IMMUNOGENICITY OF CUBAN HEPATITIS B VACCINE IN IRANIAN CHILDREN

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Background – To determine the response of Iranian children to Cuban hepatitis B vaccine.

Methods – A total of 538 children who had received three doses of Cuban hepatitis B vaccine were classified into 4 groups of 6, 12, 24, and 36 months after the third dose of vaccination. Every group was subdivided into nonresponders, hyporesponders, and good-responders.

Results – Of 538 vaccinees, 240 (44.6%) were females. In Group I, of 230 (42.75%) vaccinees, 25 (10.9%) were nonresponders, 51 (22.1%) hyporesponders, and 154 (67%) good-responders. In Group II, consisting of 98 (18.2%), 18 (18.4%) were nonresponders, 38 (38.8%) hyporesponders, and 42 (42.6%) good-responders. In Group III, of 100 (18.58%) vaccinees, 8(8%) were nonresponders, 32 (32%) hyporesponders, and 60 (60%) good-responders. In Group IV, with 110 (20.4%) vaccinees, 31 (28.1%) were nonresponders, 30 (27.3%) hyporesponders, and 49 (44.5%) good-responders.

Conclusion – Of the total 538 vaccinees, 305 (56.7%) were good-responders, 149 (27.7%) hyporesponders, and 84 (15.6%) nonresponders. Both rates of vaccinees and concentration of anti-HBs in the good-responders were low and the number of hyporesponders and nonresponders were high.

Keywords • anti-HBs • hepatitis B • vaccine

Introduction

In Iran, hepatitis B infection has an intermediate endemicity and transmission patterns of hepatitis B virus (HBV) infection are mixed. The disease occurs at all ages and 3–8% of the population are chronic carriers. The most effective way to prevent HBV infection is vaccination against HBV during the first year of life. Previous studies have shown that >95% of healthy infants and children who were given non-Cuban vaccines formed protective amounts of antibody to HBsAg.

In Iran, Cuban hepatitis B vaccine became available approximately in 1994 and mass vaccination of neonates and children was incorporated in the national vaccination scheme.

However, the impact of such a vaccine in Iranian children is unknown. The aim of present study was to determine the concentration of antibody titers to Cuban HBV vaccine in Iranian children.

Patients and Methods

A descriptive and prospective study was conducted from December 30, 2000 to June 30, 2001, to evaluate immune response to the three doses of recombinant Cuban HBV vaccine administered to infants in Tehran. Postvaccinated children with different socioeconomic levels and varied ages came from different areas of Tehran. All of the children were normal on physical examination, and they were immunized with 10 μg recombinant Cuban HB vaccine (Herberbiovac HB, Heber Biotec, Havana, Cuba) in accordance with the national vaccination scheme in Iran (at birth, 1 1/2, and 9 months of age). After obtaining
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the informed consent from one of the parents, 3 mL blood samples were taken from children to determine anti-HBs (hepatitis B surface) and anti-HBc (hepatitis B core) concentrations. Prior to serological testing, sera were stored at –20°C.

All children were classified into 4 groups on the basis of their age: 6, 12, 24, and 36 months after their last vaccination. Each group was subdivided into three smaller groups, nonresponders (<10 mIU/mL), hyporesponders (> 10 < 100 mIU/mL), and good-responders (≥100 mIU/mL). Maternal hepatitis B virus marker status of all eligible children were unknown.

Detection of HBV markers

Anti-HBs and anti-HBc were detected by enzyme-linked immunosorbent assay (ELISA), using commercial kits (RADIM, Roma, Italy). Anti-HBs was quantitatively measured according to manufacturer recommendation and expressed as mIU/mL. According to Hollinger et al., anti-HBc was qualitatively measured and expressed as positive or negative.

Statistical analysis

Differences in variables were analyzed by Chi-square test and Student’s t-test. P values less than 0.05 were considered significant.

Results

A total of 538 children were evaluated for determination of anti-HBs. The minimum age of vaccinees was 15 months and the maximum 45 months; 240 (44.6%) were females and 298 (55.4%) males. Table 1 shows Group I with 230 (42.75%) children, which is the largest in number. The number of both sexes in all groups were approximately equal. The anti-HBs titer in good-responders in both genders were equal and no significant difference was observed (p = 0.63).

