamivudine, and nelfinavir used as postexposure prophylaxis (PEP) for HIV infection was prospectively evaluated among 185 patients at 11 hospitals in eastern France. After exclusion of the 106 persons who discontinued PEP either because the source patient subsequently tested HIV seronegative or because the injury was reassessed as resulting in a low risk for transmission of HIV, 67 (85%) of the patients who received such PEP experienced adverse effects, which led to withdrawal of nelfinavir in 28 (35%) of these patients.

In accordance with current guidelines [1, 2], prophylaxis can be offered to individuals in France who have recently been exposed to HIV infection. Although the benefit of a 3-drug regimen (which usually includes 2 nucleoside reverse transcriptase inhibitors and 1 protease inhibitor) has not been demonstrated, the higher antiretroviral activity and lower susceptibility to resistance that are associated with such a regimen may be advantageous [3].

Few data are available on the tolerability of such combinations among patients who are receiving prophylaxis. Results of studies of the tolerability of the combination of zidovudine, lamivudine, and indinavir among 2 cohorts of health care workers were recently reported: 74% and 66.5% of the subjects in each of the cohorts, respectively, experienced adverse effects, which resulted in discontinuation of indinavir for 47% and 40% of the subjects, respectively [4, 5]. In a cohort of older health care workers, adverse effects were reported in 94% of treated subjects [6].

We reviewed data prospectively collected from 11 hospitals in eastern France that used the combination of zidovudine, lamivudine, and nelfinavir as first-line PEP when resistance to these drugs was neither suspected nor proven in the source patient. If PEP was initiated, further medical advice was given on day 2; it was given again when adverse effects occurred and then again at the end of treatment (on day 28). Adverse effects were recorded on case-report forms. HIV seronegative status was confirmed at the time of initial presentation and was retested 3 months later. Statistical analysis was based on the χ² test and on analysis of variance, as appropriate.

From 1 May 1998 through 1 September 2000, a total of 697 individuals sought medical advice after a recent exposure event that carried a risk for HIV transmission. PEP was initiated for 262 individuals.

PEP with zidovudine, lamivudine, and nelfinavir (zlnPEP) was given to 251 individuals, including 136 health care workers who sought medical consultation after they sustained injuries that resulted in exposure to blood, 76 individuals who were exposed to HIV during sex (including 19 cases of rape), 1 injection drug user, and 38 individuals who were not health care workers but who had been exposed to blood (e.g., through contact with discarded syringes). The mean patient age (±SD) was 33.5 ± 11 years. Forty-eight percent of the individuals were women, none of whom were pregnant. The median interval between exposure to HIV and presentation was 4 h (interquartile range, 2–19 h [minimum, 0 h; maximum, 96 h]). Sixty-four percent of the individuals had previously undergone at least 1 test for determination of their HIV serostatus, and 15% had previously sought medical advice after exposure to HIV. Five individuals had previously received PEP; this group included 2 health care workers, 2 individuals who were exposed to HIV during sex, and 1 individual who had another exposure event.

The source patient was identified for 187 (74.5%) of the 251 patients to whom zlnPEP was given, but the source patient’s HIV serostatus was unknown for 49 (26%) of these patients. Of the 138 source patients whose HIV serostatus could be determined, 32 (23%) were HIV seropositive, 6 (4%) had tested negative for HIV before PEP had been initiated for the contact individual (zlnPEP was nonetheless initiated for the contact individual because the source patient indicated having had a
Table 1. Adverse effects from and discontinuation of postexposure prophylaxis with zidovudine, lamivudine, and nelfinavir among 185 patients.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Received zlnPEP&lt;sup&gt;a&lt;/sup&gt; (n = 185)</th>
<th>Discontinued zlnPEP before day 28&lt;sup&gt;b&lt;/sup&gt; (n = 106)</th>
<th>Required zlnPEP for 28 days (n = 79)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adverse effects</td>
<td>77 (41.5)</td>
<td>10 (9.5)</td>
<td>67 (85)</td>
</tr>
<tr>
<td>Total discontinuation of zlnPEP</td>
<td>8 (4)</td>
<td>—</td>
<td>8 (10)</td>
</tr>
<tr>
<td>Discontinuation of nelfinavir only</td>
<td>20 (11)</td>
<td>—</td>
<td>20 (25)</td>
</tr>
</tbody>
</table>

NOTE. zlnPEP, postexposure prophylaxis with the combination of zidovudine, lamivudine, and nelfinavir.

<sup>a</sup> Patients who were lost to follow-up were excluded.

<sup>b</sup> zlnPEP was discontinued either because the source patient tested negative for HIV or because injury was reassessed as resulting in a low risk for transmission of HIV.

recent risk of exposure), and 100 (73%) had tested negative for HIV after initiation of zlnPEP.

Sixty-six (26%) of the 251 patients to whom zlnPEP was given were lost to follow-up after the first or second (day 2) consultation. For 106 (57%) of the remaining 185 patients (74%; table 1), zlnPEP was discontinued before day 28 of PEP either because the source patient tested negative for HIV or because the injury was reassessed as resulting in a low risk for transmission of HIV. In 95 of these cases (89.5%), PEP was discontinued before day 3. Adverse effects were reported before discontinuation of zlnPEP in 10 (9.5%) of these 106 persons (including 7 patients who discontinued zlnPEP before day 3). For 8 (10%) of the remaining 79 patients (43%), zlnPEP was discontinued because of adverse effects (median treatment period, 8.5 days). Twenty patients (25%) discontinued receiving nelfinavir but continued prophylaxis with zidovudine and lamivudine (median period during which the full regimen was received, 9 days). Fifty-one (65%) of these 79 patients received zlnPEP for the full 28 days of treatment, and 39 (76%) of these 51 patients experienced at least 1 adverse effect (median treatment period before onset of adverse effects, 3 days). The most frequently occurring adverse effects were diarrhea (in 31 [79%] of the individuals who reported at least 1 adverse effect) and nausea/vomiting (in 24 [62%]). In this group of 79 patients who required zlnPEP for the full 28 days of treatment, no significant associations between tolerability and sex, age, or exposure event were found. Three months after injury, HIV serostatus was available for only 77 (31%) of the 251 patients, among whom no seroconversions were recorded.

The tolerability of zlnPEP among patients was therefore poor (resulting mainly in gastrointestinal effects) and compromised treatment efficacy. However, the rate of treatment discontinuation was slightly lower than that previously reported with use of the zidovudine-lamivudine-indinavir combination. Other, better-tolerated prophylactic antiretroviral combinations must now be evaluated.

References


