

Original article

Hepatitis B Virus Vaccine immune response in Egyptian children 15-17 years after primary immunization; should we provide a booster dose?

Background: Few studies have evaluated the seroprotection of HBV vaccines among healthy Egyptian children after receiving the primary immunization. Yet, up to our knowledge none of them has evaluated the immune status to HBV vaccine among Egyptian children older than 15 years.

Objective: To assess the seroprotection as well as immunological memory against HB virus more than 15 years after receiving the primary set of vaccination.

Methods: Serum anti-HB surface antibody was measured in 225 healthy adolescents. Their ages ranged from 16-18 year with a definite history of receiving the primary immunization for HBV at infancy. A booster dose of the HB vaccine was given to 56 of the candidates in whom serum level of anti-HB surface antibody was not protective (less than 10 mIU/ml). A second evaluation of anti-HBs was done in those 56 one month after the booster dose.

Results: Only 8.9% of our cohort have a protective anti-HBs antibody when measured 15-17 years after primary vaccination set. On the other hand, 100% of the 56 children who received the booster dose showed excellent anamnestic response.

Conclusion: Despite the loss of protective levels of anti-HBs antibody among healthy low risk adolescents 15-17 years after primary HB immunization set, strong anamnestic response indicates the presence of good immunological memory.

Keywords: Hepatitis B, vaccine, booster.

Mohammed Eladawy, Amira Gamal*, Ahmed Fouad, Amel El-Faramawy.**

Department of Pediatrics and Clinical Pathology*, Faculty of Medicine, Ain Shams University and Pediatric department, Elmatarya Educational Hospital**, Cairo, Egypt .

Correspondence:

Mohammed Eladawy, MD, Children's hospital, Ain Shams University, Abbassya, Cairo, Egypt.

E-mail:

drmohamed_eladawy@med.asu.edu.eg

INTRODUCTION

Hepatitis B virus (HBV) infection is a global public health problem. With approximately 350 million hepatitis B virus (HBV) carriers in the world, of whom over 600,000 die annually from hepatitis B-associated liver disease¹. Egypt is considered as a region of intermediate prevalence for HBV infection with reported figure of 4.5%².

In 1992, Egypt started a program of universal immunization in infancy in accordance with the WHO recommendations. The schedule adopted by Egyptian Ministry of Health was three doses of yeast-recombinant hepatitis B vaccine administered to all infants at 2, 4 and 6 months to coincide with other compulsory vaccines (Diphtheria, Tetanus, Pertussis and oral polio (DPT- OPV)³.

Few Egyptian studies have evaluated the duration of protection of HBV vaccines after receiving the primary immunization. Up to our knowledge our study is the first to evaluate the

immune status to HBV vaccine among Egyptian children more than 15 years after primary immunization. Also in this study we tried to assess the immunological memory to HBV vaccine by examining the response to a booster dose of vaccine for those who did not have protective serum anti-HBs level (lower than 10 mIU/ml).

METHODS

This cross-sectional study included two hundred twenty five (225) healthy university students affiliated to different colleges in Ain Shams University, their ages ranged from 16-18 years. They were 154 males and 71 females. They were all documented to have received 3 doses of HBV vaccine at ages 2, 4, 6 months. None of them have a history suggestive of either chronic liver disease or chronic extrahepatic disease.

All study candidates were exposed to a full history taking, thorough clinical examination and

filled up a questionnaire about the demographic data and risk factors for liver disease and chronic diseases that may affect the immune response to vaccine. Vaccination certificate were checked and receiving the full primary immunization set was confirmed for each study candidate.

Serum samples were collected from the study candidates after signing informed consent. All serum samples were studied for HBV surface antibody level using ELISA. Those with serum anti-HBs higher than 10 IU/ml were considered immune. Others with serum anti-HBs less than 10 IU/ml were given a booster dose (10 mcg/1.0 ml) of HBV vaccine [Hepatitis-B Vaccine, B.P (r-DNA), genetically engineered recombinant vaccine, *VACSERA*] manufactured by *VACSERA* under license of *SHANTHA BIOTECHNIC*. This dose was given to test for anamnestic reaction and HBsAb titer was measured again after one month.

HB surface antigen and HB core antibodies were to be done for every patient who did not show a good anamnestic response to the booster dose to exclude HBV infection.

