ORIGINAL ARTICLE

Seroprotection after hepatitis B vaccination in children aged 1 to 15 years in central province of Iran, Semnan

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Key words

Hepatits B antibody • Vaccination • Children

Summary

Introduction. *There are controversies over the long-term persistence of post vaccination immunity to hepatitis B and the need for booster doses of the vaccine. The aim of this study was to verify antibody levels of antibody against hepatitis B virus surface antigen (anti-HBs) in children aged 1 to 15 years who received vaccination against hepatitis B in the central province of Iran, Semnan.*
Materials and methods. *We performed a seroepidemiological survey (n = 210) of anti-HBs in 2011 in the central province of Iran, Semnan using enzyme-linked immunosorbent assay (ELISA). The levels of anti-HBs < 10 mIU/mL were considered to be negative and samples showing an anti-HBs titer ≥ 10 mIU/mL was considered protective.*
Results. *Protective antibody levels were detected in 88% of the children less than 5 year after vaccination, decreased to 78% between 5 to 10 years after vaccination, and further declined to 74% in 10 years after vaccination, respectively.*
Conclusion. *The vaccination program has been proven effective in Semnan and immunological protection against hepatitis B infection was found in the majority of children even more than 10 years after being vaccinated.*

Introduction

The vaccine against hepatitis B virus (HBV) is included in the routine immunization schedule for children in most countries with the ultimate goal of reducing the prevalence of chronic hepatitis B carriers, as well as preventing the occurrence of acute hepatitis B [1]. Although long-term reduction of chronic HBV after hepatitis B vaccination has been reported [2], decreasing the levels of antibody against hepatitis B surface antigen (anti-HBs) over the time can be alarming [3].
Hepatitis B virus (HBV) prevalence has decreased dramatically in Iranian population since 1993 when the mass vaccination program was started. The geographic distribution of HBV infection in Iran showed heterogeneous patterns of HBV prevalence from the highest prevalence rates of more than 3% in northeastern region of our country to less than 2% in central and western regions of Iran [4].
Several hundred million doses of plasma-derived HB vaccines are produced in the Republic of Korea, China, Vietnam, Myanmar, India, Indonesia, Iran and Mongolia [5, 6]. Engerix-B® (SmithKline Beecham, 1992) and Recombivax HB® (Merck & Co.) are considered as the two major yeast-derived hepatitis B vaccines that are licensed in most countries [5].
There are controversies over the long-term persistence of post vaccination immunity to HBV and the need for booster doses of the vaccine [7].
The aim of this study was to verify antibody levels of anti-HBs antibodies in children aged 1 to 15 years who received vaccination against HBV in accordance with the standard method in the central province of Iran, Semnan.

Materials and methods

In this cross-sectional study, all children between ages of 1 and 15 years residing in Semnan, Iran in Amiralmoemenin hospital were tested for anti-HBs during 2009.
Informed consent was obtained from all children and/or their parents or guardians who agreed to participate in the study. The questionnaire was completed about the child's general data (e.g., family history of contact with HBV and knowledge about the possibility for the child to have any immunosuppressive disease, such as HIV, type 1 diabetes mellitus, or chronic renal failure).
We included immunocompetent participants without history of previous HBV infection.The participants were excluded from the study on the basis of
the following criteria: (a) were not screened for serologic markers of HBV infection (HBsAg) before vaccination; (b) born to HBsAg carrier mothers; (c) had predisposing factors for any immunosuppressive disease such as HIV positive.
After blood sample collections, plasma samples were collected and tested for anti-HBs using enzyme-linked immunosorbent assay (ELISA)(Delaware Biotech Inc.

Dover, DE, USA) following the manufacturer's protocol.
The antigen and antibody formed a sandwich complex with the conjugated antibodies with the peroxidase (horseradish peroxidase) and the enzymatic activity was detected with the specific chromogen/substrate 3,3',5,5' -tetramethylbenzidine (TMB).
The TMB levels were quantified at 450 nm and the concentrations of the anti-HBs were determined on the standard curve. The levels of anti-HBs < 10 mIU/mL were considered to be negative and samples showing an anti-HBs titer ≥ 10 mIU/mL was considered protective [1].
The Chi-square test and Fisher's exact test were used with the SPSS 16 Package program (Chicago, IL, USA). Data were presented as mean ± SD or, when indicated, as an absolute number and percentage. Student's t-test was used for statistical analysis to compare the means between the two groups.

