Universität Basel

Research Project

Physiologically based pharmacokinetic modeling of antiretroviral agents in special populations

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Project title Physiologically based pharmacokinetic modeling of antiretroviral agents in special populations
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The use of combined antiretroviral therapy has dramatically reduced the morbidity and mortality related to HIV infection. As a result, HIV-infected individuals live longer and the proportion of older individuals within the HIV infected population is constantly growing. Thus, the management of HIV infection will become more complex as age-related decline in the function of organs may impact the pharmacokinetic of antiretroviral agents and thereby affect dosage requirements. Furthermore, due to improved health outcomes, HIV-infected individuals are becoming increasingly overweight or obese at a rate similar to the general population. Thus, obesity represents a new challenge in the treatment of HIV infection because the actual recommended drug doses may not be sufficient. Finally, the epidemiology of HIV infection has changed over the years so that women represent now a substantial proportion of infected adults. Thus, as more effective and tolerable antiretroviral drugs have become available, and as the prevention of mother-to-child transmission has becomes an achievable goal, more and more HIV-infected women are choosing to become pregnant and to have children. Even though the physiological changes associated with pregnancy are well known to cause pharmacokinetics alterations, there is a scarcity of data on dose optimization strategies for antiretroviral drugs during pregnancy. All together, the issue of antiretroviral drug dosing in these special populations relates to the fact that recommended doses are usually issued from clinical trials including a “standard” HIV-infected population which does not reflect the physiological changes and thereby pharmacokinetic changes occurring in the above mentioned conditions.

The aim of this project is to characterize the dosing requirements in special populations using a physiologically based pharmacokinetic (PBPK) modeling. This technique allows prediction of drug pharmacokinetics in virtual patients using *in vitro* data and a mathematical description of drug distribution thus offering the possibility to simulate clinically relevant scenarios such as therapy optimization in special populations. This project is of clinical importance as, with the prolonged lifespan of HIV-infected individuals, the number of patients that will potentially require dose adjustments will gradually increase.

Keywords antiretroviral drugs, dosage adjustment, special populations
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