Anti HBs antigen levels greater than 10 mIU/ml were considered protective⁴. A good anamnestic response was defined as serum anti-HBs antibodies level changing from less than 10 mIU/ml to more than 10 mIU/ml one month after booster dose⁵.

RESULTS

Median age of the studied population was 17.8 years with a range of 16-18 years. Study candidates were born in different Egyptian governorates and have received their primary vaccination set in their place of birth. Most of the studied candidates (91.1%) showed serum HBsAb level below 10 IU/ml (not protected) whereas only 20 (8.9%) had a protective level of serum HBsAbs. The mean serum HBsAb was 5.4 ± 2.1 IU/ml. Those with protective HBsAb titer were not different in age, gender or social class when compared with the other group without protective level. Table 1 shows the distribution of serum HBsAbs level among the studied candidates before receiving a booster dose of HBV vaccine.

A booster dose was given to 56 (around 25%) of the study candidates whose serum HBsAb was less than 10 mIU/ml. These candidates were randomly selected and were 20 males and 36 females with median age 17.9 ± 0.2 years (range 16 – 18 years). HBsAb was measured one month after the booster dose.

All the 56 study candidates showed good anamnestic response with serum HBsAb higher than 10 mIU/ml (protective value). Table 2 shows the HBsAb serum level before and one month after booster dose in the 56 study candidates. Age, gender and social class had no significant effect on the anamnestic response.

Table 1. Distribution of serum HBsAbs level among the studied candidates before booster dose of HBV vaccine.

HBsAbs level (IU/ml)	Number of candidates	%
0-2	33	14.7%
3-4	54	24%
5-6	63	28%
7-8	47	20.9%
9-10	8	3.5%
Above 10	20	8.9%

Table 2. Effect of booster dose of HBV vaccine on antibody titer among the 56 candidates who received the booster dose.

Total Number : 56	Serum anti-HB surface antibody titer (mIU/ml)		Significance P value
	Range	Mean \pm SD	
Before booster dose	1-9	5.46 ± 2.1	< 0.0001*
After booster dose	10-1000	785 ± 308	

DISCUSSION

Hepatitis B vaccination is a well-established, safe and effective method of conferring long-term protection against hepatitis B viral infections, liver cirrhosis and hepatocellular carcinoma (HCC) worldwide. It is recommended by World Health Organization (WHO) for all infants⁶. Inclusion of hepatitis B vaccine into national infant immunization programs could prevent >80% of HBV-related deaths⁷. One hundred and seventy nine countries have introduced a hepatitis B vaccine in their national infant immunization schedules by the end of 2010, including parts of India and the Sudan⁸.

Neonatal HBV vaccination is the best effective measure for prevention of HBV infection in countries with intermediate to high level of HBV endemicity. The duration of protection induced by plasma-derived and recombinant vaccines against HBV was investigated by several authors. Even if there is a decline of antibody titers over time, there is evidence that immunological memory persists for at least 9–15 years after immunization^{9,10}.

In our study, the seroprotection at 15-17 years after immunization was 8.9% of the studied population. Other studies for evaluation of immunogenicity and efficacy of HBV vaccination were done among Egyptian children but at shorter intervals from the primary immunization set. Afifi et al studied 245 vaccinated children aged 6–7 years and 9-11 years; they reported seroprotection in 47.5% and 39.3% of them respectively¹¹. Also, Elsayed et al studied 200 vaccinated children who were divided into two groups. Group A, 100 child aged 6 years and group B, 100 child 11 years old; and they reported similar figures of seroprotection¹². These two studies in addition to our study revealed progressive pattern of waning of humoral immunity to HBV in vaccinated children with the increase in time lapsed after the primary immunization set.

Immune memory to HB vaccine has been studied through measuring the humoral immune response to a single dose of HB vaccine or in vitro testing for T and B cell activation⁵. In our study, 56 adolescents who initially had non protective HBVs antibodies titer showed excellent anamnestic response to a booster dose with a significant increase in serum anti HB antibody mean from 5.46 ±2.1 to 785±308 mIU/ml. That response is similar to other reports^{13,14} and indicates immune memory to HBV vaccine.

