Evaluation of 4 Weeks’ Neonatal Antiretroviral Prophylaxis as a Component of a Prevention of Mother-to-Child Transmission Program in a Resource-Rich Setting


PURPOSE OF THE STUDY. A 6-week course of neonatal antiretroviral prophylaxis has been standard in most developed countries. In the same settings, a 4-week rather than 6-week intervention might reduce toxicity and reduce cost.

STUDY POPULATION. The study involved a cohort that included all HIV-exposed live births in Ireland from January 1999 through December 2008 with a minimum of 18-months of follow-up.

METHODS. This was a 10-year observational study of the Irish experience in their use of a 4-week rather than 6-week neonatal antiretroviral regimen.

RESULTS. Of the 916 infants with known outcome, 1% were infected. If analysis was limited to the 910 infants whose mothers received at least 4 weeks of antiretroviral therapy, the vertical transmission rate was 0.4%. These numbers are consistent with those found in other areas in which the standard 6-week regimen is followed.

CONCLUSIONS. The current clinical practice of using a 4-week neonatal antiretroviral prevention regimen seems to be as effective as a 6-week regimen.

REVIEWER COMMENTS. Although it is reasonable to surmise that a 4-week regimen is as effective as a 6-week regimen in preventing vertical transmission of HIV, the data presented here are unlikely to convince the public health authorities of other countries to move in this direction. This was not a controlled trial, and the patient population might differ in other countries.

Cardiac Effects of Antiretroviral Therapy in HIV-Negative Infants Born to HIV-Positive Mothers: NHLBI CHAART-1 (National Heart, Lung, and Blood Institute Cardiovascular Status of HAART Therapy in HIV-Exposed Infants and Children Cohort Study)


PURPOSE OF THE STUDY. HIV is known to cause a cardiomyopathy. In addition, the mitochondrial abnormalities reported in children exposed to antiretroviral therapy but not infected with HIV might also be associated abnormal
To accurately identify these at-risk patients with conventional tests has limited efforts to control TB. The purpose of this study was to identify novel biomarkers of active disease by using genomic techniques.

**STUDY POPULATION.** The investigators generated genome-wide transcriptional profiles from the blood of patients with active TB (before treatment), patients with latent TB, and healthy controls. This study was conducted at St Mary’s Hospital in London, United Kingdom, and the University of Cape Town in South Africa.

**METHODS.** Whole blood was obtained from healthy volunteers and patients with TB before starting antimicrobial therapy. A subset of patients diagnosed with active TB were also sampled 2 and 12 months after starting therapy. RNA was extracted from the whole blood of these subjects and used in a genome-wide microarray analysis. Extent of disease was assessed by plain chest radiographs.

**RESULTS.** The authors identified a distinct 393-transcript signature that defined patients with active disease. In addition, this transcript signature strongly correlated with extent of disease in patients with active TB. It is interesting to note that between 10% and 25% of patients with latent TB had similar transcript profiles to those patients with active disease, which suggests that this profile might identify those at risk for developing active disease. After 2 months of therapy, the transcriptional signature in patients with active TB reverted back to that of healthy controls, which suggests that this signature could be used to monitor the course of the disease. Using data-mining strategies, the authors found that the largest set of transcripts that changed in active TB were those induced by type I interferon (IFN) or IFN-γ in cells that were likely of neutrophil and monocyte origin.

**CONCLUSIONS.** A unique, treatment-sensitive, genome-wide transcriptional signature predominantly in phagocytes is associated with active TB and might predict those patients at risk of developing active disease. Type I IFN might play a larger role in the pathogenesis of TB than was previously appreciated.

**REVIEWER COMMENTS.** Development of an accurate biomarker for disease progression and treatment response would be a quantum leap forward in the global fight against TB and would potentially be useful for other similar diseases. This study is the first to associate active TB with a specific gene-expression signature that could be used to monitor those patients on therapy and identify those at risk of treatment failure. More research is needed to determine whether this signature could be used as a marker to identify those with latent TB and at risk of going on to develop active disease. This signature could be extremely valuable in aiding the diagnosis and
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