Original article

Prevalence of anti hepatitis B surface antibody among children in Ahvaz, Iran, five years after vaccination

Ahmad Shamsizadeh, MD[1,2]*, Manoochehr Makvandi, PhD[1], Gholamali Shoshtari, MD[2]

[1]*Jundishapur Infectious and Tropical Diseases Research Centre, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran*
[2]*Abuzar Children's Hospital, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran*

How to cite this article:
Shamsizadeh A, Makvandi M, Shoshtari G. Prevalence of anti hepatitis B surface antibody among children in Ahvaz, Iran, five years after vaccination. Jundishapur J Microbiol. 2011; 4(2): 49-54.

Received: June 2010 **Accepted:** September 2010

Abstract

Introduction and objective: The public vaccination program of hepatitis B virus was started in 1993 in Iran, and all children received three doses of hepatitis B vaccine in 0, 2 and 6 months of age routinely. The objective of this study was to determine the prevalence of antibody to hepatitis B surface (anti-HBs) five years after vaccination.

Materials and methods: In a cross-sectional study, anti-HBs was determined in six year old girl and boy students of selected elementary schools of Ahvaz with enzyme-linked immunosorbent assay (ELISA) method in 2006. All children had received complete course of hepatitis B vaccination in the first year of age.

Results: Four hundred and twenty seven students (223 girls and 204 boys) were enrolled in the study. Of them, 75.4% were anti-HBs positive (>10 mIU/mL). The prevalence of anti-HBs was statistically different between males and females (P=0.02).

Conclusion: The study detected anti-HBs in 75.4% of children and because of possibility of presence of anamnestic responses in seronegative subjects, a booster dose of vaccine is not necessary at least five years after primary vaccination. Further studies are needed to evaluate hepatitis B immunity in older age groups.

Keywords: Anti-HBs; Children; Vaccination; Iran

*Address for correspondence:
Dr. Ahmad Shamsizadeh, Jundishapur Infectious and Tropical Diseases Research Centre, Ahvaz Jundishapur University of Medical Sciences, Ahvaz, Iran; Tel: +98611 2215365;
Fax: +98611 444711, Shamsizadeh@ajums.ac.ir

Introduction

It is estimated that about one third of the world's population has been infected with hepatitis B virus (HBV). Of which, 350 million are believed to be chronic carriers [1]. Approximately one million deaths each year are attributable to HBV complications including hepatocellular carcinoma, liver cirrhosis, chronic and acute hepatitis [2]. Active immunization is the most effective way to decrease the rate of HBV infection. Vaccination against HBV has started since 1982 in many countries, at first as a plasma-derived vaccine and from 1984 onwards as a recombinant one [3].

In Iran, hepatitis B immunization program was started in 1993 by a recombinant vaccine (Cuban). The vaccination schedule consists of three doses of 0, 2 and 6 months intramuscularly in the deltoid or thigh areas of infants. There are a lot of studies about immunogenicity of hepatitis B vaccine from different areas of the world [4-9]. Some studies in Iran showed persistence of antibody to hepatitis B surface Antigen (anti-HBs) in 47-80% of persons 10-16 years after vaccination [10-12]. This study was conducted to evaluate the persistence of anti-HBs in children five years after primary vaccination in Ahvaz, south-west of Iran.

Materials and methods

In a cross-sectional descriptive study, students of first grade of elementary schools of Ahvaz were tested for anti-HBs. The study was performed in several stages and the last sampling terminated in December 2006. The schools were selected randomly from four educational districts of Ahvaz (two girls' elementary schools and two boys' elementary schools from each district). In each school, about half of six years students enrolled in the study. Our plan was to obtain samples from boys and girls equally, but because of lack of assistance of some schools' managers and resistance of some students to sampling, we could not carry out our plan. Informed consent to take sample was obtained from students' parents.

All students had received complete course of hepatitis B vaccination by Cuban vaccine five years ago (in the first year of age). After checking of students' vaccination card, 5ml of blood was obtained from each subject. Sera were prepared and stored at -20ºC, coded and further tested in the virology laboratory of Ahvaz Medical School. At the end of the study, anti-HBs was detected using a commercial immunoenzymatic method (anti-HB kit, Radim, Italy) according to the manufacturer's instructions.

