**Induction of zidovudine glucuronidation and amination pathways by rifampicin in HIV-infected patients.**

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**AIMS:** The objective of the study was to determine the effect of multiple doses of rifampicin on the steady-state pharmacokinetics of zidovudine and its 5'-glucuronosyl (GZDV) and 3'-amino (AMT) metabolites.

**METHODS:** Eight asymptomatic HIV-infected patients (seven male, one female) participated in this three-period longitudinal study. Each patient received zidovudine (200 mg every 8 h) for 14 days (period 1), followed by rifampicin (600 mg every 24 h) with zidovudine for 14 days (period 2), and then zidovudine alone for a further 14 days (period 3). Blood and urine samples were collected over 6 h on the last day of each period for measurements of zidovudine and GZDV by h.p.l.c.-u.v. and AMT by h.p.l.c.-m.s-m.s.

**RESULTS:** Compared with zidovudine-alone values in period 1, 14 days of co-administration with rifampicin significantly increased zidovudine oral clearance (89%) and formation clearances to GZDV (100%) and AMT (82%). Correspondingly, there were decreases in maximum plasma concentration (43%), AUC (47%) and urine recovery (37%) of zidovudine. GZDV/zidovudine and AMT/zidovudine AUC ratios increased by 99% and 36%, respectively, despite a significant 29% decrease in AMT AUC. After stopping rifampicin for 14 days, values of these pharmacokinetic parameters returned to within 26% of baseline. Over the three periods AMT plasma levels were <18 ng ml-1 (n=6) and <40 ng ml-1 (n=2), and molar AMT/zidovudine AUC ratios ranged from 1.7% to 4.5%.

**CONCLUSIONS:** Rifampicin induced zidovudine glucuronidation and amination pathways resulting in decreased plasma and urine exposures to zidovudine. AMT plasma exposure decreased because induction was more pronounced for the major GZDV metabolite. The magnitude of the residual inductive effect was minimal at 14 days after stopping rifampicin.

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