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Original Articles

Immune Response to Hepatitis B Virus Vaccine in Term and Preterm Babies Received As Per EPI Schedule

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Abstract

Objective: To determine the immune response of hepatitis B virus (HBV) vaccine given according to EPI schedule and to compare the antibody response among term and preterm babies.

Setting: EPI centre, Paediatric OPD and Department of Virology, Bangabandhu Sheikh Mujib Medical University (BSMMU).

Duration: May 2006 to April 2007.

Study Population: Thirty preterm and thirty term babies who received 3 doses of HBV vaccination according to EPI schedule.

Outcome variables: Immune response to HBV vaccine according to gestational age, according to birth weight and comparison of immune response among term and preterm babies.

Results: Thirty three percent infants were non-responder in all the groups and 50% infants were good responders in 34-36 weeks and above. Total response was 80% among preterm and 86.6% among term infants.

Conclusion: Most of the infants showed positive immune response and there was no significant difference among term and preterm babies.

***Key words**: Efficacy of HBV vaccine, immune response, poor responder, good responder.*

Introduction

Viral hepatitis is recognized as a clinical disease since antiquity[1]. Approximately 350 million people are chronically infected by hepatitis B virus globally and are at risk of serious illness i.e., cirrhosis of the liver and primary liver cancer. Ninety five percent of the infected neonates with immature immune system became asymptomatic carriers as compared with 30% of children infected after the neonatal period[2].

World Health Organization (WHO) recommends immunization of all children with 3 doses of 10 µgm of Hepatitis B Virus (HBV) vaccine given intramuscularly at 6 weeks, 10 weeks and 14 weeks along with DPT and oral polio vaccine[3].

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Similarly, in Bangladesh Hepatitis B vaccination is recommended at 6 weeks, 10 weeks and 14 weeks along with DPT and oral Polio vaccine by Govt. of Bangladesh in the Expanded Programme on Immunization (EPI). This schedule is proposed for decreasing the number of visits for vaccination and also to increase the compliance[4,5]. The full term as well as preterm infants, immune system is physiologically weaker, but it is more marked in the preterm and particularly sick or stressed infant[6].

Though the recommended schedule is practiced routinely in our country but to the best of our knowledge the antibody response against HBV vaccine has not been evaluated in the vaccinated infants.

Lau et al. and Losonsky et al. reported low response to hepatitis B vaccine among preterm babies[7,8]. American Academy of Pediatrics (AAP) in the year 1994 also recommended a delay of HBV vaccination in preterm infants until they reach 2000 gm of weight or 2 months of age[9]. Later in 2003 AAP recommended first dose at 1-2 months of chronological age, may be administered as early as 30 days of chronological

age if medically stable or at hospital discharge even before 30 days of chronological age[10]. But some other studies found no significant difference between term and preterm babies in terms of efficacy of vaccine[11-15].

This study was designed to evaluate the immune response to HBV vaccine among the infants and to compare the antibody response among preterm and term babies.

Materials and Methods

It was a prospective observational study done in the EPI corner of Paediatric outpatient department and the department of Virology, Bangbandhu Sheikh Mujib Medical University (BSMMU), Dhaka. Duration of the study was one year, from May 2006 to April 2007. Eighty five infants aged between 105 days attending EPI corner, BSMMU, born to HBsAg negative mothers and received 3 doses of HBV vaccine were enrolled in this study. Infants with major congenital anomalies, infants having history of maternal jaundice and infants of mothers whose hepatitis B status was unknown were excluded from the study.

Operational Definitions

Gestational Age: It was defined as the number of completed weeks of gestation calculated from last menstrual period.

Term gestation was defined as a gestational age of at least 37 completed weeks.

Preterm gestation was defined as a gestational age less than 37 completed weeks.

After giving 3rd dose of vaccines, informed consent was taken and a pre-prepared, structured questionnaire was filled up. Birth weight was recorded from birth records. Parents were counseled about the study and requested to come with their babies after 6 weeks of 3rd dose of vaccine for determining anti HBSAg antibody titre. When these infants came after 6 weeks they were divided into 2 groups. Group A included 40 infants born at term, Group B included 45 infants born preterm.

When infants came after 6 weeks 2 ml of blood was collected with all aseptic precaution. Samples were centrifuged at 3000 rpm for 3 minutes in the department of Virology, BSMMU. After centrifugation the serum was pipetted into the eppendorf tube and labeled properly. All samples were stored at minus 20 degree Celsius in the department of virology, BSMMU until tests were done. Tests were done by anti-HBs immunoassay kit (Diasorin, Italy) following instruction of the manufacturer. Serum levels of anti-HBs <10 IU/L were taken as evidence of non response, while levels of 10-100 IU/L and >100 IU/L were considered as poor response and good response respectively.

Data analysis was done using SPSS for Windows (version 10.2; SPSS Inc, Chicago). Strength of association was determined by calculating odds ratio (OR) using 95% confidence interval (CI).

Results

A total of 85 babies were enrolled in the study. Initially twenty three infants did not come timely for assessment of antibody titre. Among them 10 were term and 13 preterm. Another 2 preterm infants were excluded from the study randomly for keeping equal number in both the groups. So ultimately Group A and Group B both had 30 infants.

Mean gestational age of preterm and term infants were 34.8±1.6 weeks and 38.7±0.7 weeks respectively. Mean birth weight was 1886±318 gms and 2673.3±343.5 gms respectively. Male: female ratio was same in both the groups (Table-I).