The statistical analysis was performed using SPSS (Version 13) software. Chi-squared test was done, and a p-value of <0.05 was considered statistically significant. The study was approved by the appropriate ethic committee.

Results

Four hundred and twenty seven six year old students were enrolled in the study. There were 223(52.2%) females and 204(47.8%) males. Generally, according to anti-HBs levels, all hepatitis B vaccine recipients were divided into three groups: 1) non-responders have peak anti-HBs levels of $\leq$ 10mIU/ml, 2) low responders have peak anti-HBs levels of 10-100mIU/ml, and 3) good responders have peak anti-HBs levels of $\geq$100mIU/ml [13].

There was not any significant statistical difference between females and males in low responders group, but the difference between females and males in good responders group was statistically significant (P=0.036). Table 1 shows the levels of anti-HBs in females and males. Since the protective level concentration of

anti-HBs considers >10mIU/ml [13,14], 322(75.4%) of children were seropositive and 105(24.6%) were seronegative (Table 2).

Table 1: Anti-HBs levels in female and male

Sex	Anti-HBs levels			Total
	> 100 IU/ml	10-100 IU/ml	<10 IU/ml	
Female	82 (36.8%)	94 (43.5%)	44 (19.7%)	223 (100%)
Male	59 (28.9%)	84 (41.2%)	61 (29.9%)	204 (100%)
Total	141 (33.1%)	181 (42.3%)	105 (24.6%)	427 (100%)

Table 2: Prevalence of anti-HBs in male and female

Sex	Positive	Negative	Total
Female	179 (80.3 %)	44 (19.7%)	223 (47.8%)
Male	143 (70.1 %)	61 (29.9%)	204 (52.2%)
Total	322 (75.4 %)	105 (24.6%)	427 (100%)

There was a statistically significant difference in the prevalence of anti-HBs between females and males. Female subjects had a better antibody response than males (P=0.02)

Discussion

In this study, 75.4% of children aged six years were anti-HBs positive five years after HBV vaccination. The persistence of antibody against HBV after vaccination has been determined by many studies worldwide. Most of the studies are from southwest of Asia, an endemic area of hepatitis B infection. In some studies from Taiwan, the rate of anti-HBs 7-20 years after vaccination ranged from 50.5-77% [15-18]. In these studies, a "waning-off" effect of anti-HBs seropositivity acquired from the hepatitis B vaccination program has been observed.

In one study on Alaskan natives, 85% of study subjects were anti-HBs positive 16 years after primary hepatitis B vaccination [19]. In Australia, immunity to hepatitis A and B antibodies six years after vaccination of adolescents (aged 12-15 years) with a combined hepatitis A and B (HAB) vaccine was assessed. About 85% of subjects had anti-HBs concentration > or = 10mIU/ml [20]. In a similar study to ours in Turkey, 87% of children had protective levels of anti-HBs (≥10mIU/ml) five years after vaccination [21]. In a study performed in Saudi Arabia, a total of 527 children (aged 4-14 years) were tested for anti-HB and overall, 74% of them were seropositive. All of children had received complete course of vaccination in the first year of age [22].

In a study carried out in Rafsanjan, Iran, blood samples were collected from 146 healthy 10-11 year old children who received primary course of hepatitis B vaccination at 0, 1.5, 9 months of age. Anti-HBs were detected in 47.9% of children [10]. In another study in health care workers of Oil Company Hospital, Tehran, Iran, 80.7% of subjects were anti-HBs positive 16 years after vaccination [12]. The results of most studies on immionogenicity of

HBV have shown: that despite low anti-HBs concentration, HBV infections (as measured by the presence of markers of infection such as HBs Ag or anti-HBc) are uncommon in persons known to have responded to primary vaccine series [23-25].

Some studies have shown presence of an anamnestic response in persons with low or undetectable anti-HBs levels following challenge with HB vaccine. In the other hand, production of anti- HBs in circulating B-cells confirmed the presence of immune memory among vaccines [26]. In most studies after injection of a dose of hepatitis B vaccine to seronegative vaccinated subjects, the titer of anti-HBs increased dramatically [15,27,28].

