

## The prevalence of hepatitis A antibodies in HIV exposed and/or infected children and adolescents

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Recent data from the National STD/AIDS Program show that there are around 600,000 cases of HIV in Brazil, with the South and Southeast regions being home to around 85% of these cases. Currently, terminal liver disease is considered one of the most important causes of death among hospitalized adult HIV patients, and it is estimated that around 40% of patients infected by HIV also have a co-infection by hepatitis B and/or C viruses. The inter-relationships of viral hepatitis with HIV are complex since HIV can modify the natural history of hepatitis infections and make possible behavior similar to that of opportunist diseases. There are *in vitro* and *in vivo* studies and controlled clinical trials demonstrating the harmful effects of these associations. Although there is growing interest in recognizing these co-infections, there are many peculiarities related to the diagnosis and treatment of viral hepatitis in patients infected by HIV and not all have been fully resolved. There can be: a) difficulties with serological diagnosis of hepatitis when significant immunodeficiency is present (T-CD4+ < 200 cells/mm<sup>3</sup>), b) a greater risk of hepatitis becoming chronic, c) a greater chance of vertical transmission of HCV, d) faster progression to cirrhosis, e) increased viral replication (B, C, HIV), and f) a greater chance of progressing to fulminating hepatitis when an HIV+ patient is co-infected by the hepatitis A virus.

Data on viral hepatitis and HIV co-infection for the pediatric population are very scarce and are generally on hepatitis B and/or C; aspects of infection by hepatitis A (HAV) are rarely described. For this reason alone the study of the prevalence of HAV antibodies in children and adolescents exposed to and/or infected by HIV, published in this issue of the *Jornal de Pediatria* would be of great interest. However, there are more reasons for congratulating the authors. Until recently, it was claimed that there was no consistent evidence of exacerbated acute liver disease due to HAV in patients with HIV. Gouvêa et al.<sup>1</sup> present a succinct review of the literature together with interesting data from their own study which demonstrate the relevance of the association between HIV and HAV. They performed a

retrospective analysis of the medical records of 352 patients receiving outpatients treatment at the Pediatric Infectology Department Clinic at the UNIFESP/EPM, in São Paulo. None of these patients had been vaccinated against HAV. There was a greater prevalence of total HAV antibodies in the HIV group for all age groups and no association was observed between immunological category and the presence of HAV antibodies.<sup>1</sup>

Despite the decline in HAV incidence over recent years in certain Latin American countries, there are still high rates of disease and even occasional epidemics, indicating that HAV remains an important Public health problem in our country.<sup>2</sup> Studies of pediatric HIV patients' response to hepatitis A vaccination are very rare. Individuals infected by HIV constitute a special group and, therefore, vaccination strategies should also be developed differently.

Since the introduction of Highly Active Anti Retroviral Therapy (HAART) drugs there has been a radical change in the management of HIV-infected patients with a recognized reduction in opportunist infections patient mortality. This protection appears to suggest that the increase in CD4+ cells in patients who are given HAART may indicate a restoration of immune system function. It is against this background that the complexities of HIV-infected patients' response to vaccination should be viewed. Although there are reports of increases in viral replication in peripheral blood after vaccination against influenza<sup>3,4</sup> the same thing does not take place after vaccination against hepatitis A.<sup>5,6</sup> It is known that the hepatitis A vaccine provokes different rates of seroconversion in patients with chronic diseases, when compared with normal subjects. With respect of children with Down Syndrome and chronic liver disease, we have previously shown that, despite responding with lower antibody titers, these patients exhibit adequate rates of seroconversion.<sup>7,8</sup>

The observation made by the authors that just 26% of those patients exposed to and/or infected by HIV exhibited antibodies against HAV is extremely interesting. The need to offer patients the desirable vaccinal prophylaxis should also take account of the stage of HIV infection. Thus, some authors have observed marked differences in vaccinal response depending on the severity of HIV infection. Santagostino et al.<sup>9</sup> found a clear relation between response to the vaccine and the stage of HIV infection when studying hemophilic patients with and without HIV infection, observing antibodies 12 months after vaccination (two

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subcutaneous doses), in 76% of cases, but in just 40% of those with progressive HIV-associated symptoms. All of the uninfected hemophiliacs developed antibodies. It has been reported that even patients with significant CD4+ cell depletion can respond to vaccines. In a recent study, Lederman et al. demonstrated 28% seroconversion after a first dose and 46% after a second dose of the hepatitis A. The group that responded had a mean of CD4+ cells of 254, in comparison with a mean of 212 for patients who did not respond. The number of CD4+ cells was also a determinant of vaccinal response in a patient sample analyzed by Kemper et al.<sup>10</sup> Seroconversion at the ninth month was observed in 68% of those with > 200 cells/mm<sup>3</sup> and just 9% of the patients with lower CD4+ counts ( $p = 0.004$ ). The safety effect of HAV immunization was analyzed by Bodsworth et al.,<sup>5</sup> 1 year after the administration of the first of two doses (1 and 6 months) of Havrix 1,440 U/E. A case-control study was undertaken of 90 HIV+ adults who were paired for CD4+ lymphocyte percentage and evaluated with respect of the development of AIDS, survival and T-cell subclasses. There were no differences between the groups.

