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Oral presentation

Early virological suppression despite high frequency NNRTI resistance following perinatal prophylaxis in HIV-infected African infants

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Background

Infants infected with HIV-1 perinatally, despite single-dose nevirapine (sd-NVP) prophylaxis, progress rapidly. Furthermore, non-nucleoside reverse transcriptase inhibitor (NNRTI) resistance mutations, following exposure to sd-NVP, may have deleterious effects on efficacy of antiretroviral therapy (ART). Data on treatment outcome in sub-Saharan African infants exposed to sd-NVP are therefore urgently required.

Methods

Infants born to HIV-infected mothers in Durban, South Africa, were tested on days 1 and 28 of life to determine intrauterine and intrapartum HIV infection, respectively. HIV-infected infants received randomised immediate or deferred (once CD4≤0%) 4-drug ART (zidovudine, lamivudine, nelfinavir and nevirapine) in a dedicated study clinic, with free outpatient and inpatient treatment of illness. Genotyping for NNRTI resistance mutations was undertaken pre-ART. Monthly follow-up to 1-year post-ART included viral load (VL) and CD4 count measurement. Adherence was assessed at every appointment by caregiver verbal recall and by measured medication returns.

Results

All 63 HIV-infected infants were exposed to sd-NVP. 20/51 (39%) infants with baseline genotyping results had NNRTI resistance (most frequently Y181C; 20%). Median pre-ART viral load was 952,000 copies/mL. 43 infants were randomised to immediate ART. Of these, 3 were lost to follow-up pre-ART; 40 started ART (on median day 28; range 8-164) and 36/40 completed 1 year of ART. 20 infants were randomised to deferred ART. 16 reached the treatment threshold of CD4≤20% (at median day 99) and 13/16 started ART during infancy (on median day 142; range 81-227). Verbal and measured adherence was 99% and 95%, respectively. One year post-ART, 49/49 (100%) infants had VL<400 copies/mL and 46/49 (94%) had VL<50 copies/mL; 9 infants (18%) required second-line ART due to virological failure (n=4), TB treatment (n=4) or both (n=1). Time to VL<50 correlated with maternal CD4 (r=–0.42; P=0.005) and infant pre-ART VL (r=0.64; P<0.001). NNRTI mutations had no significant effect on

virological suppression. Infants starting immediate compared to deferred ART had fewer illness episodes (median 7 vs 12 illness episodes per infant; P=0.003), but no significant difference in mortality, virological suppression or CD4 repletion.

Conclusions

Excellent adherence and virological suppression are achievable in infants, despite high-frequency NNRTI mutations, high viral loads and rapid disease progression. Infants are currently relatively neglected in roll-out programmes and ART provision must be expanded. Immediate therapy may be preferable to delayed ART, to reduce morbidity and prevent loss to follow-up.