Progression of disease in HIV-infected children slowed after the first year of life

The European Collaborative Study. **Fluctuations in symptoms in human immunodeficiency virus-infected children: the first 10 years of life.** Pediatrics. 2001 Jul;108:116-22.

QUESTION

In children with HIV infection at birth, what are the clinical and immunologic manifestations of disease progression during the first 10 years of life?

DESIGN

Cohort study with a median of 5.8 years of follow-up.

SETTING

11 pediatric centers in 7 European countries.

PATIENTS

170 HIV-infected children who were born to mothers known to be infected with HIV at the time of delivery.

ASSESSMENT OF PROGNOSTIC FACTORS

Children were categorized into 3 cohorts according to the treatment policy at the time of their birth. Cohort 1 consisted of children born during 1985 to 1988 when no recommendations for treatment existed; cohort 2 consisted of children born during 1989 to 1994 when the treatment policy was restricted to monotherapy for symptomatic children; and cohort 3 consisted of children born during 1995 to 1999 when the initiation of combination therapies was recommended at an early stage. Children were allocated to Centers for Disease Control and Prevention (CDC) categories for clinical manifestations (N = asymptomatic; A = mildly symptomatic; B = moderately severe symptoms, including lymphoid interstitial pneumonitis; C = severe symptoms; and D = death) and immunologic classes (1 = normal, 2 = moderate immune suppression, and 3 = severe immune suppression) at each visit to the clinic.

MAIN OUTCOME MEASURES

Death and severity of disease progression with actual treatment received.

MAIN RESULTS

45 children (26%) died of AIDS during follow-up, and 2 children died of non–HIV-related causes. 70 children (41%) progressed to AIDS. 10 of 55 children (18%) who never received antiretroviral therapy (ART) were asymptomatic (category N), 8 (15%) were mildly symptomatic (category A), and 37 (67%) had more severe HIV-related signs and symptoms (category B). An estimated 15% of infected children will have progressed to severe disease (category C) or death (category D) by 1 year of age, after which the rate would be 7% annually to just under 40% by 5 years. An estimated 50% of children would have progressed to moderate immune suppression (category 2) by 1 year of age and > 90% by 5 years. The children in all 3 cohorts differed in their rate of disease progression, and the children in cohort 3 were the least likely to progress to serious disease (category C). It was estimated that by 1 year of age, > 25% of cohort 1 would have progressed to severe disease (category C) compared with 15% in cohort 2 and only 5% in cohort 3 ($P = 0.011$).

CONCLUSIONS

In children with HIV infection at birth, progression to clinical and immunologic manifestations of severe disease slowed after the first year of life. Children did not have serious symptoms or signs for most of the time.

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COMMENTARY

Doing studies to evaluate the effectiveness of ART in HIV-infected children has been difficult for several reasons. The largest barrier is that most infected children live in countries where ART is not affordable. In wealthier countries, perinatally infected children are usually a heterogeneous group, and their course of ART depends on where and when they were diagnosed with HIV infection. This heterogeneity has made it difficult to obtain useful results from large randomized controlled trials.

The results of cohort studies, including those of the European Collaborative Study, are consistent, showing that since 1995 a major improvement has occurred in the prognosis of children with HIV infection, particularly in the first year of life (1, 2). This change reflects not only an increasing use of combination ART but also an increasing use of *Pneumocystis carinii* pneumonia (PCP) prophylaxis (3). Prevention of PCP accounts for a substantial decrease in AIDS and death in infants with HIV infection (4). Most HIV specialists start combination ART in all HIV-infected children identified in their first year of life. Although this strategy is clearly beneficial for infants who would otherwise have developed serious disease before 1 year of age, it may not be optimal for children who would have remained asymptomatic for many years without therapy. As seen in adult populations, as we improve survival with the longer use of combinations of ART, we will also see an increase in the long-term complications of drug therapy. To balance the benefits and harms of long-term ART, we need information to help us determine in which children this therapy could safely be started later.

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