A population pharmacokinetic model is beneficial in quantifying hair concentrations of ritonavir-boosted atazanavir: A study of HIV-infected Zimbabwean adolescents.

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Abstract

Background

Adolescents experience higher levels of non-adherence to HIV treatment. Drug concentration in hair promises to be reliable for assessing exposure to antiretroviral (ARV) drugs. Pharmacokinetic modelling can explore utility of drug in hair. We aimed at developing and validating a pharmacokinetic model based on atazanavir/ritonavir (ATV/r) in hair and identify factors associated with variabilities in hair accumulation.

Methods

We based the study on secondary data analysis whereby data from a previous study on Zimbabwean adolescents which collected hair samples at enrolment and three months follow-up was used in model development. We performed model development in NONMEM (version 7.3) ADVAN 13.

Results

There is 16% / 18% of the respective ATV/r in hair as a ratio of steady-state trough plasma concentrations. At follow-up, we estimated an increase of 30% /42% of respective ATV/r in hair. We associated a unit increase in adherence score with 2% increase in hair concentration both ATV/r.

Thinner participants had 54% higher while overweight had 21% lower atazanavir in hair compared to normal weight participants. Adolescents receiving care from fellow siblings had atazanavir in hair at least 54% less compared to other forms of care.

Conclusion

The determinants of increased ATV/r concentrations in hair found in our analysis are monitoring at follow up event, body mass index, and caregiver status. Measuring drug concentration in hair is feasibly accomplished and could be more accurate for monitoring ARV drugs exposure.

Full Text

Due to technical limitations, full-text HTML conversion of this manuscript could not be completed. However, the manuscript can be downloaded and accessed as a PDF.

Figures
Figure 1

Schematic representation of the structural population PK model used to predict atazanavir and ritonavir concentrations measured in hair.
Basic goodness-of-fit plots for the final model for atazanavir (panel A) and ritonavir (panel B). Upper left panel: The observations are plotted versus the population predictions. Upper right panel: The observations are plotted against the individual predictions. Lower left panel: The individually weighted residuals are plotted versus time after dose. Lower right panel: The conditional weighted residuals are shown versus the individual predictions. The open black circles represents observed data. The red line is a locally weighted scatter-plot smoother (LOESS), while the solid line is identity or zero.