...g and after maternal valacyclovir therapy in conjunction with antiretroviral HIV-1 prophylaxis in a randomized clinical trial.

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Abstract

BACKGROUND: Maternal administration of the acyclovir prodrug valacyclovir is compatible with pregnancy and breastfeeding. However, the safety profile of prolonged infant and maternal exposure to acyclovir in the context of antiretrovirals (ARVs) for prevention of mother-to-child HIV-1 transmission (PMTCT) has not been described.

METHODS: Pregnant Kenyan women co-infected with HIV-1/HSV-2 with CD4 counts > 250 cells/mm(3) were enrolled at 34 weeks gestation and randomized to twice daily 500 mg valacyclovir or placebo until 12 months postpartum. Women received zidovudine from 28 weeks gestation and single dose nevirapine was given to women and infants at the time of delivery for PMTCT. Infant blood was collected at 6 weeks for creatinine and ALT. Breast milk specimens were collected at 2 weeks postpartum from 71 women in the valacyclovir arm; acyclovir levels were determined for a random sample of 44 (62%) specimens. Fisher's Exact and Wilcoxon rank-sum tests were used for analysis.

RESULTS: One hundred forty-eight women were randomized and 146 mother-infant pairs were followed postpartum. PMTCT ARVs were administered to 98% of infants and all mothers. Valacyclovir was not associated with infant or maternal toxicities or adverse events, and no congenital malformations were observed. Infant creatinine levels were all normal (< 0.83 mg/dl) and median creatinine (median 0.50 mg/dl) and infant growth did not differ between study arms. Acyclovir was detected in 35 (80%) of 44 breast milk samples collected at 2 weeks postpartum. Median and maximum acyclovir levels were 2.62 and 10.15 mg/ml, respectively (interquartile range 0.6-4.19).

CONCLUSIONS: Exposure to PMTCT ARVs and acyclovir after maternal administration of valacyclovir during pregnancy and postpartum to women co-infected with HIV-1/HSV-2 was not associated with an increase in infant or maternal toxicities or adverse events.