

MECHANISMS OF VIROLOGIC FAILURE IN HIV-INFECTED PATIENTS

A case-control study evaluated genotypic resistance, treatment adherence, and degree of viral load rebound to identify mechanisms of virologic failure in HIV patients following induction therapy with a zidovudine/lamivudine/indinavir (triple drug) regimen. Patients ($n = 58$) who reached virologic failure (HIV viral rebound > 500 copies/mL in two consecutive samples) were randomized to maintenance therapy with the triple-drug regimen, a zidovudine/lamivudine regimen, or a zidovudine/indinavir regimen and matched to control patients ($n = 58$) with sustained reduction in viral load < 500 copies/mL. Virologic and pharmacologic studies were based on plasma sample one (S1), taken at initial virologic failure, and plasma sample two (S2), taken 6 weeks after S1. The only primary resistance mutation in the reverse transcriptase gene was the M184V substitution, which was found in four of six S1 samples and three of six S2 samples in the triple-drug arm and 22 of 22 S1 samples and 20 of 21 S2 samples in the zidovudine/lamivudine arm. In the zidovudine/lamivudine control arm, M184V was found in 11 of 13 S1 samples and 10 of 11 S2 samples. Based on plasma drug measurements, overall adherence to zidovudine and indinavir in the maintenance phase was significantly lower in case patients compared with control patients. The study concluded that virologic failure during the maintenance phase was not associated with primary zidovudine or indinavir resistance mutations and that poor adherence was associated with virologic failure in the triple-drug maintenance arm and zidovudine/indinavir arms.

Descamps D, Flandre P, Calvez V, et al: Mechanisms of virologic failure in previously untreated HIV-infected patients from a trial of induction-maintenance therapy. JAMA 2000;283:205-211.

CERVICAL SHEDDING OF HERPES SIMPLEX VIRUS IN HIV-INFECTED WOMEN

A study analyzed HIV-1-seropositive women ($n = 273$) who were also seropositive for herpes simplex virus type 1 (HSV-1) and type 2 (HSV-2) to evaluate the influence of contraceptive use, pregnancy, and serum vitamin A levels on cervical shedding of HSV DNA. Polymerase chain reaction detected HSV DNA in 46 (17%) cervical swabs. In univariate analyses, cervical shedding of HSV DNA was significantly more frequent in women using oral contraceptive pills than in women using no contraception or nonhormonal forms of contraception (30% versus 11%, respectively). Pregnant women also shed HSV with greater frequency than nonpregnant women and women using nonhormonal contraception (45% versus 11%, respectively).

Prevalences of cervical HSV shedding among 178 women who were not pregnant, were not using hormonal contraception, and had serum vitamin A levels of < 20 , 20–29, 30–39, and ≥ 40 $\mu\text{g}/\text{dL}$ were 29%, 18%, 8%, and 2%, respectively. The study concluded that genital tract shedding of HSV in HIV-1-infected women was significantly associated with hormonal contraceptive use, pregnancy, and vitamin A deficiency and that further studies should evaluate HSV shedding in HIV-1-uninfected hormonal contraceptive users and the effect of vitamin A supplementation on genital shedding of HSV.

Mostad SB, Kreiss JK, Ryncarz AJ, et al: Cervical shedding of herpes simplex virus in human immunodeficiency virus-infected women: effects of hormonal contraception, pregnancy, and vitamin A deficiency. J Infect Dis 2000;181:58-63.

HEPATOTOXICITY ASSOCIATED WITH ANTIRETROVIRAL THERAPY AND HEPATITIS VIRUS INFECTION

A prospective cohort study evaluated HIV-infected patients ($n = 298$) to determine the incidence of severe hepatotoxicity after antiretroviral therapy initiation and to assess the role of chronic viral hepatitis in the development of antiretroviral-associated hepatotoxicity. Eighty-seven patients received nucleoside analog (NA) regimens and 211 patients received protease inhibitor (PI)-containing regimens. Severe (grade 3 or 4) hepatotoxicity was found in 31 (10.4%) of 298 patients, and ritonavir use was associated with 48% of all cases of severe hepatotoxicity. Hepatotoxicity of any grade was found in 83 (54%) of 154 patients infected with hepatitis C virus compared with 56 (39%) of 144 uninfected patients. Overall, 13 (9.4%) of 138 patients with hepatitis C or B virus in the non-ritonavir PI and NA arms developed severe hepatotoxicity compared with three (2.7%) of 110 uninfected patients. After multivariate adjustment, only ritonavir use and an increase in CD4 cell count greater than $0.05 \times 10^9/\text{L}$ during treatment were associated with severe hepatotoxicity. The study concluded that ritonavir was associated with the greatest risk of hepatotoxicity compared with nelfinavir, indinavir, and NA regimens, but further studies are needed to confirm and further define the mechanism of interaction between drug-induced hepatotoxicity and chronic viral hepatitis.

Sulkowski MS, Thomas DL, Chaisson RE, Moore RD: Hepatotoxicity associated with antiretroviral therapy in adults infected with human immunodeficiency virus and the role of hepatitis C or B virus infection. JAMA 2000;283:74-80.

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