DECLINE OF MATERNAL HEPATITIS A ANTIBODIES DURING THE FIRST 2 YEARS OF LIFE IN INFANTS BORN IN TURKEY

ALABAZ DERYA,* AKSARAY NECMI, ALHAN EMRE, AND YAMAN AKGÜN
Infectious Disease Unit, Department of Pediatrics, Cukurova University Faculty of Medicine, Balcalı, Adana, Turkey; Microbiology Department, Cukurova University Faculty of Medicine, Balcalı, Adana, Turkey

Abstract. Selective immunization of at-risk groups may reduce the incidence of hepatitis A infection, but only the inclusion of hepatitis A vaccine in a routine universal childhood immunization schedule would guarantee control of the infection. But the interference by maternally derived hepatitis A antibodies (anti-HAV) with the immunogenicity of inactivated hepatitis A vaccine is still important in the determination of the optimal age for hepatitis A vaccination. The hepatitis A vaccines have not been assessed widely in children under the age of 2 years and are not currently licensed for this age group in many countries. A prospective trial was performed to detect seroprevalence of maternal hepatitis A antibodies during the first 2 years of life among young infants born to hepatitis A antibody positive mothers in Turkey. We measured at-birth anti-HAV in 147 infants born in our hospital and in their mothers and then from the offspring at months 3, 6, 9, 12, 15, 18, 21, and 24. The prevalence of seropositivity among the mothers at birth were found similarly high (93.9%) to the studies previously done among the adults in our area. The prevalence of anti-HAV among children aged 0, 9, 12, 15, 18, and 21 months were 93.9%, 62.6%, 36.1%, 13.6%, 6.1%, and 0.7%, respectively. Although a proportion of infants still had measurable antibodies at 9 and 12 months of age, two thirds of the infants over the age of 12 months were at high risk of acquiring hepatitis A infection, as living in an endemic region.

INTRODUCTION

Hepatitis A virus (HAV) infection in children (<6 years old) is mostly asymptomatic or characterized by nonspecific symptoms.1,2 Almost all children in developing countries with poor conditions of sanitation and hygiene become seropositive before 5 years of age.3-4 Because it does not cause chronic infection, there is a common misconception that hepatitis A is not a serious disease and thus the morbidity of hepatitis A is often underestimated. Furthermore, young children infected with hepatitis A in daycare centers, for example, can serve as a reservoir of infection for adolescents and adults, who are much more likely to develop clinical illness with a high morbidity and mortality.1,5 Selective immunization of at-risk groups may reduce the incidence of the disease, but because of their high disease rates and importance as a reservoir of transmission to others, children should be the primary focus of vaccination. However, the appropriate timing of vaccination has not been defined. Hepatitis A vaccines are not yet licensed for infants, thus the possibility of interference by maternally derived hepatitis A antibodies (anti-HAV) with the immune response of the infant has not yet been ruled out.6-8 Further knowledge about the decay of maternal antibodies in infants is important to help determine the optimal age for vaccination against hepatitis A to overcome this interference.4,9 Optimum immunization age should be determined for each country.

The current study evaluated the seroprevalence of HAV antibodies in women at delivery in a region of moderate endemicity, Turkey, and the decline of passively acquired maternal HAV antibodies in the first 2 years of life in infants born to HAV-positive mothers.

MATERIALS AND METHODS

All 165 healthy women who delivered between December 1999 and December 2000 at the Obstetrics Unit of Cukurova University, Adana, Turkey, were enrolled into the study. All infants were followed for 24 months at the Well Baby Clinic. Infants with an acute or chronic illness or with congenital abnormalities were excluded from the study. Blood samples were collected from all women at delivery and from all infants at birth and at the age of 3, 6, 9, 12, 15, 18, 21, and 24 months. Sera were stored at −20°C until they were tested. Total anti-HAV antibody levels were measured using an enzyme immunoassay ELISA inhibition assay. The study was approved by the hospital’s ethics committee, and informed consent was obtained from all the parents of the children involved.

Statistical analysis was carried out using nonlinear regression analysis to test the relationship between age and seropositivity.

RESULTS

Eighteen of 165 infants were excluded from the study either because they were lost to follow up, migrated, or their mothers did not consent for drawing blood samples. The results refer to a total of 147 infants. No clinically manifest hepatitis infections were detected during 2 years of follow-up.

Seropositivity (positive for anti-HAV antibody) was found in 138 (93.9%) of 147 infants and their mothers in their earliest serum specimens, at birth, whereas 9 (6.1%) infants and their mothers were seronegative at birth. The latest recorded seropositivity was at the age of 21 months in one infant (0.7%). In the following of the seropositive 138 infants, the seropositivity rates at 3, 6, 9, 12, 15, and 18 months of age were 90.5%, 84.4%, 62.6%, 36.1%, 13.6%, and 6.1%, respectively, with corresponding patient numbers of 133, 124, 92, 53, 20, and 9, respectively (Figure 1).

DISCUSSION

Because the severity of illness increases with age and because of the crucial role of children in HAV transmission, children should be the main target of immunization strategies aimed at lowering disease incidence and avoiding creating a pool of susceptible older subjects.2,5 Indeed, only the inclu-
passive immunity. The current study demonstrates that 93.9% of the infants born in Turkey have passively acquired antibodies against HAV, because of high rates of maternal HAV seropositivity, which may be preferred even though the remaining antibodies at the last resort, at 18 months of age in the routine childhood immunization program. It is concluded that if children in Turkey are to be vaccinated against hepatitis A, the first dose may possibly be added to the immunization schedule after 12 months of age combined with varicella or MMR vaccine or alone, otherwise, at the last resort, at 18 months of age in the routine child immunization schedule when the maternal antibodies disappear.

In light of these data that 36.1% of infants at age 12 months and only 6.1% at 18 months had remaining maternal antibodies, two thirds of the infants over the age of 12 months are at high risk of acquiring HAV infection in Turkey, considered to be an endemic region for hepatitis A.

We consider that vaccination beginning after 12 months may be preferred even though the remaining antibodies at the first vaccination time (12–18 months of age) may render an ineffective response; the last-dose vaccination (18 months of age or over) will be administered after the disappearance of any potentially interfering maternal antibodies and will provide satisfactory protection against HAV in endemic regions like Turkey. It will be useful to develop and test a new clinical study of mass immunization along these modalities.

FIGURE 1. Prevalence of anti-HAV by age among Turkish children in Adana.

REFERENCES


