

Title: The effects of short-term zidovudine treatment on mother to child hiv-1Transmission

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Abstract: Vertical transmission accounts for the majority of pediatric HIV-1 infections. Immunological, obstetrical, co-infection with other diseases and maternal viral load are some of the factors that influence this mode of transmission. It is not clear which of these factors are important in determining whether a mother will infect her infant. The long-term treatment of mothers with Zidovudine (AZT) during pregnancy reduced the infection rate by 70%. However, drug resistance variants are generated and can be vertically transmitted during long-term treatment. In Kenya, the use of a short-term treatment reduces transmission by 67% but whether this treatment could induce drug resistance is not known. This study investigated the induction and transmission of drug resistance variants during a short-term treatment with AZT. A part of the pol (697bp) region encoding the reverse transcriptase of six HIV-1 isolates from positive mothers (three on AZT and three untreated) and their infected infants was analyzed. Proviral DNA was amplified by nested PCR, the products cloned, sequenced and phylogenetically analyzed. Some natural point mutations at codons known to confer resistance to AZT were observed in some mothers' but none were transmitted to the infants. However, in one case (BU025) of a child whose mother was on AZT, lysine was substituted for serine at codon 70 (K70S) but, serine is not documented to confer any resistance to AZT. Selective transmission was observed in both treatment and non-treatment groups (KSO51, KSO06, BU025 and KSO04), supported by high bootstrap values of 914, 995, 898 and 914 and 995 respectively. However, multiple transmissions were also observed where the mothers' population was heterogeneous and homogeneous in mother-child pairs KSO04 and BU069 respectively. In mother-child pair KSO12, the infant's viral population clustered away from the mothers but the bootstrap value was low (421). Phylogenetic analysis revealed that four mothers were infected with HIV-1 subtype A and remaining two mothers were dually infected. Mother KSO12 was infected with two distinct subtype A viruses and the other mother KSO04 with subtype A and D. The dually infected mothers transmitted subtype A virus to their infants. In cases of mixed infection, our results suggest that there is selective transmission of genotypes and/or phenotypes. None of the three mothers' on short-term AZT treatment transmitted resistant variants to their infants. In addition, there were no differences in the transmission patterns between the AZT-treated and non-term AZT treatment for prevention of vertical transmission of HIV-1 is effective and safe.