Group II, with 98 (18.2%) children, in which the mean ± SD concentration of anti-HBs was higher in males (p = 0.01). In Group III, there were 100 (18.85%) children. The response of females was higher than that in males (p = 0.01). In Group IV, with 110 (20.4%) children, there were no significant differences in mean titers of anti-HBs between female and male responders (p = 0.33).

In general, the total number of good-responders was 305 (56.7%), 143 (47%) of which were females and 162 (53%) males, with a total anti-HBs concentration of 393 ± 273 and 409 ± 294 mIU/mL (mean ± SD), respectively, and in 149 (27.7%) hyporesponders, 67 (45%) were females and 82 (55%) males with a total anti-HBs concentration of 59 ± 22 and 52 ± 22, respectively.
and also of 84 (15.6%) nonresponders, 34 (40.5%) were females and 50 (59.9%) males.

Discussion

Numerous studies of various populations have been conducted over the past several years to investigate the protection provided by European HB vaccine.9 – 11 Immunization of healthy adults and neonates with HB vaccine resulted in a long-lasting protective immunity in the vast majority of the vaccinees. A small proportion of vaccinated normal subjects failed to respond and did not develop good-response of anti-HBs levels.12 – 13 The rate of unresponsiveness has been variable in different studies.14

The number of children in all nonresponder groups were different. The number of nonresponders in Group I, in comparison with other groups, had no significant correlation with postvaccination age. It seemed that all vaccinees in four groups were originally nonresponders.

The number of hyporesponder subjects in the first group was more than in the other groups. Therefore, antibody concentration was not related to postvaccination age and, perhaps, all vaccinees in four groups were originally hyporesponders. Also, the number of good-responder children in all groups varied. The percentage of Groups I and III were approximately similar, whereas, the number of Group III was more than Group II and the number of vaccinees in Groups II and IV were similar. So, postvaccination age did not influence the number of responders. Therefore, it seems that vaccinees in all groups were originally good-responders.

The results of present study suggest that immunization with Cuban hepatitis B vaccine produced good immunity in 305 (56.7%) children. should one at here to the recommendation of the international group7 then both non- and hyporesponders, 233 (43.3%) have to be immunized again.

Davilla et al15 demonstrated the persistence of anti-HBs in 97.1% of children who were immunized with European HB vaccine (Engerix-B) five years ago in 97.1% of subjects, and concentration of anti-HBs in vaccinees of good-responders. In comparison with present study, anti-HBs persistence in Group I was demonstrated in 154 (67%) (mean anti-HBs titer = 447.8, 100 – 1,406 mIU/mL) and 49 (44.5%) of 110 children in Group IV (mean anti-HBs titer = 461.6, 100 – 1,123 mIU/mL). As noted, the percentage of vaccinees in good-responders was low. Hadler et al16 believed that the higher the level of anti-HBs the longer the duration of persistence of antibody. Another study based on the decline of antibody titers 4 to 5 years after immunization with recombinant vaccine (Engerix-B), has recommended that persons with peak titers < 500 mIU/mL should receive another dose immediately; those with titers of 500 to 4,000 mIU/mL should receive a booster dose at 5 years; and those with anti-HBs titers greater than 4,000 mIU/mL should not receive a booster dose for at least 10 years.17 On the other hand, Amani et al18 reported 31% of Iranian infants who were immunized with Engerix-B vaccine were high-responders (1,000 – 10,000 mIU/mL; mean ± SD titer = 5,654 ± 3,080) and 15.6% intermediate-responders (100 – 1,000 mIU/mL; mean ± SD titer = 482 ± 279).

Concentration of anti-HBs in the majority of good-responders in all groups were approximately 423.8 ± 313.26 mIU/mL (range, 100 – 1,406 mIU/mL). Therefore, the decline of concentration of anti-HBs must be expected in future or as recommended by another study,17 majority of Iranian vaccinees should receive a booster dose of vaccine.

The persistence of anti-HBs depends on the peak antibody level achieved after three doses.16, 19 Unresponsiveness to HBsAg has been attributed to a number of environmental and genetic factors, the most important ones being the haplotype of HLA antigens and immunological tolerance.20 A variety of HLA classes I and II antigens have been reported to be associated with unresponsiveness to HBsAg in different ethnic populations.21 In this study both rates of vaccinees and concentration of anti-HBs in good-responders were low and the rate of hyporesponders and nonresponders were high. This suggests that anti-HBs titer should be measured in all Iranian vaccinees after the third dose of vaccination by Cuban HB vaccine so that the health authorities can decide which scheme, booster dose, or national vaccination to implement.

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References