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An Evaluation of the Responses to the Standard Hepatitis B Vaccination among 8-18-Month-old Children in North East of Iran

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Abstract

Background: Vaccination of children against hepatitis B virus (HBV) is the most effective strategy to prevent infections in their future life. However, the real response to HBV vaccination in infancy is still unclear. The aim of this study was to evaluate the status of immune response to HBV vaccine among children aged 8 to 18 months in east coast of the Caspian Sea, Bandar-e Turkmen, Golestan, Iran.

Methods: In this cross-sectional study, 565 children from Bandar-e Turkmen ranging from 8 to 18 months of age, vaccinated in a routine vaccination program were included. The serum samples were collected from all children and HBsAb titers were measured using ELISA.

Results: Out of 565 children, 12 (2.12%) had anti-HBs titers <10 IU/L (non-responder) while 553 (97.88%) had anti-HBs titers >10 IU/L (responder) ($p<0.05$). Among these responder children, 92 (16.3%) had anti-HBs titers 10-100 IU/L (poor responder) and 461(81.6%) had anti-HBs titers >100 IU/L (good responder). The negative children were revaccinated (3-doses) and 11 of them became protected against HBV infection (anti-HBs titers >10 IU/L). Only 1 of the included children was non-responder, after routine vaccination and 3 doses revaccination.

Conclusion: The results of this study indicated that the HBV vaccination program in this region of Iran is effective and most of the children showed positive immune responses after three doses of vaccination. Importantly, revaccination of non-protected individuals is recommended.

Key Words: Children, HBsAb, Hepatitis B vaccination, Immune response.

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1- INTRODUCTION

Hepatitis B virus (HBV) is an enveloped DNA virus, which belongs to the *Hepadnaviridae* family (1). The virus is hepatotropic and causes a multitude of clinical conditions ranging from acute viral hepatitis to cirrhosis and hepatocellular carcinoma (2). The HBV infection is considered as a major public health problem in the world. More than 350 million people are infected with chronic HBV, and around 1 million deaths each year are considered to be related to HBV infection (3). The prevalence of HBV infection varies considerably in different countries. In Iran, it is reported that 2-7% of the population are infected with HBV, and Iran is considered to be an endemic region (4).

HBV is normally transmitted from person to person via blood or body fluids, and mother-to-child transmission is one of the main transmission routes, especially in developing countries (5). Different vaccination programs for controlling the HBV infection have been performed by different countries depending on the prevalence of the HBV infection in each country (6). The widespread vaccination program against HBV, especially in pediatrics, reduced the occurrence of chronic HBV infection and hepatocellular carcinoma (7). In Iran, the HBV vaccination was initiated in 1993 as a part of the national immunization schedule in newborns with injections at 0, 1, and 6 months of age (8). This program resulted in a significant reduction in the rate of acute symptomatic HBV infection among children (9).

Vaccination of infants against hepatitis B using the HBV standard vaccine is effective in preventing the infection in early childhood and there is growing evidence of long-term protection with no need for booster doses (10). However, the persistence of immunity against HBV after vaccination in infancy is still of debate (11). Up to now, no need for a booster dose has been identified in healthy subjects; and further follow-up studies continue to determine the long-term protection (12). In the present study, we evaluated the antibody response to HBV vaccination in children aged 8-18 months in the east coast of the Caspian Sea, Bandar-e Turkmen, Golestan, Iran.

2- MATERIALS AND METHODS

2-1. Participants

This cross sectional study was conducted in the Department of Microbiology, Golestan University of Medical Sciences, Gorgan, Iran. A total of 565 healthy children from Bandar-e Turkmen of either sex between the ages of 8 to 18 months, documented to have received 3-doses of standard HBV vaccine, according to the Iranian vaccination schedule (at birth, 1 and 6 months), were recruited to the study. Signed informed consent was provided by at least one parent or a legally acceptable representative of each participant. A clinical questionnaire was used to collect the required data of all participants including age, gender, weight, height, ethnicity, residence location, and vaccination status of the mother. In the present study, the infants with no infectious disease and completely vaccinated with Euvax B, a Korean HBV vaccine (manufactured by LG Chem. Pharmaceutica DIV; one pediatric dose of 0.5 ml containing 10 micrograms of hepatitis B surface antigen [HBsAg], 3 doses) were included. This study was approved by the ethical committee of Golestan University of Medical Sciences (ethics code: 773A2032980).

2-2. Serology

Blood samples were collected from all participants to evaluate the status of HBsAb titers after standard vaccination. The level of serum HBsAb was measured by ELISA kit (Diapro, Italy) with 100%

sensitivity and according to the manufacturer's instruction. The ELISA tests were performed in duplicate for all of the samples. Children with HBsAb titers >10 IU/L were considered to be immune. Those with HBsAb levels <10 IU/L were provided with 3-doses of standard vaccination. The second serum sample was obtained following the revaccination and the HBsAb titers were also measured.

2-3. Data analyses

Statistical analyses were performed using SPSS version 23 (IBM, Chicago, IL). *p* values < 0.05 were considered significant.

