Timing of HAART Defines the Integrity of Memory B Cells and the Longevity of Humoral Responses in HIV-1 Vertically-Infected Children


PURPOSE OF THE STUDY. HIV infection induces a progressive decline in immune function that affects not only T-cell but also B-cell activities, including the progressive decline in memory B cells, markedly elevated serum immunoglobulin levels, impaired responsiveness to routine immunizations, and loss of specific antibodies previously generated. Treatment of adults with highly active antiretroviral therapy (HAART) reduces immunoglobulin levels and increases B-cell numbers. However, several studies indicate that the B-cell compartment does not recover completely and patients maintain impaired antibody responses to immunizations. The purpose of this study was to determine whether the timing of HAART initiation affected pediatric patients’ ability to generate and to maintain protective levels of antibodies to routine immunizations.

STUDY POPULATION. Seventy children perinatally infected with HIV were studied with 50 healthy control subjects.

METHODS. Patients and control subjects received childhood immunizations according to the national (Italian) vaccine protocol. Patients who started HAART within the first year of life were categorized as “early treated”; children treated after the first year of life were considered “late treated,” and this group was subdivided into individuals with controlled virus and those who developed virological failure. Peripheral blood cells were evaluated with standard flow cytometry for B-cell subsets, including memory B cells. Antigen-specific B-cell functions were measured with an enzyme-linked immunosorbent spot assay. Plasma antibody titers against measles, tetanus, and pneumococcal antigens were assayed with enzyme-linked immunosorbent assays.

RESULTS. Early-treated patients maintained high percentages of memory B cells, compared with levels observed in healthy control subjects; patients who started HAART later showed lower percentages. Patients treated early maintained the capacity to generate antigen-specific memory B cells, and early HAART resulted in maintenance of multiple antibody levels above protective thresholds in HIV-infected children. Of concern, 25% of patients treated late failed to generate protective levels of antibodies to measles, and this number increased to >40% among those who experienced failure of antiretroviral therapy. In addition, >60% of subjects who received late HAART failed to maintain protective levels of antibodies to antigens including measles and tetanus; similar findings were noted in antibody responses to pneumococcal antigens.

CONCLUSIONS. Early HAART is essential for maintenance of normal B-cell functions in perinatally HIV-infected children. Regardless of T-cell numbers and/or clinical status, the results of this study strongly indicate that newborns infected with HIV should be treated as early as possible to preserve immune functions.

Maraviroc for Previously Treated Patients With R5 HIV-1 Infection


PURPOSE OF THE STUDY. Although there are now >20 anti-HIV medications, new agents are still needed. HIV drug resistance is highly prevalent and 15% of newly infected patients in the United States have drug-resistant virus. In addition, enhanced safety and tolerability and improved convenience would enhance adherence to antiretroviral regimens. HIV uses 1 of 2 chemokine receptors, in addition to CD4, to gain entry into a cell, chemokine receptor 5 (CCR5) and α-chemokine receptor 4 (CXCR4). HIV that uses CCR5 is the primary type of virus that is transmitted through sexual or perinatal exposure. CCR5 antagonists are a new class of anti-
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