Table-I

Clinical characteristics of study population (n=60)

Clinical criteria	Preterm (n=30)	Term (n=30)
Gestational age (wks) Mean±SD (Range)	34.8±1.6 (31 to 36.8)	38.7±0.7 (37 to 40)
Birth Weight (gms) Mean±SD (Range)	1886±318 (1300 to 2500)	2673.3±343.5 (2000 to 4000)
Male/Female	18/12	17/13
Type of Delivery (Normal/CS)	25/5	18/12

The immune response against HBV vaccine according to gestational age in the preterm babies revealed that 33.3% infant were non-responder in all the age groups (<34 weeks, 34-36 weeks and 36 weeks 6 days). But 50% infants were good responder in 34-36 weeks group and 36 weeks 6 days group (Table-II).

Table-II

Immune response to HBV vaccine according to gestational age in preterm babies (n=30)

Gestational age	Non Responder n=6 n (%)	Poor Responder n=6 n (%)	Good Responder n=18 n (%)	O.R* (C.I)**	P value
<34 weeks	2 (33.3)	2 (33.3)	0	5.5 (0.39-87.0)	0.17
34-36 weeks	2 (33.3)	1 (16.6)	9 (50)	0.7 (0.07-6.01)	1.0
36 weeks+6days	2 (33.3)	3 (50)	9 (50)	0.5 (0.05-4.24)	0.66

* OR: Interval Odds Ratio; ** CI: Confidence interval

Table-III

Antibody (anti-HBs) response in relation to birth weight (n=60)

Response	Birth weight (gm) <2500 (n= 35) n (%)	Birth weight (gm) ≥ 2500 (n= 25) n (%)	OR (C.I)	P value
Non responder	10 (28.5)	2 (8)	4. 6(0.9-23.25)	0.045
Poor responder	9 (25.7)	2 (8)	3.98 (0.78-20.35)	0.159
Good responder	16 (45.7)	21 (84)	0.1 6(0.04-0.56)	0.003
Total responder	25 (71.4)	23 (92)	0.22 (0.04-1.10)	0.045

Table-IV

Immune response to HBV vaccine in term and preterm infants (n=60)

Immune response	Preterm (n=30) n (%)	Term (n=30) n (%)	O.R (C.I)	P value
Negative	6 (20)	4 (13.3)	1.6(0.3-8.0)	0.72
Poor	6 (20)	4 (13.3)	1.6(0.3-8.0)	0.72
Good	18 (60)	22 (73.3)	0.6(0.2-1.9)	0.4
Total Responder (poor+good)	24 (80)	26 (86.6)	0.6(0.1-2.9)	0.7

Out of 25 babies in ≥ 2500 gm birth weight group, 92% were responder to HBV vaccine, whereas it was 71.4% in <2500gm birth weight group. Good responder was also high in the ≥2500gm birth weight babies. These findings were statistically significant (Table-III).

Comparison of the immune response to HBV vaccine among term and preterm babies showed that total response was 80% among preterm and 86.6% among term infants. The differences between the groups were not statistically significant (Table-IV).

Discussion

This study was carried out with the aim to evaluate antibody response to HBV vaccine in term and preterm infants who received the vaccine as per EPI schedule.

In this study immune response after HBV vaccine did not have statistically significant difference among the preterm babies when gestational age was taken into consideration. But when birth weight was taken into consideration good responders and total responders were statistically higher among normal birth weight (≥2500gm) infants. D'Angio showed similar findings

in his study[11], where seroconversion was 91% and 100% in preterm infants weighing more than 2000gms and term infants respectively. American Academy of Pediatrics (AAP) recommended a delay of hepatiis B vaccination in premature infants until they reach 2000 gm of weight or 2 months of age in 1994[9]. Later on in the year 2003 AAP recommended first dose of HBV vaccine to the infants <2000gms at 1-2 months of chronological age, and it may also be administered as early as 30 days of chronological age if medically stable or at hospital discharge even before 30 days of chronological age[10]. However we did not classify our low birth babies (<2500gms) further. It included less than 2000gms as well, as the range of birth weight in this age group was 1300gms to 2500gms.

When immune response among term and preterm babies were assessed, present study found more seroconversion in term (86%) than in preterm (80%) babies. But these findings were not statistically significant. Bhave et al[12] and Rostami et al[13] also showed similar findings, where there was no statistically significant different immune response to HBV vaccine among term and preterm babies. A number of studies also showed similar findings and they recommended that there is no need to delay vaccination in preterm babies[14-18]. It is to be noted here that their studies found more immune response than our study. Most series showed more than 90% seroconversion even in preterm infants whereas we found 80% and 86% seroconversion in preterm and term infants. This small difference could be explained by the genetic and racial variations[19].

This study shows that preterm infants are capable of developing almost similar immune response to HBV vaccine as to that of term babies. However, birth weight is shown to be an important factor in determining the immune response.

Conclusion

It may be concluded from this study that our HBV vaccination programme as practiced in EPI schedule may be equally effective in both the term and preterm babies. Even in case of low birth weight babies (including <2000gms) we can follow American Academy of Pediatrics (AAP) recommendation i.e., first dose at 1-2 months of chronological age, may be administered as early as 30 days of chronological age if medically stable or at hospital discharge even before 30 days of chronological age.

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