Prognosis

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, who received differing treatment protocols, what are the clinical and immunological manifestations during the first 10 years of life?

Design

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

Setting

11 paediatric centres 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 categorised into 3 cohorts according to the treatment policy at the time of birth. Cohort 1 consisted of children born from 1985–8 when no recommendations for treatment existed; cohort 2 consisted of children born from 1989–94 when the treatment policy was restricted to monotherapy for symptomatic children; and cohort 3 consisted of children born from 1995–9 when the initiation of combination therapies was recommended at an early stage. Children were allocated to Centres 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 immunological classes (1 = normal immune suppression, 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

70 children (41%) progressed to AIDS. 45 children (26%) died of AIDS during follow up, and 2 children died of non-HIV related causes. 45 of 55 children (82%) who never received antiretroviral treatment developed HIV related signs and symptoms. It was estimated that >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 and just under 50% by 10 years. Also, 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 immunological manifestations of severe disease slowed after the first year of life. Children were without serious symptoms or signs for most of the time.

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COMMENTARY

The European Collaborative Study is an important longitudinal study providing rich information about the clinical patterns and immunological progression of HIV in children infected perinatally in 11 European centres since 1985.

Analysis of such data is complicated because of the ever changing treatments for HIV, but the investigators analysed the effect of treatment changes in their study by dividing the sample into 3 groups according to treatment policy at the time of birth. Clinical status was measured using the CDC classification system at each visit. Nurses are interested in broader aspects of clinical response including symptom distress; number, type, and severity of infections; and developmental outcomes.¹

Immune status did not reflect clinical stage at any age and progress of disease was difficult to predict by immune status. CD4 count poorly reflects virological activity, which fluctuates because the count is affected by treatment. Currently, viral load is used as an indicator of disease progression. However, it may not be a good indicator in children <3 years of age. After 3 years of age, HIV1 RNA plateaus and is a more useful indicator. Assessment and follow up of young children with HIV should be done at centres whose staff is experienced in assessing and treating such children.

Of particular note from this study is that children with HIV may do better than we thought. The overall progression of disease slows after the first year of life, is less rapid from 1–5 years of age, and slows even more from 5–10 years. It will be increasingly important to provide support to children and families using models of chronic illness care rather than treating HIV as a terminal illness. Developmental outcomes, preventive health care, adherence to treatment, and maintaining contact with healthcare providers are all issues that should be closely monitored in HIV infected children. As the children reach school age, their parents will need help in telling them about their illness. Furthermore, healthcare professionals working with adolescents with HIV are challenged by how to help them manage complicated issues, including sexuality, as they live with HIV.

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1 Holditch-Davis D, Miles MS, Burchinal M, *et al*. Parental caregiving and developmental outcomes of infants of mothers with HIV. *Nurs Res* 2001;50:5–14.