ORIGINAL ARTICLE

The Efficacy of Hepatitis B Vaccination among School Age Children in Southern Iran

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Abstract

Background: Primary prevention by vaccination to increase herd immunity remains the main thrust in the control of hepatitis B virus (HBV) infection and many countries such as Islamic Republic of Iran have incorporated HBV vaccination into their national expanded program of immunization. This study was performed to determine the vaccine efficacy of hepatitis B infection between vaccinated and non-vaccinated school-aged children.

Methods: Three hundred and ninety four students aged 6 to 8 years who received the hepatitis vaccine in the infancy and 314 students aged 9 to 10 years who did not receive it in Sepidan, southern Iran were enrolled. We also determined the titer of anti HBs Ab in the vaccinated students.

Results: Two students (0.5 %) were HBV infected (positive HBC Ab) and none were a chronic carrier. Two hundred and forty nine students (63.2%) had anti HBs titer greater than 10 IU/ml. One hundred and seventeen students (30%) had anti HBs titer between 1 and 10 IU/ml and only 28 children had anti HBs titer less than 1 IU/ml. Five (1.6%) were HBV infected (positive HBc Ab) and 2 (0.6%) were chronic carriers (positive HBs Ag). The efficacy of the vaccine 6-8 years after vaccination was 67.9 %(95 CI 78-92).

Conclusion: Our results showed that similar to other studies, vaccination could not reduce the infection rate but had a significant effect on the reduction of chronic infection and carrier state, emphasizing on the role of vaccination in the control of HBV infection in an endemic region.

Keywords: Hepatitis B; Vaccination; Efficacy; Southern Iran

Introduction

Hepatitis B virus (HBV) infection is a one of the most important global health problems, infecting 2 billion people worldwide, of whom 350 million are suffering from chronic HBV infection. HBV infections result in 500,000 to 1.2 million deaths per year induced by chronic hepatitis, cirrhosis, and hepatocellular carcinoma, the last accounting for 320,000 deaths per year and being the 10th leading cause of death worldwide.[1] According to the available data in Iran, 2-3% of the population are infected with this virus and approximately 350,000 individuals have chronic hepatitis, cirrhosis or hepatocellular carcinoma.[2,3] These figures emphasize the burden this infection afflicts so that World Health Organization recommended universal neonatal vaccination to be carried out in all countries to control the disease progression and reduce the complications.

Hepatitis B vaccination is the simplest and most effective intervention to prevent mortality in adults. Although safe and effective vaccination has been available since 1980, universal vaccination is still postponed in many countries. Only 130 of 216 countries and territories had introduced HBV vaccine by the beginning of 2001.[4] The reason behind inhibition or weakness of social commitment to preventive vaccines is lack of public awareness and cost of vaccination. In Iran, the vaccination program to control the

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disease started in March, 1992, and all of the newborns were vaccinated. The short and intermediate term goals of vaccination are to prevent the chronic and acute symptomatic infection and to reduce healthcare costs. The long term goals are prevention of the chronic complications, such as cirrhosis, hepatocellular carcinoma and death.

The potential impact of vaccination programs and vaccination efficacy has been evaluated in many countries. Ayoola reported a decrease in the carriage rate from 8.8% before introducing vaccination to 0.9% after it in a hyperendemic region in south western Saudi Arabia in children aged less than 1 year.[5] Another report from Taiwan showed that among 1200 children who had received HBV vaccination in infancy, protective antibodies could be found in 71.1% at age 7 and 37.4% at age 12.[6]

In order to get some information about the efficacy of the immunization program against HBV in Iran, a serological survey was performed from March to April 2002 among the school children in Sepidan born from 1990 to 1994. The objective was to evaluate the frequency of the HBS Ag positivity and to measure the humoral immunity by anti-HBs and Anti-HBc antibody titration.

Materials and Methods

The trial was undertaken in March 2002 in Sepidan, Fars province, southern Iran. This town has a well defined population with a low rate of in and out migration. All of the families had health records in one of the two health centers of the town. All vaccinations in the town were done in these two centers. HBV vaccination has been afforded completely since March 1994 in this town so that children aged less than 8 years at the time of the study had completed their vaccination according to the records. The study included 726 primary school children born from 1990 to 1994 and lived in Sepidan. All children presented a written consent from their parents. All underwent routine physical examination and the basic demographic and health information were obtained from their health records including identity: Sure name, first name, sex, date of birth, school; medical history of the children and their families, especially HBs antigen (HBs Ag) carriage in the mother, if mentioned in the health records; vaccination status provided from the health records in the local health offices of Sepidan. All children in the city had precise health records in the local health offices about vaccination status, previous diseases, growth and development chart and other related data.

Any child with chronic disease such as diabetes mellitus, congenital heart disease, chronic renal failure, thalassemia major or any hematologic disease leading to blood transfusion was excluded from the study. Due to the starting time of immunization program against hepatitis B in Iran, some of the children (356) were unvaccinated and the others (395) were vaccinated at time of the study.

The vaccine used in this area was ENGERIX-B®-Hepatitis B Vaccine (Recombinant), manufactured by GlaxoSmithKline Biologicals, Rixensart, Belgium, and distributed by GlaxoSmithKline, Research Triangle Park, NC 27). The vaccination was according to the national schedule program (three or four doses injection).