Results

A total of 210 children were participated in this study. Totally, 67 cases (32%) were under 5 years, 67 (32%) were between 5 to 9 years old and 76 (36%) were more than 10 years. The male to female ratio was 1. Distribution of anti-HBs levels according to sex, age and duration after vaccination are shown in Table 1. Eighty four cases (80%) in the female group and 82 cases (78%) in the male group had protective levels of anti-HBs > 10 mIU/mL, with no statistically significant difference in anti-HBs positivity and genders (p = 0.735). Anti-HBs positivity was seen in 87% of cases less than 5 years, 81% of cases between 5 and 10 years and 71% of cases more than 10 years.
Protective antibody levels were detected in 88% of the children less than 5 year after vaccination, decreased to 78% between 5 to 10 years after vaccination, and further declined to 74% in 10 years after vaccination, respectively.

Discussion

The immunity derived from the HBV vaccine was assessed by measuring the antibody in 210 children who were vaccinated in a routine vaccination program in central province of Iran, Semnan.
In our study, among 210 cases, 166 children (79%) had antibodies levels ≥ 10 mIU/mL. Protective antibody levels were detected in 88% of the children less than 5 year after vaccination, 78% in cases between 5 to 10 years after vaccination, and 74% in cases at 10 years after vaccination. Generally, 3-30% of vaccinated individuals lost their protective anti-HBs titres five years after the hepatitis B vaccination [8]. Long-term follow-up studies demonstrated that antibodies might become negative in 15-50% among the vaccine responders within 5 to 10 years [9, 10].
According to several studies among healthy children who had received a complete hepatitis B immunization program, the protective titer of anti-HBs antibody > 5 years after the last dose were seen in 50-100% of individuals [7, 11-13]. It has been reported that the variability in the anti-HBs antibody might be due to is the type of vaccine used, the amount of antigen delivered and the population immunized [14-17].
The HBV vaccination started in infants in two provinces (Zanjan and Semnan) in 1989, and since 1993 the vaccination was introduced in the expanded program on immunization in Iran. After implementation of HBV vaccination in our country, the coverage has reached an appropriate level 94% in 2005 compare with 62% in 1993 [18].
Jafarzadeh et al. found that 81.5% of children had protective levels of antibody [19] at five years after primary hepatitis B immunization while 47.9% of children had protective levels of antibody 10 years after primary vaccination [20].
In Aghakhani et al. study, protective antibody levels were detected in 65% of children one year after vaccination, which declined significantly over time to 24% in 15 years after vaccination [21].

Tab. I. Distribution of anti-HBs levels according to sex, age and duration after vaccination.

		Anti-HBs ≥ 10 mIU/mL		Anti-HBs < 10 mIU/mL		Total
		N	%	N	%	N
Sex	Male	82	78	23	22	105
	Female	84	80	21	20	105
Age	< 5 years	58	87	9	13	67
	5-10 years	54	81	13	19	67
	≥ 10 years	54	71	22	29	76
Duration after vaccination	< 5 years	62	87	9	13	71
	5-10 years	54	78	15	22	69
	≥ 10 years	52	74	18	26	70

In Gilca et al. study, 88.2%, 86.4% and 76.7% of cases had a titer ≥ 10 IU/L after 5, 10 and 15 years post-vaccination [13].

In our study similar to other studies, no differences were observed between sex, age and anti-HBs titer following the vaccination [8, 21].

There are controversies over the long-term persistence of post vaccination immunity to hepatitis B. According to meta-analysis, protection which was provided by three or four doses of monovalent HB vaccine persists for at least two decades in the great majority of immunocompetent individuals and 3 doses of HB vaccine ensure a good protection against infection for up to 20 years [2], while some studies recommend a need for booster dose of vaccine in our country [20, 21]. Although a booster dose increases substantially anti-HBs titers, the clinical relevance of such an increase remains unknown.

In conclusion, the vaccination program has been proven effective in Semnan and immunological protection against HBV infection was found in the majority of children even more than 10 years after being vaccinated.

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