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# Simultaneous Administration of Hepatitis B Vaccine with other E.P.I. Vaccines

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**Abstract.** Development of recombinant DNA vaccine against hepatitis B grown on cultured yeast cell has made it possible to mount a world-wide effort to control and eradicate Hepatitis B infection. However, the currently recommended schedules (0, 1 & 2 months, and 0-1 and 6 months) do not coincide with the scheduled visits for other E.P.I. vaccines, and necessitate additional visits for Hepatitis B vaccination. This study was therefore carried out to find out if adequate seroconversion occurs to Hepatitis B vaccine when given with other EPI vaccines or not?

Thirty nine infants born to Australia antigen positive mothers from among 850 screened pregnant mothers were recruited to receive Hepatitis B vaccine (Engerix B-10 micro gram each) at 0, 6 and 14 wks (group A) or at 0, 1 and 2 months (group B). Thirty-one infants were recruited in group A and 8 in group B. The cord blood was collected and the first dose of vaccine was given within 48 hours of birth. Simultaneous B.C.G. was given at the left deltoid. Other E.P.I. vaccines were given qt 6, 10 and 14 wks in group A and at 2, 3 and 4 months in group B. Repeat blood samples were collected prior to giving each dose of Hepatitis B vaccine, and 4 weeks after the last dose. All blood samples were assayed for HBsAg and HBsAb at the National Institute Of Communicable Diseases, utilizing standard ELISA kits.

The seroconversion rates following one, two and three doses of Hepatitis B vaccine were 3.33%, 55.5%, 96.15% and 0%, 62.5% and 100% in group A and B respectively. Only one infant in group A failed to develop HbsAb even after 3 doses of Hepatitis B vaccine, 5 infants in group A were available at 9 months of age and were still positive for HBsAb and negative for HBsAg. Recombinant DNA Hepatitis B vaccine (Engerix-B) is a highly effective vaccine which can safely and effectively be given together with other childhood vaccines.
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***Key words:*** *Hepatitis B; Vertical transmission; Post exposure prophylaxis; E.P.I.*

Hepatitis B is a major public health problem as the chronic carrier stage can cause long term liver damage and hepatocellular carcinoma.[1-4] Vertically acquired infection by infants from carrier mothers has an almost 90% risk of causing a chronic carrier stage.[5-7] While screening of blood donors and sterilisation of needle etc. can prevent the majority of horizontal transmissions, these measures are ineffective in curbing vertical transmission and its consequences. The recombinant DNA vaccine against Hepatitis B is an effective tool for preventing vertical transmission by vaccination of

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infants born to HBsAg carrier mothers. Three doses of vaccine given at 0, 1 and 6 months or at 0, 1 and 2 months (with booster at 12 months) as suggested by W.H.O. has been shown to have more than 90% efficacy.[3,8-10] Due to this reason W.H.O. recently has proposed the inclusion of Hepatitis B vaccine as the 'Seventh vaccine' in the National EPI Programmes of all member countries which fall in the high or intermediate risk groups.[1,5] India is classified in the intermediate prevalence category with prevalence rates between 2-7%.[2,3]

Besides epidemiological and economic considerations, for any vaccine which is to be included in the National programme, it is important to have an easily feasible schedule. Visits in the either of the currently recommended immunisation schedule for HBV, i.e. 0, 1 and 6 months or 0, 1 and 2 months do not coincide with recommended visits for EPI vaccines which are given at 0, 6 and 14 weeks and 9 months, thus necessitating additional visits which would lead to higher drop out rates and decreased compliance.[11] It would be more practical and convenient therefore if the Hepatitis B vaccine can be given at the same time as other EPI vaccine. This study was therefore carried out to study feasibility and efficacy of giving Hepatitis B vaccines at the same time as other EPI vaccines.

TABLE 1. Schedule for Follow up of Infants and Immunization of Infants Born to HBsAg Positive Mothers

| Schedule A | Schedule B |
|---|---|
| < 48 hr.<br>Cord blood<br>HB vaccine 1st dose<br>B.C.G. | < 48 hr<br>Cord blood<br>HB vaccine 1st dose<br>B.C.G. |
| *6 weeks* Blood sample<br>HB vaccine 2nd dose<br>DPT<br>OPV 1st dose | *1 month* Blood sample<br>HB vaccine 2nd dose |
| *10 weeks* DPT<br>OPV 2nd dose | *2 months* Blood sample<br>HB vaccine 3rd dose<br>DPT<br>OPV 1st dose |
| *14 weeks* Blood sample<br>HB vaccine<br>DPT<br>OPV 3rd dose | *3 months* Blood sample<br>DPT<br>OPV 2nd dose |
| *18 weeks* Blood sample | *4 months* DPT<br>OPV 3rd dose |
| *9 months* Blood sample<br>Measles vaccine | *9 months* Blood sample<br>Measles vaccine |

## Material and Methods

Eight hundred and fifty pregnant women admitted to the labour rooms of L.N.J.P.N. hospital were randomly tested for markers of Hepatitis B infection namely HBsAg and HbeAg by latex agglutination test and ELISA respectively. The former served as a rapid screening test. Liver function tests were done on the HBsAg positive women. Cord blood samples were collected at birth.

Thirty nine infants born to HBsAg positive women (as detected by latex agglutination test) were recruited for further study. These neonates were given 10 microgram Engerix B intramuscularly within 48 hours of birth into anterolateral thigh muscle. B.C.G. was given simultaneously over left deltoid region.