Based on that good anamnestic response to HBV vaccine in our study, we do not find any indication for a booster dose of HBV vaccine after finishing

the complete HBV vaccine immunization set in infancy in low risk Egyptian subjects. It is worth mentioning that most guidelines do not indicate administration of a booster dose for HBV.^{6,15,16}

In conclusion, most of the adolescents in our study showed non protective serum anti HBs antibody 17 years after finishing the primary set of HBV vaccine immunization in infancy. However, the good anamnestic response to the booster dose may indicate that fully vaccinated low risk subjects do not need a HB vaccine booster dose at 17 years after primary immunization.

REFERENCES

1. **BARNES PJ.** Immunology of asthma and chronic obstructive pulmonary disease. *Nat Rev Immunol* 2008;8(3):183-92.
2. **LAVANGHY D.** Chronic viral hepatitis as a public health issue in the world. *Best Pract Res Clin Gastroenterol* 2008;22:991–1008.
3. World Health Organization (WHO). WHO/UNICEF immunization summary. 2007. Available at http://whqlibdoc.who.int/hq/2007/who_ivb_2007_eng.pdf. last accessed July 2013
4. **MANSOUR E, ABDUL-RAHIM S, BATOUTY G, ZAGHLOUL I, ABDEL-HADI S.** Integration of hepatitis B immunization in the Expanded Program on Immunization of the Child Survival Project. *J Egypt Public Health Assoc* 1993; 68(5-6):487-94.
5. **JACK AD, HALL AJ, MAINE N, MENDY M, WHITTLE HC.** What level of hepatitis B antibody is protective? *J infect Dis* 1999, 179:489-492.
6. **LEURIDAN E, VAN DAMME P.** Hepatitis B and the need for a Booster dose. *Clinical Infectious Diseases* 2011;53(1):68–75.
7. World Health Organization (WHO). Revised WHO position paper on hepatitis B vaccine, Oct 2009, <http://www.who.int/immunization/documents/positionpapers/en/index.html#hepb>. Last accessed February 2014.
8. **GOLDSTEIN ST, ZHOU F, HADLER SC, BELL BP, MAST EE, MARGOLIS HS.** A mathematical model to estimate global hepatitis B disease burden and vaccination impact. *Int J Epidemiol* 2005; 34(6):1329-39.
9. World Health Organization (WHO). Hepatitis B Vaccines. International travel and health. Available at: <http://www.who.int/ith/vaccines/hepatitisB/en/index.html>. Last accessed Feb 2015
10. **FLOREANI A, BALDO V, CRISTOFOLETTI M, RENZULLI G, VALERI A, ZANETTI C, TRIVELLO R.** Long-term persistence of anti-HBs after vaccination against HBV: an 18 year experience in health care workers. *Vaccine_2004* ;22(5-6):607-10

11. **SAFFAR MJ, REZAI MS.** Long-term antibody response and immunologic memory in children immunized with hepatitis B vaccine at birth. *Indian Pediatric* 2004; 41: 1232-7.
12. **AFIFI S, MAHRAN M, SAID Z, SALAMA I, EL KHAYAT H.** Serum level of anti-hepatitis b surface antigen among newborns and fully vaccinated infants and children aged 6 to 11 years. *Australian Journal of Basic and Applied Sciences* 2009; 3(4): 3239-45.
13. **EL-SAYED B, EL-GUINDI M, EL-SHAARAWY A, SALAMA E, SOBHY G.** Long-term Immunogenicity of Hepatitis B Vaccination in children. *Zagazig Journal of Occupational Health and Safety.* 2009;2 (2): 17-28.
14. **PETERSEN KM.** Duration of hepatitis B immunity in low risk children receiving hepatitis B vaccinations from birth. *Paediatric infectious diseases journal* 2004;23(7): 650-5
15. **CHANG Y, WANG J, CHEN Y, LIN J, CHENG C, CHU G.** Hepatitis B virus vaccination booster does not provide additional protection in adolescents: a cross-sectional school-based study. *BMC Public Health* 2014, 14:991
16. Immunization NACo. Revised guidelines for booster vaccination against hepatitis B. *CMAJ* 1992; 147:1029–1030.
17. European Consensus Group on Hepatitis B Immunity. Are booster immunizations needed for lifelong hepatitis B immunity? *Lancet* 2000; 355:561–565.