Ritonavir-Boosted Atazanavir May Be Efficacious in HIV-Infected Patients Concurrently Receiving Omeprazole

To the Editor—Optimal absorption of atazanavir is highly dependent upon an acidic gastric pH. In a small study of healthy volunteers, coadministration of omeprazole (40 mg per day) and a combination of atazanavir (300 mg per day) and ritonavir (100 mg per day) reduced the minimum concentration \( C_{\text{min}} \) and area under the plasma concentration-time curve (AUC) for atazanavir by 78% and 76%, respectively [1]. Because antiretroviral efficacy of protease inhibitors generally correlates with \( C_{\text{min}} \) and AUC [2], Bristol-Myers Squibb recommended that omeprazole and atazanavir should not be coadministered [3]. However, there are no established pharmacokinetic parameters for atazanavir that predict virologic suppression. In addition, recent data suggest that this adverse omeprazole-atazanavir interaction does not occur in some HIV-infected patients [4, 5]. We describe a 50-year-old HIV-infected African American man who maintained virologic suppression with an atazanavir-ritonavir-based regimen despite omeprazole use.

The patient’s virologic history included an HIV load of <400 copies/mL for the previous 6 years (4 years of stavudine-lamivudine-nelfinavir-based indinavir therapy, followed by 2 years of stavudine-lamivudine-nelfinavir therapy). The patient had no genotypic evidence of protease-resistance mutations. Atazanavir-ritonavir was substituted for nelfinavir because of worsening hyperlipidemia. At that time, the patient’s CD4+ cell count was 1095 cells/mL (CD4+ cell percentage, 21.2%) and an HIV load of <75 copies/mL suggests that he did not experience any adverse interaction between omeprazole and atazanavir, despite 12 weeks of coadministration. Several possibilities exist for this observation. First, atazanavir pharmacokinetics and omeprazole-atazanavir pharmacokinetics can vary significantly from person to person, such that adequate atazanavir \( C_{\text{min}} \) and AUC may be achieved for some HIV-infected patients and not for others [4]. Second, the patient had no genotypic evidence of protease-resistance mutations, and his virus likely retained susceptibility to atazanavir, even at lower drug concentrations. Third, the omeprazole-atazanavir interaction may not compromise virologic outcomes in patients who are already immunosuppressed [5]. Fourth, lower dosages of omeprazole, such as 20 mg per day, may not significantly affect atazanavir absorption [4, 5]. Fifth, the short period of concurrent omeprazole and atazanavir administration may have been insufficient to develop clinical resistance and viral rebound, especially in this patient, who had a high CD4+ cell count and longstanding viral suppression. To date, the earliest reported virologic failure occurred after 16 weeks of concurrent therapy [5]. Sixth, it is also conceivable, but less likely, that taking atazanavir twice per day may have blunted the effect of the patient’s morning omeprazole-atazanavir coadministration. These issues were discussed with our patient; he chose to resume nelfinavir treatment, because the available data suggest that there is no adverse pharmacokinetic interaction with omeprazole. His case underscores the need for additional data to conclusively determine the effect of omeprazole and atazanavir coadministration on virologic outcomes in HIV-infected patients.

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References


The Queen of Punt

To the Editor—The photograph of the grotesquely fat female figure on the cover of the 15 December issue of Clinical Infectious Diseases that was taken from a bas-relief and correctly identified as the Queen of Punt was incorrectly ascribed to be consistent with the clinicopathological features of lymphatic filariasis “elephantiasis” [1]. In the past, the clinical diagnosis was
made solely on the basis of the deformities of the limbs observed [2]. More recently, the Queen of Punt syndrome, clinically described as a rugged face, gluteal femoral obesity, hyperlordosis, and symmetrical deposits of fat on the trunk, limbs, and thighs, seems to be a more unifying explanation for the graphic representation of the Queen [3]. This syndrome appears to be a single phenotype grouping several dermatological pathologies (Launois Bensaude lipomatosis, Dercum disease, neuropathogenesis, congenital lipodystrophy, acondroplasia, familial obesity, Proteus syndrome, and X-linked dominant hypophosphatemic rickets) [4–6]. Clearly, in the absence of any genetic or bioanthropological evidence of a mummy, the clinical diagnosis that should be ascribed to the Queen of Punt still remains elusive after 34 centuries.

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References


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Reply to Bodi et al.

To the Editor—We congratulate Dr. Bodi and colleagues for their recent article [1], which demonstrates a significant association between the use of guideline-concordant antibiotics and mortality for patients with community-acquired pneumonia who require hospitalization in an intensive care unit. However, we wish to correct an error in their article regarding our recent article [2] in the American Journal of Medicine. In the discussion, the authors state that “the effects of other factors such as age, presence of comorbidities, and complications associated with pneumonia (e.g., septic shock and receipt of mechanical ventilation) were not analyzed” [1, p. 1714]. This is incorrect. Comorbid conditions and age are part of the pneumonia severity index developed by Fine et al. [3], which was included in our multivariable models. The pneumonia severity index is a validated prediction rule for 30-day mortality for patients with community-acquired pneumonia. This rule is based on 3 demographic characteristics, 5 comorbid illnesses, 5 physical examination findings, and 7 laboratory results and radiographic findings obtained at the time of presentation. Age, chronic renal disease, liver disease, congestive heart failure, prior stroke, and neoplasia are all components of the pneumonia severity index.

Regarding adjusting for complications associated with pneumonia, although we did not adjust for these 2 factors directly, we included a dichotomized variable for the need of hospitalization in an intensive care unit as one of the factors in our multivariable analyses. We found that need for hospitalization in an intensive care unit was a much stronger predictor of mortality than was either septic shock or mechanical ventilation as individual variables. In addition, we were unable to put all of these factors in the same multivariable models as a result of collinearity, because both septic shock and mechanical ventilation are reasons for admission into an intensive care unit.

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Improvement of Dyslipidemia during Different HAART Regimens: Tenofovir versus Stavudine-Containing Antiretroviral Combinations

To the Editor—Schewe et al. [1] recently analyzed the switch from antiretroviral regimens that contain stavudine to those