AIDS briefs

Early, abrupt weaning of infants of HIV-positive mothers potentially harmful

In low-resource settings, many programmes recommend that women who are infected with the human immunodeficiency virus (HIV) stop breastfeeding early. In this study researchers conducted a randomised trial to evaluate whether abrupt weaning at 4 months compared with the standard practice has a net benefit for HIV-free survival of children.

In this study researchers enrolled 958 HIV-infected women and their infants in Lusaka, Zambia. All the women planned to breastfeed exclusively to 4 months; 481 were randomly assigned to a counselling programme that encouraged abrupt weaning at 4 months, and 477 to a programme that encouraged continued breastfeeding for as long as the women chose. The primary outcome was either HIV infection or death of the child by 24 months.

In the intervention group, 69.0% of the mothers stopped breastfeeding at 5 months or earlier; 68.8% of these women reported the completion of weaning in less than 2 days. In the control group, the median duration of breastfeeding was 16 months. In the overall cohort, there was no significant difference between the groups in the rate of HIV-free survival among the children; 68.4% and 64.0% survived to 24 months without HIV infection in the intervention and control groups, respectively (p=0.13). Among infants who were still being breastfed and were not infected with HIV at 4 months, there was no significant difference between the groups in HIV-free survival at 24 months (83.9% and 80.7% in the intervention and control groups, respectively; p=0.27). Children who were infected with HIV by 4 months had a higher mortality by 24 months if they had been assigned to the intervention group than if they had been assigned to the control group (73.6% v. 54.8%; p=0.007).

Early, abrupt cessation of breastfeeding by HIV-infected women in a low-resource setting, such as Lusaka, Zambia, does not improve the rate of HIV-free survival among children born to HIV-infected mothers and is harmful to HIV-infected infants.

Kuhn L, *et al. NEJM* 2008; 359: 130-141.

Extended antiretroviral prophylaxis reduces HIV transmission in breastmilk

Effective strategies are urgently needed to reduce mother-to-child transmission of human immunodeficiency virus type 1 (HIV-1) through breastfeeding in resource-limited settings.

In this study, women with HIV-1 infection who were breastfeeding infants were enrolled in a randomised, phase 3 trial in Blantyre, Malawi. At birth, the infants were randomly assigned to one of three regimens: single-dose nevirapine plus 1 week of zidovudine (control regimen) or the control regimen plus daily extended prophylaxis either with nevirapine (extended nevirapine) or with nevirapine plus zidovudine (extended dual prophylaxis) until the age of 14 weeks. Using Kaplan-Meier analyses, the authors assessed the risk of HIV-1 infection among infants who were HIV-1 negative on DNA polymerase chain reaction assay at birth.

Among 3 016 infants in the study, the control group had consistently higher rates of HIV-1 infection from the age of 6 weeks through 18 months. At 9 months, the estimated rate of HIV-1 infection (the primary end point) was 10.6% in the control group compared with 5.2% in the extended-nevirapine group (p<0.001) and 6.4% in the extended-dual-prophylaxis group (p=0.002). There were no significant differences between the two extended-prophylaxis groups. The frequency of breastfeeding did not differ significantly among the study groups. Infants receiving extended dual prophylaxis had a significant increase in the number of adverse events (primarily neutropenia) that were deemed to be possibly related to a study drug.

Extended prophylaxis with nevirapine or with nevirapine and zidovudine for the first 14 weeks of life significantly reduced postnatal HIV-1 infection in 9-month-old infants.

Kumwenda NI, *et al. NEJM* 2008; 359: 119-129.

Co-trimoxazole prophylaxis reduces mortality in HIV-infected adults with TB

The aim of this study was to assess the impact of prophylactic oral co-trimoxazole in reducing mortality in HIV-positive Zambian adults being treated for pulmonary tuberculosis, using a double-blind placebo-controlled randomised clinical trial.

Two groups of antiretroviral treatment-naïve adults with HIV infection were enrolled: patients newly diagnosed as having tuberculosis and receiving tuberculosis treatment either for the first time or for retreatment after relapse; and previously treated patients not receiving treatment. The intervention was oral co-trimoxazole or matching placebo daily.

A total of 1 003 patients were randomised: 835 (416 co-trimoxazole, 419 placebo) were receiving treatment for tuberculosis, 762 (376 co-trimoxazole, 386 placebo) of them newly diagnosed, previously untreated patients and 73 (40 co-trimoxazole, 33 placebo) receiving a retreatment regimen; 168 (84 co-trimoxazole, 84 placebo) were not on treatment but had received treatment in the past. Of 835 participants receiving tuberculosis treatment, follow-up information was available for 757, with a total of 1 012.6 person years of follow-up. A total of 310 (147 co-trimoxazole, 163 placebo) participants died, corresponding to death rates of 27.3 and 34.4 per 100 person years. In the Cox regression analysis, the hazard ratio for death (co-trimoxazole:placebo) was 0.79 (95% confidence interval 0.63 - 0.99). The effect of co-trimoxazole waned with time, possibly owing to falling adherence levels; in a per protocol analysis based on patients who spent at least 90% of their time at risk supplied with the study drug, the hazard ratio was 0.65 (0.45 - 0.93).

The conclusions were that prophylaxis with co-trimoxazole reduces mortality in HIV-infected adults with pulmonary tuberculosis. Co-trimoxazole was generally safe and well tolerated.

Nunn AJ, *et al. BMJ* 2008; 337: a257.

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