Original Article

PHASED INTRODUCTION OF HEPATITIS B VACCINATION IN PAKISTAN

Khalida Kazmi[1], M. Aman Ullah Khan[2]

ABSTRACT

Objectives: The study was undertaken to assess the level of sero-protection of children up to five years of age who had received at least one dose of HB vaccination in their infancy.

Methodology It is a cohort study to follow up vaccinated children from four weeks after completion of vaccination to one, three and five years of age of the children. The study was conducted in three districts of North West Frontier Province (N.W.F.P) from August 1991 to 1996. WHO/EMRO supplied single dose of vaccine for HBV in 1991. Five hundred randomly selected children fulfilling the inclusion criteria of having received at least one dose and 100 each of those children having received two or one dose of the vaccine: serology was conducted by using commercial ELISA. (Abbott).

Results: Anti HBs was detected in 70% of infants who had received all the three doses, four weeks after completion of vaccination. After one year the sero-protection was raised to 90%, it fell to 80% after 3 years and 70% after 5 years. The group with two doses of the vaccine had anti HBs positive rates of 70%, 50% and 16% after one, three and five years respectively. The group having one dose had anti HBs positive rates of 50%, 30% and 6% and one, three and five years respectively.

Conclusion: Sero conversion was best in children who had received full course and was significantly lower in those having received partial vaccination.

KEY WORDS: Hepatitis B vaccination, EPI, Phased Introduction.

Pak J Med Sci October - December 2007 (Part-II) Vol. 23 No. 6 913-916

1. Dr. Khalida Kazmi, PhD,
Scientific Research Officer,
Pakistan Medical Research Council,
National Institute of Health,
Islamabad - Pakistan.
2. Prof. M. Aman Ullah Khan, PhD
Prof. of Community Medicine,
Fatima Memorial Hospital
College of Medicine & Dentistry,
Shadman,
Lahore - Pakistan.

Correspondence

Prof. M. Aman Ullah Khan
27-S, D.H.A,
Lahore - Pakistan.
Email:amans786@hotmail.com

* Received for Publication: March 6, 2007
* Revision Received: August 6, 2007
* 2nd Revision Received: October 5, 2007
* Final Revision Accepted: October 6, 2007

INTRODUCTION

Hepatitis B is globally endemic,[1-3] with more than one million deaths per year due to this disease.[1] About 400-500 million people in the world are carriers of Hepatitis B. Human being are the only reservoir and the disease has no zoonotic involvement.[1] The vaccine against this disease has shown promising results in many countries.[3] Studies in Pakistan have shown that 32% of patients with liver diseases were suffering with hepatitis B and 80% of patients with liver cancer were positive for Hepatitis B.[1,4,5] The exposure rate to Hepatitis B and C in normal population has been assessed to be between 24-35%.[6,7] Vertical transmission has been found to play major role in Hepatitis B.[8,9]

The immunization program against Hepatitis B requires good vaccine coverage to be main-

tained for decades. The World Health Organization (WHO) in 1991 recommended that every country should adopt hepatitis B vaccination as a strategy by year 1997, as an integral part of Expanded Program on Immunization (EPI). The global advisory group (GAG) advised that the vaccination of all the infants should be considered in populations with chronic carrier rate of over 2%.[10,11] A demonstration project for integration of hepatitis B vaccination into E.P.I schedule was implemented during 1990-1991. This report is the out come of that demonstration project in the district of Peshawar, Char Sadda and Mardan. The project was undertaken to demonstrate the feasibility of HB vaccination into EPI schedule through examining the level of sero protection of children up to five years of age who had received at least one dose of HB vaccine in their infancy.

METHODOLOGY

From a general population of the area of study which included 4,127,000 persons, and an estimates live births in 1990-1991 of 1,49,000 children, a random cluster sample of 500 children of age under 5 years were selected. Three hundred of those had received all the three prescribed doses of the vaccine, 100 had two and 100 had only one dose. The vaccine was confirmed by examining vaccination cards.

An informed consent was obtained from the parents of children to be selected in the study. One ml of blood was collected each time according to the following schedule:

* First sample at 4-6 weeks after completed or incomplete immunization
* Second sample after one year
* Third sample after three years
* Fourth sample after 5 years

Sera was separated and kept at -20C until tested by three commercial ELISA kits of Abbot (Chicago), AUSZYME for HBs Ag, CORZYME for anti HBc and ASUAB for anti HBs, standard control with anti HBs 10% IU/ml 100, 1000 and 10,000 were run to plot a graph titres of anti HBs were evaluated by s/n ration of OD and plotting in the graph against the level of anti-HBs, HBV markers (HBc Ag & anti HBs).

The cut off values were adopted on the following basis;

a) Anti HBs <10 mIU/ml – Non Responders.
b) Anti HBs level >10 mIU/ml < 100 m IU/ml- Responders
c) Anti HBs level > 100 mIU/ml – High responders
d) HBs Ag positive-infected.
e) Anti-HBs positive but HBs negative- exposure to HBV without disease.

Statistical Validation: The difference between the percentages of sero-conversion and sero-protection antibody concentrations were subjected to Chi-square test for significance.

