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Predictors of severe hyperbiliruniaemia in HIV-infected patients treated with atazanavir (ATV)

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Purpose of the study

Hyperbilirubinemia is the most common laboratory abnormality in patients treated with ATV; bilirubin plasma levels have been correlated with ATV plasma concentration [1]. In this study we analysed the relationships between hyperbilirubinemia, Gilbert's syndrome and ATV plasma concentration.

Methods

HIV-infected subjects on ATV/ritonavir containing stable HAART regimen were included. ATV plasma concentrations were measured 24 hours after the last dose by HPLC with UV detector. Polymorphism at the uridin-glocoronosyl-transferase 1A1 (UGT1A1) was examined in DNA extracted from blood mononuclear cells, to identify subjects with Gilbert's syndrome. The correlation between bilirubin plasma levels, ATV concentration and polymorphism of UGT1A1 (defined as the presence than at least one TA7 allele) were evaluated by multivariate linear regression (other covariates included: gender, age, CD4 count, months of ATV exposure). Predictors of severe hyperbilirubinemia (>2.5 μmol/l; grade 3) were evaluated by multivariate logistic regression (polymorphism at UGT1A1, Cmin, BMI, age included as covariates).

Summary of results

44 patients, 27.3% females, median age of 42.5 years, median BMI of 23.88 (IQR 21.8–25.8) were analysed. The distribution of different polymorphism at UGT1A1 was: 45.4% TA6/TA6, 40.9% TA6/TA7, 13.7% TA7/TA7. The median ATV exposure was 17 months (IQR 7–32), the median Cmin ATV plasma concentration was 0.60 ng/ml (IQR 0.41–0.97) and the median plasma bilirubin level was 2.48 mg/dL (IQR 1.24–3.95). Twenty-two (50%) patients experienced severe hyperbilirubinemia; among those, the proportion of patients with polymorphism was higher: 72% vs. 36% without severe hyperbilirubinemia (chi-square p = 0.01). In multivariate linear regression analysis total bilirubin was directly correlated to polymorphisms at UGT1A1 (β 1.52 SE 0.61 p = 0.01), to Cmin ATV plasma levels (β 1.42, SE 0.47 p = 0.04) and to age (β 0.08, SE 0.03 p = 0.007). Polymorphism at UGT1A1 (AOR 6.6, 95%CI 1.34–32.6, p = 0.02) and BMI (for every additional unit AOR 0.66, 95%CI 0.45–0.97, p = 0.03) were the only independent predictors of severe hyperbilirubinemia.

Conclusion

Screening for Gilbert's syndrome could be an important tool in patients with a ATV/ritonavir-containing HAART regimen, in order to predict severe hyperbilirubinemia.

References

1. Rodriguez-Novao S, *et al.*: *AIDS* 2007, **21**:41-46.