In our study, females showed a higher antibody response than males. However in some studies, male was associated with persistence of higher anti-HBs levels after vaccination [19-22]. At least in two studies, anti-HBs titer was significantly higher in females than males [12,29]. Our study was limited because we could not administer a booster dose of HB vaccine to seronegative participant to evaluate the level of anti-HBs after booster vaccination.

Conclusion

In this study 75.4% of children were seropositive five years after hepatitis B vaccination. However, lack of cold chain in preservation of vaccine, poor vaccine administration technique may have a role in decreased response to vaccination. But, as studies have shown, because of the presence of immune memory, most of seronegative children may be immune against hepatitis B and booster vaccine is not necessary after primary vaccination of hepatitis B. Further studies are needed to evaluate efficacy of primary hepatitis B vaccination in the older age groups.

Acknowledgements

We thank Dr. Shoshtari for using of his thesis project design and are grateful to all the participant children and their families, whose participation allowed to conduct the study. We also thank Mrs. Shohreh Nabidavoodi for the preparation of the manuscript.

References

1) Su FH, Chen JP, Cheng SH, Sung KY, Jeng JJ, Chu FY. Waning off effect of serum hepatitis B surface antibody amongst Taiwanese university students. 18 years post implementation of Taiwan's national hepatitis B vaccination programme. *J Viral Hepat*. 2008; 15(1): 14-9.
2) Su FH, Cheng SH, Li CY, *et al*. Hepatitis B seroprevalence and anamnestic response amongst Taiwanese young adults with full vaccination in infancy, 20 years subsequent to national hepatitis B vaccination. *Vaccine*. 2007; 25(47): 8085-90.
3) Giambi C, Bella A, Barale A, *et al*. A cohort study to evaluate persistence of hepatitis B immunogenicity after administration of hexavalent vaccines. *BMC Infect Dis*. 2008; 8: 100.
4) Poovorawan Y, Chongsrisawat V, Theamboonlers A, Book H, Leyssen M, Jacquet JM. Persistence of antibodies and immune memory to hepatitis B vaccine 20 years after infant vaccination in Thailand. *Vaccine*. 2010; 28(3): 730-6.
5) Bialek SR, Bower WA, Novak R, *et al*. Persistence of protection against hepatitis B virus infection among adolescents vaccinated with recombinant hepatitis B vaccine beginning at birth: a 15 year follow up study. *Pediatr Infect Dis J*. 2008; 27(10): 881-5.
6) McMahon BJ, Dentinger CM, Bruden D, *et al*. antibody levels and protection after hepatitis B vaccine: results of a 22 year follow up study and response to a booster dose. *J Infect Dis*. 2009; 200(9): 1390-6.
7) Lu JJ, Cheng CC, Chou SM, Hor CB, Yang YC, Wang HL. Hepatitis B immunity in adolescents and necessity for boost