Recently a number of different authors have been pointing to the need for HAV vaccination for HIV+ individuals, irrespective of whether they are using potent antiretroviral drugs.<sup>5,10,11</sup> On the other hand, compliance with hepatitis A and B vaccination by those infected with HIV is not usually good. A study by Tedaldi et al.<sup>12</sup> of HIV outpatients reported that just 32.4% of the 612 eligible to receive vaccination against hepatitis B and 23.3% of the 716 identified for vaccination against hepatitis A received a dose. The number of patients that completed the entire vaccination scheme was very small.

The conclusions of the authors of the Brazilian study with respect of the need for vaccinal hepatitis A prophylaxis for children and adolescents with HIV are judicious and opportune. We must be alert to the implementation of this measure which will probably have a positive impact on the quality of life of this group of patients who are so vulnerable.

## References

- Gouvêa AF, de Moraes-Pinto MI, Machado DM, do Carmo FB, Beltrão SC, Cunegundes KS, et al. Prevalência de anticorpos contra o vírus da hepatite A em crianças e adolescentes expostos e/ou infectados pelo HIV. *J Pediatr (Rio J)*. 2005;81:205-8.
- Costa Clemens SA, da Fonseca JC, Azevedo T, Cavalcanti AM, Silveira TR. Soroprevalência para hepatite A e hepatite B em quatro centros no Brasil. *Rev Soc Bras Med Trop*. 2000;35:1-100.
- Günthard HF, Wong JK, Spina CA. Effect of influenza vaccination on viral replication and immune response in persons infected with human immunodeficiency virus receiving potent antiretroviral therapy. *J Infect Dis*. 2000;181:522-31.
- O'Brien WA, Grovit-Ferbas K, Namazi A. HIV type 1 replication can be increased in peripheral blood of seropositive patients after influenza vaccination. *Blood*. 1995;86:1082-9.
- Bodsworth NJ, Neilsen GA, Donovan B. The effect of immunization with inactivated hepatitis A vaccine on the clinical course of HIV-infection: 1-year-follow-up. *AIDS*. 1997;11:747-9.
- Hess G, Clemens R, Bienzle U, Schonfeld C, Schunck B, Bock HL. Immunogenicity and safety of an inactivated hepatitis A vaccine in anti-HIV positive and negative homosexual men. *J Med Virol*. 1995;46:40-2.
- Ferreira CT, Taniguchi NA, Vieira SM, Lima JP, Silveira TR. Prevalência do anticorpo da hepatite A em crianças e adolescentes com hepatopatia crônica. *J Pediatr (Rio J)*. 2002;78:503-8.
- Ferreira CT, Leite JC, Taniguchi A, Vieira S, Pereira-Lima J, Silveira TR. Immunogenicity and safety of an inactivated Hepatitis A Vaccine in children with Down Syndrome. *J Pediatr Gastroenterol Nutr*. 2004;39:337-40.
- Santagostino E, Gringeri A, Rocino A, Zanetti A, de Biasi R, Mannucci PM. Patterns of immunogenicity of an inactivated hepatitis A vaccine in anti-HIV positive and negative hemophilic patients. *Thromb Haemost*. 1994;72:508-10.
- Kemper C, Haubrich R, Frank I, Dubin G, Buscarino C, McCutchan JA, et al. California Collaborative treatment group. Safety and immunogenicity of hepatitis A Vaccine in Human Immunodeficiency virus-infected patients: a double blind, randomized, placebo-controlled trial. *J Infect Dis*. 2003;187:1327-31.
- Valdez H, Smith KY, Landay A, Connick E, Kuritzkes DR, Kessler H, et al. Response to immunization with recall and neoantigens after prolonged administration of an HIV-1 protease inhibitor-containing regimen. ACTG 375 team. *AIDS Clinical Trials Group*. *AIDS*. 2000;14:11-21.
- Tedaldi EM, Baker RK, Moorman AC, Wood KC, Fuhrer J, McCabe RE, et al. HIV Outpatient Study (HOPS) Investigators. Hepatitis A and B vaccination practices for ambulatory patients infected with HIV. *Clin Infect Dis*. 2004;38:1478-84.