RESULTS

The EPI coverage record for HB Vaccination was 71%, 67% and 62% for the first, second and third dose of the vaccine respectively. The 300 infants tested four weeks after the completion of the full course of vaccine were HBs Ag negative in all the vaccines. Anti-HB were deteced in 210 (70%) of the infants, the rest (30%) were suspected to be non-responders. Among the subjects with anti-HBs positive 2% had anti-HBs titre <10mIU/ml. The protective level of anti HBs was developed in 270 (90%) after one year, in 240 (80%) after 3 years and in 210 (70%) after five years of vaccinations.

In the infants having received two doses of vaccine, the sero-protection was 70% (out of 100) after one year, 50% (out of 100) after three years and 16% (out of 100) after 5 years of vaccination.

None of the infants with two doses of the vaccine had HBs Ag positive, only four infants out of 100 were anti-HBC positive (4%). The group having only one dose of the vaccine, 50% of them had anti-HBs> 10miu/ml after one year, 30% (30/100) after three years and only 6% (6/100) after five years of age but one was found positive for anti-HBc of HBs Ag.

Table-I. Sero conversion rate in infants followed for 5 years

No. of Doses	No. of Infants	Sero Conversion in Infants				HBs Status	
		At 4 weeks No.(%)	1 year No. (%)	3 years No. (%)	5 years No. (%)	HBs Ag+ve No. (%)	Anti HBc +ve No.(%)
3	300	210 (70%)	270 (90%)	240 (80%)	210 (70%)	---	---
2	100	---	70 (70%)	50 (50%)	16 (16%)	---	4 (4%)
1	100	---	50 (50%)	30 (30%)	06 (6%)	---	---

DISCUSSION

Hepatitis B infection is a world-wide public health problem; as no easy treatment is available. The most effective regime is the vaccination of neonates in the endemic areas of hepatitis B. Hepatitis is a disease that can grossly be controlled or even eradicated as its reservoir is exclusively human and potent vaccines are also available. The elimination of hepatitis from countries or regions, although is theoretically possible, it requires good vaccination programs to be continued for decades. In order to advance towards the eradication of HBV infection, it is essential to create awareness in general public. In Pakistan sero-prevalance surveys were carried out all over the country and the results established.[1-3] A policy of mass immunization against Hepatitis B, was approved by the National Assembly of Pakistan.

The situation analysis of HBV in Pakistan was clearly spelled out in the prevalence of HBV infection in normal population,[2,12] in blood donors[11,13] in pregnant females[14] and in health care personnel.[5,15] The spectrum of liver disease in the country and the mode of transmission [6-10] were established. WHO/ EMRO supplied 507,782 single doses vials for the HBV integration project. The coverage of vaccine was 71%, 67% and 62% for first, second and third doses of HBV vaccine respectively.

The sero-protection rate in the vaccines was 70% when tested after four weeks of vaccination with complete course of three doses. It was 90%, 80% and 70% after one year, three years and five years of vaccination respectively. The sero-protection rate was recorded as the highest after one year of complete vaccination. Under-weight infants, malnourishment and possible trans-placental antibodies might be responsible for these low rates. After one year of complete vaccination sero-protection was highest, with no evidence of HBV infection in the group. The infants who had two doses of the vaccine and could not get the third dose were also tested for antibody titer after one year, three years and five years of age. The results showed a rapid decline in sero-protective antibodies with one dose and two doses of the vaccine but they did not acquire HBV infection during the five years of study period. The infants who had 3 injection-course, had a gradual decline in anti-HBs protective level. This shows that infants at an early age need full course of vaccination for long lasting sero-protection. There were no major barriers in integrating HBV vaccines in the current EPI schedule.

It was not easy to contact the infants during the first week of life as most of the deliveries are conducted at home by the traditional birth attendants and it is a tradition that the baby should not be taken out of house before forty days. However it is not customary in other parts of the country. The results of the project clearly demonstrated the feasibility of integration of HBV vaccine into the current EPI Schedule without major costs.

In Taiwan the mass immunization had decreased the carrier rate from 18% to 8% in a period of seven years. Since 1992 hepatitis vaccine has been a part of Thailand's EPI programme.[12] Thailand started immunization programme in 1992, the rate of coverage of Hepatitis B vaccination was 71.3%-94.3% for three and two doses of the vaccine. Later only 0.7% of the children born after implementation of the novel EPI strategy were HBV carriers. In South Africa after the mass immuniza-

tion against HBV, the frequency of HBV infection was reduced.[16,17] Hepatitis B and its complications are among the most common diseases in Iran.[18] National mass immunization of neonates was started in 1991. They compared the schedule of vaccine as intramuscular and intradermal with reduced (2ug) ID and 10ug IM. It was concluded that interdermal vaccination with 20% of the standard dose was as effective as intramuscular vaccination with evaluated at 18 months of age.[18] The rate of developing hepatitis squalae from acute to chronic hepatitis cirrhosis and hepato cellular carcinoma are inversely proportional to the age at which infections occurs. Five percent of adults, 20% of young and 90% of neonates may lead to chronic hepatitis[10,16] hence prevention of hepatitis B infection in neonates is expected to reduce the prevalence of serious liver disease in the population.

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