

Response to the provision of hepatitis B booster in children aged 10-15 years with non-protective anti-HBs titer.

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Abstract

Introduction: Several studies have demonstrated that titer of protective anti-HBs (≥ 10 mIU/ml) begins to wane at age 10 and declines rapidly due to age. Approximately 10% of Indonesia's population was infected with hepatitis B.

Objective: To determine the response to the provision of Hepatitis B vaccine among children aged 10-15 years with titer of non protective anti-HBs.

Method: Consecutive study conducted from October to December 2015 among the children aged 10-15 years from 10 schools in Tuminting Regency, North Sulawesi. Before study conducted, titer of anti-HBs was checked with the result titer of non-protective anti-HBs (<10 mIU/ml). The inclusion criteria was Parents signed inform consent, the children were administered a booster dose of hepatitis B immunization and were rechecked within 1-3 months after administration. The study was approved by Ethic Committee of Medical Faculty of Sam Ratulangi University.

Result: A total 74 out of 82 children who had non-protective titer of anti-HBs complied with inclusive criteria. 60 children (81.1%) got protective titer of anti-HBs after receiving a booster dose of hepatitis B immunization. While 14 children (18.9%) got non-protective titer of anti-HBs (non-responder). Among 60 children who got protective titer of anti-HBs, only 4 children (6.7%) were found with titer of anti-HBs ranging 10-100 mIU/ml (hyporesponder) and 56 children (93.3%) were found with titer of anti-HBs >100 mIU/ml (good responder).

Conclusion: Provision of a booster dose of hepatitis B to the non-protective children presented a good result.

Keywords: Hepatitis B, Vaccination, Titer anti-HBs, Booster.

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Introduction

Hepatitis B Virus (HBV) infection is highly prevalent in the society. There are 240 millions people are suffered from chronic infection of Hepatitis B and 780.000 death every year from causes both chronic and acute Hepatitis B infections [1]. In areas of high endemicity, such as Southeast Asia, Africa and Brazil, more than 8% of the population are detected as Hepatitis B patients [2]. Indonesia with 235 millions of population is included into high endemicity areas because 9.4% among the population are Positive-Hepatitis B [3,4]. In areas of high endemicity, the infection is often acquired during the preschool years and transmitted vertically from mother to the infant or horizontally from HB-carrier who lives in the same house with the infant [5].

Primary Hepatitis B vaccination could prevent Hepatitis B virus infection with rate as high as 90% to 95%.⁶ In Indonesia, since 2006, HB-0 HB-0 monovalent vaccine (uniject) has been given after the birth. It has been continued by receiving combination of DTWP/HB/HIB vaccine at age 2, 3 and 4 months [6,7]. Although vaccines have been given for a long period of time, According to the data from Ministry of Health of Indonesia in 2013, presentage of HB-0 administration is only 79.1% and DPT-HB-3 is 75.6% [8]. Immune system memory remain until 15 years after hepatitis B initial administration. However, several studies have demonstrated that titer of protective anti-HBs (≥ 10 mIU/ml) begins to wane at age 10 and declines rapidly due to age [9,10]. This, for sure, increases the risk of hepatitis B exposure, moreover approximately 10% of Indonesia's population is infected

with hepatitis B. Therefore, booster hepatitis B vaccine is needed for prevention of hepatitis B infection.

The aim of the study was to determine the response to the provision of Hepatitis B vaccine among children aged 10-15 years with titer of non protective anti-HBs.

Materials and Methods

The study design was consecutive study among the children aged 5-15 years from 10 schools (Elementary, Junior, and Senior High School) in Tuminting Regency, Manado, North Sulawesi. It was an advanced study from previous study. The previous study showed that among 105 children who were observed, only 23 children had titer of protective anti-HBs and 82 children did not have titer of non-protective anti-HBs [9]. The inclusion criteria was parents signed inform consent, children were administered a booster dose of HBS and were rechecked within 1-3 months after administrations. The study was approved by Ethics Committee of Medical Faculty of Sam Ratulangi University.

2 ml of blood sample was drawn by needle connected to vacuumtainer. Then, Titer of anti-HBs from the sample was checked using Chemiluminescent Microparticle Immunoassay (CMIA). Titer of anti-HBs levels <10 mIU/ml was categorized as non-responder and titer of anti-HBs levels ≥ 10 mIU/ml was categorized as responder. Responder was determined into hyporesponder (titer of anti-HBs levels 10-100 mIU/ml) and good responder (titer of anti-HBs levels >100 mIU/ml) [11]. Data was analyzed by using descriptive analysis and Chi-square of SPSS ver. 22.

Result

A total 74 out of 82 children whom had titer of non-protective anti-HBs from previous study complied with the inclusive and exclusive criteria. There were 8 children excluded from the study. Three of them did not receive a booster dose of hepatitis B vaccine. Five of them, eventhough they were administered with a dose of titer of anti-HBs, did not show up for rechecking the titer of anti-HBs within 1-3 months after administrations. 74 children who complied the criteria of the study consisted of 17 male (23%) and 57 female (77%). Thus, They were determined into various range of age. There were twelve of ten years old (16.2%), twelve of eleven years old (16.2%), eleven of twelve years old (14.9%), 15 of 13 years (20.3%), 12 of 14 years (16.2%) and 12 of 15 years old (16.2%). There were 60 children (81.1%) had protective titer of anti-HBs (titer of anti-HBs ≥ 10 mIU/ml) after receiving a booster dose of hepatitis B immunization, while 14 children (18.9%) had non-protective titer of anti-HBs (titer of anti-HBs < 10 mIU/ml). Among the children who were protective, four children (6.7%) had titer of anti-HBs between 10-100 mIU/ml (hyporesponder) and 56 children (93.3%) had titer of anti-HBs >100 mIU/ml (good responder). 14 out of 56 children who were good responder had titer of

anti-HBs >1000 mIU/ml. Table 1 shows characteristic of the subject of the study.