vaccination: 23 years after nationwide hepatitis B virus vaccination program in Taiwan. *Vaccine*. 2009; 27(47): 6613-8.
8) Alfaleh F, Alshebri S, Alansari S, *et al*. Long-term protection of hepatitis B vaccine 18 years after vaccination. *J Infect*. 2008; 57(5): 404-9.
9) Gabbuti A, Romano L, Blanc P, *et al*. Long-term immunogenicity of hepatitis B vaccination in a cohort of Italian healthy adolescents. *Vaccine*. 2007; 25 (16): 3129-32.
10) Jafarzadeh A, Montazerifar SJ. Persistence of anti-HBs antibody and immunological memory in children vaccinated with hepatitis B vaccine at birth. *J Ayub Med Coll Abbottabad*. 2006; 18(4): 4-9.
11) Jafarzadeh A, Zarei S, Shokri F. Low dose revaccination induces robust protective anti-HBs antibody response in the majority of healthy non-responder neonates. *Vaccine*. 2008: 26(2): 269-76.
12) Alavian SM, Mansouri S, Abouzari M, Assari S, Bonab MS, Miri SM. Long-term efficacy of hepatitis B vaccination in healthcare workers of Oil Company Hospital, Tehran, Iran (1998- 2005). *Eur J Gastroenterol Hepatol*. 2008; 20(2): 131-4.
13) Sherlock S, Dolley J. Diseases of the liver and biliary system. 10th ed. Oxford, Blackwell Science. 1997; 274-86.
14) Petersen KM, Bulkow LR, McManon BJ, *et al*. Duration of hepatitis B immunity in low risk children receiving hepatitis B vaccination from birth. *Pediatr Infect Dis J*. 2004; 23(7): 650-5.
15) Wang LY, Lin HH. Short-term response to a booster dose of hepatitis B vaccine in anti-HBs negative adolescents who had received primary vaccination 16 years ago. *Vaccine*. 2007; 27(41): 7160-7.
16) Lin YC, Chang MH, Ni YH, Hsu HY, Chen DS. Long-term immunogenicity and efficacy of universal hepatitis B virus vaccination in Taiwan. *J Infect Dis*. 2003; 187(1): 134-8.
17) Su FH, Chen JD, Cheng SH, Lin CH, Liu YH, Chu FY. Seroprevalence of hepatitis B infection amongst Taiwanese university students 18 years following the commencement of a national hepatitis B vaccination program. *J Med Viral*. 2007; 79(2): 138-43.
18) Ni YH, Huang LM, Chang MH, *et al*. Two decades of universal hepatitis B vaccination in Taiwan: impact and implication for future strategies. *Gastroentrology*. 2007; 132(4): 1287-93.
19) McMahon BJ, Bruden DL, Petersen KM, *et al*. Antibody levels and protection after hepatitis B vaccination: results of a 15 year follow up. *Ann Intern Med*. 2005; 142(5): 333-41.
20) Burgess MA, McIntyre PB, Hellard M, Ruff TA, Lefevre I, Bock HC. Antibody persistence six years after two doses of combined hepatitis A and B vaccine. *Vaccine*. 2010; 28(10): 2222-6.
21) Kurugol Z, Erensoy S, Aksit S, Egemen A, Bilgic A. Low-dose intradermal administration of recombinant hepatitis B vaccine in children: 5 year follow up study. *Vaccine*. 2001; 19(28-29): 3936-9.
22) Jabber SM. Prevalence of anti-hepatitis B and anti hepatitis A antibodies among school aged children in Western Saudi Arabia. *Saudi Med J*. 2006; 27(10): 1515-22.
23) Hammitt LL, Hennessy TW, Fiore AE, *et al*. Hepatitis B immunity in children vaccinated with recombinant hepatitis B vaccine beginning at birth. A follow up study at 15 years. *Vaccine*. 2007; 25(39-40). 6958-64.
24) Yven MF, Lim WC, Chan AO, Wong DK, Sum SS, Lai CL. 18-year follow up study of a prospective randomized trial of hepatitis B vaccination without booster doses in children. *Clin Gastroenterol Hepatol*. 2004; 2(10): 941-5.
25) Zanetti AR, Mariano A, Romano L. Long-term immunogenicity of hepatitis B vaccination and policy for booster: an Italian multicentre study. *Lancet*. 2005; 366(9494): 1337-8.
26) Manatvala JE, Van Damme P. hepatitis B vaccine- do we need boosters? *J Viral Hepat*. 2003; 10(1): 1-6.

27) Lu CY, Chiang BL, Chen PJ, *et al*. Humoral and cellular immune responses to a hepatitis B vaccine booster 15-18 years after cellular immunization. *J Infect Dis*. 2008; 19(10): 1419-26.
28) Kao JT, Wang JH, Hang CH, *et al*. Long-term efficacy of plasma- derived and recombinant hepatitis B vaccination in a rural township of central Taiwan. *Vaccine*. 2009; 27(12): 1858-62.
29) Chen CC, Yen CH, Wu WY, *et al*. Epidemiology of hepatitis B virus infection among young adults in Taiwan, China after public vaccination program. *Chin Med J*. 2007; 120(13): 1155-8.