Thereafter, these infants were followed up into 2 groups using 2 schedules 'A' and 'B'. The main aim of the study was to recruit 30 infants into schedule 'A' and only after that was achieved, were any further infants born to HBsAg positive mothers were taken up under schedule 'B'. This was not intended as a controlled trial. The schedule of vaccination and blood sampling under the 2 schedules is shown in Table 1.

Antibodies against HBs antigen was tested before each dose of HB vaccine, and 4 weeks after the last dose by the ELISA technique. Adequate serological response was indicated by presence of anti HBs in infant's sera.

The infants were examined and weighed at each visit. Any adverse reaction to vaccination was enquired into and recorded.

An attempt was made to follow these infants at 9 months to look for persistence of HBs antibodies.

## Results

The age range of women recruited for study varied from 16-38 years with a mean of 23.68 yrs. The parity varied from 0 to 12 with a mean of 3.68.

Thirty nine (4.58%) of the 850 mothers tested were positive for HBsAg by latex agglutination test, while 54 (6.34%) were positive for HBsAg by ELISA. Only 7 (17.94%) of these 39 mothers who were positive for HBsAg were also positive for HBeAg.

Cord samples of one (i.e. 2.55%) of 39 infants born to HBsAg positive mothers, was also positive for HBsAg. Subsequent blood samples of this child were negative

Table 2. Serological Status of Children Before and After Different Doses of Hepatitis B Vaccine

| | Group A | | | Group B | | |
|---|---|---|---|---|---|---|
| | No. under follow-up | Anti HBs +ve | Sero conversion | No. of under follow-up | Anti HBs +ve | Sero conversion |
| Cord blood | 31 | 0 | – | 8 | 0 | – |
| After 1st dose | 29 | 1 | 3.33 | 8 | 0 | 0 |
| After 2nd dose | 27 | 15 | 55.3 | 8 | 5 | 62.5 |
| After 3rd dose | 26 | 25 | 96.5 | 8 | 8 | 100 |

for HBsAg.

**Followup.** About 31 infants received the 1st dose of Engerix B at birth under schedule A, 30, 29, 27 and 26 infants were available for 2nd and 3rd dose of vaccine, and for follow up and blood sampling at 18 wks respectively (Table 2).

Only 8 infants were recruited in group B and all of these infants reported for all their scheduled visits at 1, 2 and 3 months.

**Seroconversion.** Seroconversion rates under schedule A was 3.33%, 55.5% and 96.15% after 1st, 2nd and 3rd dose of vaccine. Under schedule B, 0%, 62.5% and 100% seroconversion response was seen after 1st, 2nd and 3rd dose of vaccine (Table 2).

Failure to develop anti HBs was seen in only one of the infants, i.e. 2.55% under schedule A. One infant of the 31 recruited infants in group A developed HBs antigenemia on follow up despite showing seroconversion to 3 doses of vaccine

**Side effects.** No significant side effects were noticed following vaccination in either group.

## Discussion

This study was aimed at studying efficacy of 3 doses of Engerix B, given at 0, 6 and 14 weeks with BCG, DPT and OPV. After sufficient infants were recruited under schedule A, remaining infants were taken up under schedule B.

HBsAg positivity among pregnant women was 4.58% in this study which is comparable to reports from other parts of the country where different studies have reported prevalence rates varying from 0.6-3.7%. The prevalence rates have varied depending on the kind of test used. Generally higher results have been obtained using micro ELISA. In our study also, 54 (6.34%) mothers were positive for HBsAg when tested by micro ELISA. China, Hong Kong, Taiwan have been shown to have higher HBsAg prevalence (7-10%) while U.K., U.S.A. have lower prevalence rates.[1,12,13,14]

HBeAg positivity which is an indicator of high infectivity was noted in 17.94% of HBsAg positive pregnant women,[2,3] which denotes a high degree of infectivity.

Only one cord blood sample was found positive for HBsAg. This was most likely due to accidental contamination with maternal secretions and not to intrauterine transmission, as consequent samples of this child were negative for HBsAg. In schedule A, anti HBs was seen in 3.33% of infants after 1st dose, 55.5% infants after 2nd dose and 96.15% of infants after 3rd dose, which is similar to the 0, 1 and 6 month schedule shown by others.[1,15-18] It is as efficacious as those schedules which use a combination of HB vaccine and HBIG.[13] The results of schedule A was comparable to that of schedule B also where in seroconversion was seen in 0%, 62.5% and 100% of infants after 1st, 2nd and 3rd dose of vaccine respectively.

Failure to respond to three doses of vaccine was seen in only one infant which may be due to either intrauterine infection, inherent inability of the recipient to respond to vaccination, or simply a longer phase period prior to development of antibodies. Such failures have been reported by other authors also.[19-21]

Two recent studies from Senegal[22,23] have also shown that HB vaccine was quite effective when given at the same time as DPT & Polio or with Tetanus Toxoid and did not interfere with the seroconversion of other simultaneously administered anti-

gens. Hence, it can be concluded that Engerix B is a safe, efficacious vaccine which can be administered along with other vaccines of EPI schedule as and when such a policy is taken up. However, before a decision is taken regarding inclusion of HB vaccine in National EPI Programme more studies on cost benefit analysis and epidemiology of HBV in our country are needed as well as logistical problems of reaching every newborn within 48 hours of birth as domicilliary deliveries still account for more than 80% of births in our country.

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## *THE FAMILY OF TOMORROW*

### A Message from a World Famous Author

In order to be successful, the family ought to embrace several generations, since it is essential for the young and the less young to live together, understand one another and help one another. I have no doubt that the future will see the "extended" family being recreated, in the sense that it will not be based simply on the notion of blood relations but rather on ties of affection.

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