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Pharmacokinetics for Pediatrics, Pregnancy, and Other Special Populations

Placental transfer of antiretroviral drugs in HIV-infected women: a retrospective study from 2002 to 2009.

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Background: The rate of mother-to-child transmission (MTCT) of HIV-1 is as low as 0.5% in non-breast-feeding mothers who delivered at term while receiving HAART with a plasma RNA < 500 c/mL in the French ANRS perinatal cohort. The degree of fetal exposure depends largely on the amount of placental transfer of drugs. The TDM of antiretroviral drugs (ARV) in HIV-infected pregnant women was used to detect adherence difficulties or intolerance.

Objectives: to evaluate the in vivo maternofetal transfer of ARV used to prevent MTCT based on the determination of concentrations in different compartments of the maternofetal unit.

Materials & Methods: paired maternal and cord blood and amniotic fluid samples were collected at delivery from HIV-1 infected women to determine steady-state plasma concentrations of ARV using HPLC coupled with UV-PDA or fluorimetric detection. Results from gemellary pregnancy were excluded from the study. The in vivo placental transfer of ARV was calculated as the ratio of cord (CP) to maternal plasma (MP) concentrations. Median ratio are presented and compared to the results of the ex vivo double perfusion of placental cotyledon reported in the literature. Other in vivo transfer ratio including amniotic fluid (AF) concentrations were calculated as AF/MP and AF/CP in a subgroup of patients.

Results: A total of 354 paired CP and MP were obtained from HIV-1 infected women (31.4 yrs) between 2002 and 2009. Among them, 65 had an AF sample collected. The main triple ARV combination found was LPV/r + ZDV/3TC (43%). CP/MP ratio were: ZDV (with pre-labour infusion 1.1, n=195 and without 167, n=78); 3TC (1.2, n=267); ABC (0.8, n=37); ddI (1.0, n=21); TFV (0.7, n=20); IDV (0.65, n=19); RTV (0.15, n=294); LPV (0.13, n=204); NFV (0.13, n=14); M8 (0.23, n=14); SQV (0.03, n=30); APV (0.21, n=12); NVP (0.81, n=21) and T20 (0.01, n=5). These in vivo results were statistically associated to the ex vivo results using the double perfusion of placental cotyledon reported in the literature. Other in vivo transfer ratio including amniotic fluid (AF) concentrations were calculated as AF/MP and AF/CP in a subgroup of patients.

Conclusions: Triple drug regimens reported in this study were in accordance with the successive French Guidelines to prevent MTCT. High transfer of NRTI, NVP and IDV in cord blood (Ratio > 0.7) was found regarding to their low protein binding, low liposolubility and low Molecular Weight. The ex vivo model of double perfusion of placental cotyledon might be a good predictor of the in vivo placental transfer. Because of high placental transfer, NRTI accumulation in amniotic compartment was found.

No conflict of interest