3- RESULTS

A total of 565 participants were enrolled in the study, among whom 309 (54.69%) and 256 (45.31%) were male and female, respectively. The mean age, weight, and height of children were 13.67±6.84 months, 9.5±1.4 kg and 74.24±7.57 cm, respectively. Of all children, 421 (74.51%) resided in rural areas, and 99.11% of them had Turkmen ethnicity.

Out of 565 children, 12 (2.12%) had anti-HBs titers <10 IU/L (non-responder) while 553 (97.88%) had anti-HBs titers >10 IU/L (responder) (p<0.05). From among these responder children, 92 (16.3%) had anti-HBs titers 10-100 IU/L (poor responder) and 461(81.6%) had anti-HBs titers >100 IU/L (good responder). The negative children were revaccinated (3-doses) and 11 of them became protected against HBV infection (anti-HBs titers >10 IU/L). Only 1 of the included children was a non-responder, after routine vaccination and 3 doses revaccination. The only non-responder participant was male with 17 months of age, 78 cm of height, and 11 kg of weight, and resided in a rural area. No statistical correlation was observed between response to vaccination and other variables such as age, gender, weight, height, ethnicity, residence location, and the vaccination status of the participant's mother.

4- DISCUSSION

Vaccination is considered as an effective approach to prevent HBV infection worldwide (13). The reduction of HBV prevalence in pediatrics has been observed in countries where standard vaccination programs have been fulfilled (14). Various independent studies in Iran have assessed the immune response to HBV vaccination in children. However, the real status of immune response following vaccination in some districts of Iran is not well described (9). The current study has assessed the real status of immune response to HBV standard vaccine among children aged 8 to 18 months in Bandar-e Turkmen, Golestan. Overall, we found that most of the children demonstrated effective responses to the 3-doses of vaccination.

Results of the current study revealed that among the children aged 8 to 18 months in Bandar-e Turkmen, 97.88% had protective responses and only 2.12% were not responder against HBV after the administration of 3-doses of vaccination. A previous study in Gorgan on children aged 7 to 12 months showed that 94.8% of the vaccinated children had protective anti-bodies against HBV (15). Rostami et al. in Mazandaran reported that 85% of children were protected, after routine vaccination (16). Zamani et al. in Tehran studied on the 12-to-24-month-old children and reported that 94.8% of the vaccinated children had protective responses against HBV (17). Another study in Kerman indicated that 96.1% of children have protective antibodies a year after the vaccination (18). The results of the mentioned studies were consistent with those of the present study. Another study in Babol showed that 87.6% of children were protected against HBV (19). The results can be affected by many factors such as the vaccine type, the HBV

prevalence and the virus carrier mothers in the region (1, 20). The literature regarding the efficacy of HBV vaccination in Iranian children is summarized in **Table 1**.

Table-1: The literature regarding the efficacy of HBV vaccination in Iranian children

Study (year)	Old	Main findings	Ref
Kazemi et al. (1999)	1-4-year-old children	98% were responder	(20)
Zamani et al. (2001)	12-24-month-old children	94.8% were responder	(17)
Jafarzadeh et al. (2001)	Neonates	96.1% were responder	(18)
Esmaili et al. (2003)	Under 7-year-old children	87.6% were responder	(19)
Rostami et al. (2006)	Preterm and neonates	85.6% were responder	(16)
Salehi et al. (2007)	Under 9-month-old children	80.7% were responder	(21)
Moradi et al. (2009)	7-12-month-old children	98.4% were responder	(15)
Yazdanpanah et al. (2010)	5-7-year-old children	84.4% were responder	(22)
Reazaei et al. (2014)	Under 5-year-old children	88% were responder	(23)
Salehifard et al. (2017)	6-18-year-old students	38.5% were responder	(24)
Arefkhah et al. (2019)	Under 12-year-old children	85.1% were responder	(25)
Dowran et al. (2021)	Under 19-year-old students	38.5% were responder	(26)

There are also studies that have targeted children older than 2 years. A study in Zanjan showed that 98% of children had protective anti-bodies against HBV, 36 months after the vaccination (20). Yazdanpanah et al. in Kohgiluyeh and Boyer-Ahmad reported that 84.4% of 5-to-7-year- old individuals had protective anti-bodies against HBV (22). It seems that the protection period after HBV vaccination depends on the vaccination plan consisting of the age at which the first dose was administered, the interval times, the number of vaccine repetitions and the dose. It can also be dependent on the type of vaccine, the HBV prevalence in the region and the virus carrier mothers (19).

Considering the mentioned studies, it can be concluded that the response to the vaccine can be affected by immunological deficiencies, lack of suitable genetic background for the correct response, incorrect storage of vaccine and vaccine type. On the other hand, the social culture and nutrition of children have important influences on their response to vaccines. In this case breast feeding is of significance. The genetic background also affects the way an individual responds to the vaccine or an infection (19). In the present study, regarding the culture of the population, all of these factors can be involved in the outcomes.

5- CONCLUSION

In conclusion, our results clearly confirm that the administration of three doses of HBV vaccine is effective and produces robust immune responses. Importantly, revaccination of non-responder children is recommended. Also to increase the effectiveness of the vaccine, it can be recommended that the vaccine should be stored in optimal conditions, the vaccine type should be chosen carefully, and the vaccine administration and transportation process must be performed correctly.

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7- CONFLICT OF INTEREST

None.

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