Blood samples were drawn from all of the students by venepuncture, using appropriate aseptic precautions. The sera were separated and stored at -20°C before being tested. Each sample was first tested for anti-HBc antibodies (HBV core). These antibodies indicate any past or current HBV infections. Also all samples were tested for anti-HBs antibody titers in order to identify the children with a vaccinated profile and to measure their immune protection. Anti-HBc positive samples were tested for HBs Ag to evaluate the probable chronic carriage of the virus. HBs Ab and HBc Ab levels were measured by Radim kit with cat. KHB31WB through immunoenzymometric assay (IEMA) and Radim kit with cat. KHB2EWB through competitive enzyme immunoassay (EIA), respectively.

The protective level concentration of serum anti HBs Ag was considered >10 mIU/ml.[7] Infection was defined by the presence of anti-HBc. If infection was found in a person vaccinated, it was considered as a breakthrough infection. All the data were fed into an access data bank. SPSS version 13 (Chicago, IL, USA) was used for the analysis of the data.

Results

The study recruited 708 children, of whom 55.6% (394) were vaccinated at birth, and 44.4 %(314) were unvaccinated. The mean age was 7.5 years (range: 6.2–8.8 years) for the vaccinated and 9.3 years (range: 8.2-10.4 years) for the unvaccinated group. The three injections schedule (M0–M1–M6) was applied for vaccination.

Effective vaccine protection levels of anti HBs level >10 mIU/ml; anti HBs level 1-10 mIU/ml; and anti HBs level <1 mIU/ml were noticed in 63.2%, 29.7% and 7.1% of the vaccinated children. Possible ineffective immunization (absence of anti-HBs antibodies, or anti-HBs titer lower than 10 IU/L) was found in 36.2% of the children (143 out of 394) and only 0.5 % (2 out of 394) had Anti-HBc antibody and developed breakthrough infection. None of them were HBs Ag positive. One of Anti-HBc positive students had a protective level of anti-HBs antibodies and the other one had a serum level smaller than 10 IU/l.

According to the history and health records, 314 children did not have immunization against hepatitis B virus. Combining the tests, we could define 3 different profiles of 1) no infection in unvaccinated students was 98.4% (309 out of 314); 2) infected with virus: 1.6 % (5 out of 314) and 3) among the infected students 2 had positive HBS Ag (0.6%) and they were labeled as chronic carrier.

Among the 394 vaccinated children, 145 (36.8%) had a non protective anti-HBs antibody titer, that was lower than 10 IU/l, whereas 249 (63.2%) had a protective titer. The vaccine was found to be efficient in this area. To determine the vaccine efficiency, we used the following formula:

$$\text{Vaccine efficiency} = \frac{\text{Prevalence in unvaccinated} - \text{Prevalence in vaccinated}}{\text{Prevalence in unvaccinated}} * 100$$

Thus vaccine efficacy in this area was defined as 67.9% according to the findings of serologic evidence of infection among vaccinated and unvaccinated children (Table 1).

Discussion

Global neonatal vaccination is considered to be the most effective strategy in prevention of hepatitis B. Long term experiences in several countries have revealed an efficacy between 20 to 93%, depending on the time of checking anti-HBs antibody titer.[8-13] Iran is one of first countries in the middle east region that implemented this vaccination strategy in its routine free neonatal vaccination program in 1992, so it seems that its effects on the control of hepatitis B complications and chronicity to appear in the years following. It should be emphasized that the Middle East countries including Iran have a moderate prevalence of hepatitis B. In Iran, the prevalence of hepatitis B varies according to the geographical areas, that is as low as 1.07% in Shiraz and as high as 8.96% in Toiserkan.[14]

Of the 394 vaccinated children in this study, nearly 63.1% had evidence of post-vaccine protective immunity against HBV with an acceptable anti HBS titer above 10 IU/ml even more than seven years after vaccination. Our findings are similar to the results of the studies in other countries that found the range of 48 to 79% for a significant anti HBs antibody level after 5-7 years follow up.[11,15] According to these findings, the need for a booster even after 5 years after vaccination has been under question. Probably the prior response with the antibody titer > 10 mIU/mL provides protection. Also we should notice that the level of 10 IU/l for anti-HBs antibody has been criticized as a significant threshold for long term protective immunity. This threshold was originally applied in order to validate passive immunity following immunoglobulin injection and thus corresponds to a safety threshold, not taking into account vaccination as an active phenomenon.[16]

In this study, the prevalence of breakthrough HBV infection, indicated as anti-HBc reactivity, was about 0.5% in vaccinated children in comparison to 1.6% rate of HBV infection in unvaccinated children in Sepidan. However, there was no massive and significant reduction in hepatitis B prevalence among the children due to the application of the neonatal immunization program. We, of course, detected no serologic evidence of chronic infection in the vaccinated group but found 2 children (0.6%) in the unvaccinated group with positive HBs Ag. It can therefore be said that the vaccine has protective effects against chronicity. In other words, it implies that even when vaccination fails to prevent the infection; it signifi-

Table 1: Health state versus infection and antibody production among vaccinated and unvaccinated children

Status	Uninfected children No. (%)	Presence of anti-HBc antibodies No. (%)	HBs Ag positive in Anti HBc positive patients No. (%)
Vaccinated children (394)	392 (99.5)	2 (0.5)	None
Unvaccinated children (314)	309 (98.4)	5 (1.6)	2 (0.6)

cantly reduces the rate of persistent infection and probably the risk of hepatocellular carcinoma and cirrhosis in the community. Our findings are compatible with those of other surveys.[17,18]

Longer follow-ups are needed to assess the precise role of transient infection and carriage in raising the risk of liver damage and hepatocellular carcinoma. Also continued follow-ups are required to assess the necessity of a booster during adolescence.

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