

Publication

Effect of ageing on antiretroviral drug pharmacokinetics using clinical data combined with modelling and simulation

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The impact of ageing on antiretroviral pharmacokinetics remains uncertain, leading to missing dosing recommendations for elderly people living with human immunodeficiency virus (HIV: PLWH). The objective of this study was to investigate whether ageing leads to clinically relevant pharmacokinetic changes of antiretrovirals that would support a dose adjustment based on the age of the treated PLWH.; Plasma concentrations for 10 first-line antiretrovirals were obtained in PLWH ≥ 55 years, participating in the Swiss HIV Cohort Study, and used to proof the predictive performance of our physiologically based pharmacokinetic (PBPK) model. The verified PBPK model predicted the continuous effect of ageing on HIV drug pharmacokinetics across adulthood (20-99 years). The impact of ethnicity on age-related pharmacokinetic changes between whites and other races was statistically analysed.; Clinically observed concentration-time profiles of all investigated antiretrovirals were generally within the 95% confidence interval of the PBPK simulations, demonstrating the predictive power of the modelling approach used. The predicted decline in drug clearance drove age-related pharmacokinetic changes of antiretrovirals, resulting in a maximal 70% [95% confidence interval: 40%, 120%] increase in antiretrovirals exposure across adulthood. Peak concentration, time to peak concentration and apparent volume of distribution were predicted to be unaltered by ageing. There was no statistically significant difference of age-related pharmacokinetic changes between studied ethnicities.; Dose adjustment for antiretrovirals based on the age of male and female PLWH is a priori not necessary in the absence of severe comorbidities considering the large safety margin of the current first-line HIV treatments.

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