Analysis of titer of anti-HBs according to age and sex could be seen on Table 2. In age group, There was no significant differences between respondents who have protective titer of anti-HBs with respondents who had non-protective titer of anti-HBs (p=0.490) as well as the mean of age between protective and non-protective subjects (p=0.457). Nevertheless, there was no significant relationship of sex between subjects with protective titer of anti-HBs and subjects with non-protective titer of anti-HBs (p=0.220).

Discussion

Primary hepatitis B vaccination could prevent hepatitis B virus infection with rate as high as 90% to 95%. Seroprotection has been estimated to persist atleast for 15 years eventhough titer of anti-HBs has been dramatically decline to negative. Someone is still clinically protected from chronic hepatitis B because the immune memory would give in vitro protection. Therefore, booster hepatitis

Table 1. Characteristic of subjects

| Characteristic | Total (%), n=74 |
|-------------------|-----------------|
| Sex | |
| Male | 17 (23.0) |
| Female | 57 (77.0) |
| Age (years) | |
| 10 | 12 (16.2) |
| 11 | 12 (16.2) |
| 12 | 11 (14.9) |
| 13 | 15 (20.3) |
| 14 | 12 (16.2) |
| 15 | 12 (16.2) |
| Titer of Anti-HBs | |
| <10 mIU/ml | 14 (19.7) |
| 10-100 mIU/ml | 4 (5.4) |
| >100 mIU/ml | 56 (74.9) |

Table 2. Analysis of titer of anti-HBs according to age and sex

| Variable | Anti-HBs titer | | Significancy (p) |
|----------------------|-----------------------|-------------------|------------------|
| | Non-Protective (n=14) | Protective (n=60) | |
| Age, n (%) | | | |
| 10 years | 2 (14.3) | 10 (16.7) | 0.49 |
| 11 years | 2 (14.3) | 10 (16.7) | |
| 12 years | 2 (14.3) | 9 (15.0) | |
| 13 years | 4 (28.5) | 11 (18.2) | |
| 14 years | 2 (14.3) | 10 (16.7) | |
| 15 years | 2 (14.3) | 10 (16.7) | |
| Age mean (SD), years | 12.59 ± 1.71 | 12.17 ± 1.78 | 0.457 |
| Sex, n (%) | | | |
| Male | 5 (35.7) | 12 (20.0) | 0.22 |
| Female | 9 (64.3) | 48 (80.0) | |

B immunization is not necessary for the children who has received a complete hepatitis B (3-4 times) [6]. However, the fact in the field shows that even though hepatitis B immunization has been conducted since 1997 in Indonesia, there is no prevalence change of 10 % of hepatitis B patients. according to task force of Indonesian Pediatric Society (IPS), immune hepatitis B booster administration could be given to the children with age 10-12 years if the level content of protection has not been reached yet (titer of anti-HBs <10 mIU/ml) [7].

The study was continuous study from previous study with 82 children (respondents). Total 74 out of 82 children were eligible to be the subjects of the study. The subjects consisted of 17 males (23%) and 57 females (77%). 12 out of 17 males had protective titer of anti-HBs, while 48 out of 57 females had protective anti-HBs. However, there was no statistically significant differences among two sex groups. It is similar to the study conducted by Cheang et al. [12] where the result showed that sex did not affect hepatitis B seroprotective and immune response after primary hepatitis B vaccine. However, the finding is at variance with the finding from the study by Giltay et al. [13] which revealed that female showed antibody response higher than male, where male showed number of lymphocyte T declined higher than female and also IgM and IgG serum content of male was lower than female. Besides, it could be affected by sexual hormone, such as estrogen, progesterone, and testosterone which are different between male and female [14].

The study showed that there was no difference of protection level in age 10-15 years group with protection mean of 80%. It was supported by statistical analysis which did not show any significant differences. It is similar to the study carried out by Rampengan et al. [9] but at variance with the study conducted by Whittle et al. [15] which displayed that titer of anti-HBs effectiveness was affected by age, effectiveness of anti-HBs titer reduction was equal to the age of respondents.

The study was found out that among 74 of the subjects who received a booster dose of hepatitis B, 14 subjects (19.7%) had non-protective titer of anti-HBs (<10 mIU/ml) and 60 subjects (80.3%) had protective titer of anti-HBs (≥ 10 mIU/ml). Among subjects who were protective, 4 subjects (6.7%) had titer of anti-HBs between 10 to 100 mIU/ml (hyporesponder) and 56 subjects (93.3%) had titer of anti-HBs >100 mIU/ml (good responder). 19.7% non-responder was found in this study. It was displayed that immune response formed was affected not only by immune response of patients but also could be affected by another factors, such as quality and quantity of vaccine (administration method, dose, frequency of administrations, adjuvant and type of vaccine) and genetical factor which was not observed in the study [16]. According to immunization task force of Indonesian Pediatric Society, children who are non-responders could

received 3 times of hepatitis B initial administrations (0,1, and 6 months) which is considered 40% of non-responder children could form strong antibody of anti-HBs. If there is no seroconversion after 3 times immunization of hepatitis B, 2 doses of hepatitis B immunization could be considered given to the patients [6].

Conclusion

Approximately 10% of Indonesia's population was infected with hepatitis B. Provision of a booster dose of hepatitis B to the non-protective children presented a good result.

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