Successful Absorption of Antiretroviral Drugs after Gastrojejunal Bypass Surgery following Failure of Therapy through a Jejunal Tube

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Abstract

Lopinavir, an antiretroviral drug against human immunodeficiency virus (HIV), was administered through various routes to an HIV-infected patient with duodenal malignant lymphoma. Antiretroviral drugs were first administered through a jejunal tube, and then through bypass route between the stomach and jejunum that was 20 cm distal from the ligament of Treitz after surgery. Oral administration through the bypass achieved sufficient serum concentrations of lopinavir, whereas administration through the jejunal tube did not.

Key words: lopinavir, serum concentration, absorption, viral suppression, jejunal tube

(Inter Med 48: 1103-1104, 2009)
(DOI: 10.2169/internalmedicine.48.1906)

Introduction

Patients infected with the human immunodeficiency virus (HIV) can now survive longer thanks to recent advances in antiretroviral therapy (ART). Although the present case is a patient with acquired immunodeficiency diseases syndrome (AIDS)-related malignant lymphoma of the duodenum, non-AIDS-related carcinoma has been increasing among HIV-infected patients in the ART era (1). For a variety of reasons, such as metastasis in the brain and upper gastrointestinal tract, the need for enteral feeding has been increasing. The site of absorption of ART within the alimentary tract remains poorly defined in humans (2).

Case Report

A 28-year-old man was admitted to our hospital diagnosed with AIDS-related malignant lymphoma of the duodenum, of the diffuse large B cell type, stage IV. He had not received antiretroviral therapy on admission. The CD4 cell count was 113/mm³ and plasma HIV-RNA was 7.1×10⁴ copies/mL, indicating severe immunosuppression. Further examination showed Candida esophagitis, an AIDS-defining disease. Due to duodenal stenosis caused by the lymphoma, the patient was unable to take any food orally except for liquids. Furthermore, bile had to be drained by percutaneous transhepatic cholangioledrainage (PTCD) tube. Two weeks after admission, he received systemic chemotherapy including cyclophosphamide 750 mg/m² (day 1), doxorubicin 50 mg/m² (day 1), vincristine 1.4 mg/m² (day 1), and prednisolone 100 mg/day (days 1-5) with intrathecal injection of prednisolone 20 mg and methotrexate 15 mg. Completion of six cycles of the above systemic chemotherapy induced complete remission.

ART was started with a combination of two nucleotide reverse transcriptase inhibitors (NRTIs), lamivudine 300 mg/day and abacavir 600 mg/day (powder forms), and a protease inhibitor, lopinavir 800 mg/day with ritonavir 200 mg/day (LPV/r) (liquid forms). Although the patient achieved complete remission, the duodenum remained stenosed due to fibrosis. He was able to take powdered ART orally and HIV-RNA decreased from 2.4×10⁵ copies/mL to < 400 copies/mL within two weeks. Frequent vomiting was noted probably due to food-induced duodenal obstruction, and drained material through the PTCD tube contained food residues and

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Received for publication November 30, 2008; Accepted for publication March 13, 2009

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Table 1. Serum Lopinavir Concentration 12 Hours after Administration

<table>
<thead>
<tr>
<th>Administration route</th>
<th>Orally without food</th>
<th>By jejunal tube with fat food</th>
<th>Orally through bypass with fat food</th>
</tr>
</thead>
<tbody>
<tr>
<td>After ART (Weeks)*</td>
<td>2</td>
<td>7</td>
<td>11</td>
</tr>
<tr>
<td>Serum LPV concentration (mg/mL)</td>
<td>0.79</td>
<td>2.04</td>
<td>&lt;0.20</td>
</tr>
<tr>
<td>HIV-RNA (copies/mL)</td>
<td>&lt;400 **</td>
<td>&lt;400**</td>
<td>2.2 \times 10^4</td>
</tr>
<tr>
<td>CD4 (/mm^3)</td>
<td>19</td>
<td>61</td>
<td>106</td>
</tr>
</tbody>
</table>

*: weeks after initiating ART by each route
**: undetectable limit of viral load by standard Amplicor

ART: antiretroviral therapy, LPV: lopinavir

Other medications that were occasionally co-administered were cefoperazone/sulbactam, linezolid, micafungin, respectively for sepsis, and aciclovir for Herpes zoster.

powered antiretroviral drugs. Accordingly, ART was stopped at week 7.

For stable enteral drug delivery and nutrition, jejunostomy was performed two weeks after stopping oral ART. Three days later, ART with fat-containing food was started through the percutaneous jejunal tube, which was placed at ≥ 35 cm distal to the ligament of Treitz in the jejunum. The combination of ART was not changed. Serum lopinavir concentrations measured at weeks 7 and 11 were 2.04 and < 0.20 μg/mL, respectively. Although HIV-RNA decreased to 210 copies/mL at 7 weeks, it increased again to 11,000 copies/mL at 11 weeks with M184V mutation.

Based on the viral failure, ART was completely stopped through the jejunal tube at week 13 of ART. The patient underwent gastrojejunal bypass surgery two weeks before stopping ART. This bypass route was from the gastric corpus to the jejunum about 20 cm distal from the ligament of Treitz. The bypass site was more proximal than the tip of the jejunal tube. Three days after surgery, he started oral intake including fat-containing food. ART was restarted orally with LPV/r liquid monotherapy after a 10-day suspension. At 6 weeks after re-initiating liquid LPV/r, HIV-RNA decreased from 2.2×10^4 copies/mL to 280 copies/mL. Two NRTIs, abacavir and tenofovir were added subsequently. The serum concentration of lopinavir was 20.83 μg/mL at 18 weeks (Table 1). HIV-RNA finally decreased and remained below the detection level (50 copies/mL).

Discussion

Successful HIV suppression requires sufficient serum concentration of several antiretroviral drugs. To our knowledge, this case was the first report that showed that the administration site may be important to achieve a clinically sufficient serum concentration of LPV. The absolute bioavailability of LPV co-formulated with ritonavir in humans has not been established (3). Although HIV-RNA decreased to less than 400 copies/mL, the concentration of LPV/r was low. After administration by jejunal tube, the concentration of LPV was unstable and could not reach clinically effective concentrations. However, oral administration with high fat meal through gastrojejunal bypass finally achieved a sufficient concentration of LPV. Another case report showed that good absorption of LPV was obtained in a patient with gastrectomy (4). These two case reports suggest that absorption of LPV does not need gastric acid. Furthermore, in the present case, LPV was well absorbed without bile and pancreatic juice since the PTCD tube was still in place after bypass surgery.

Taken together, with regard to the site of absorption of LPV, the jejunum must be the most important; at least within 35 cm from the ligament of Treitz. We should pay more attention to the site of absorption to maintain effective drug concentrations when antiretroviral drugs are administered through an unusual route, such as a jejunal tube.

Acknowledgement

The authors thank Drs. A. Ueda, Y. Abe, R. Iwashita, and N. Tachikawa, for treatment of this patient.

References


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