IMPACT OF THE HEPATITIS B MASS VACCINATION PROGRAM IN THE SOUTHERN PART OF THAILAND

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Abstract: By 1992, hepatitis B vaccine had been included in the Expanded Program of Immunization (EPI) on a nation-wide scale in Thailand. With the results now available from Songkhla Province in the south of Thailand, we are able to fully evaluate its impact on the prevalence of HBV infection and carrier rate. The population studied comprised 180 randomly selected children aged between 2 months and 15 years who had attended Hat Yai hospital due to any acute illness affecting neither the liver nor the immune system. Their sera were examined for the hepatitis markers HBsAg, anti-HBs and anti-HBc, respectively, using a commercially available test kit. We detected anti-HBs in 106 of the 180 children (58.9 %) with its prevalence peaking within the age groups of 0-2 (94.4 %) and 3-5 years (75.6 %), respectively. Six children, five within the age groups of 6-10 and 11-15 years showed anti-HBc, one of them was diagnosed as a chronic carrier; the sixth one of the age group of 0-2 years most probably displayed passive maternal antibodies. The overall HBV carrier rate amounted to 0.55%. The hepatitis B mass vaccination program has proved highly efficient in protecting newborns from infection and heralds the promise of eventually eradicating hepatitis B virus in the not so far future.

INTRODUCTION

Hepatitis B virus (HBV) infection constitutes a health problem on a worldwide scale, particularly in Southeast Asia and Africa, causing a wide range of liver diseases which frequently either turn chronic or culminate in fatal outcomes. The global estimate as to the number of HBV carriers lies between 400 and 500 million and over a million deaths are attributed yearly to the consequences of HBV infection (Moradpour and Wands, 1995; Anonymous, 1988).

Perinatal transfer of HBV from an asymptomatic carrier mother to her fetus is considered a major mode of transmission responsible for 35-40 % of HBV infections encountered worldwide annually (Maynard *et al,* 1988; Ghendon, 1987). Women seropositive for hepatitis B surface antigen (HBsAg) as well as precore antigen (HBeAg) harbor high titers of HBV thereby increasing the risk of infecting their children (Alter *et al,* 1976; Hindman *et al,* 1976; Shikata *et al,* 1977) to such extent that 65-93 % of neonates born to these mothers become chronic HBV carriers within the first 12 months (Beasley *et al,* 1977; Stevens *et al,* 1975; Beasley *et al,* 1983; Wong *et al,* 1984; Xu *et al,* 1985; Pongpipat *et al,* 1985; Lo *et al,* 1985). Especially in Asia, even children of HBsAg positive mothers that have not been infected during their first year continue to be at risk in that by the age of four years, 40 % born to HBeAg positive mothers and 75 % born to HBsAg positive mothers exhibit symptoms characteristic of HBV infection (Beasley and Hwang, 1983).

In order to reduce the frequency of hepatitis B infections and to eventually eliminate the disease altogether hepatitis B vaccine administered to newborns on a global basis ought to be made imperative as the reservoir of chronic carriers responsible for spreading HBV can thereby be diminished. In recognition of this requirement it has been recommended by the World Health Organization that all countries adopt such a preventive strategy by the year 1997 (WHO, 1991).

Hence, hepatitis B vaccine ought to display high as well as long-lasting protective efficacy in newborns of mothers positive for HBsAg and HBeAg if the ultimate aim of HBV eradication is to be attained. In Thailand, the Ministry of Public Health (MOPH) initiated the program for mass administration of HB vaccine as a pilot project conducted in 2 provinces, Chiang Mai and Chon

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Buri, in 1988. Hepatitis B vaccine to be delivered in three doses, one each at birth, 2 and 6 months of age, respectively, was introduced as part of the expanded program on immunization (EPI) and evaluated over a four-year period (Chunsuttiwat *et al,* 1997). In 1991, MOPH extended the project to 10 additional provinces including Songkhla Province in the south of Thailand, until in 1992 mass HB vaccination had become part of the EPI on a nationwide scale. With the data as to its evaluation now for the first time being comprehensive, we report here the impact of the hepatitis B vaccination program on the HBsAg and HBeAg carrier rate among the population in Thailand's south.

MATERIALS AND METHODS

Population study

The population examined comprised children between the age of 2 months and 15 years all of whom were residents of Songkhla Province and attended the pediatric department at Hat Yai Hospital due to acute illness. The exclusion criteria were chronic illness, compromised immune response or history of medication with immunosuppressive drugs, as well as lack of reliable history regarding vaccination. Of the 354 children within the respective age group, 16 were excluded due to unreliable history of vaccination. Out of the remaining 338, 180 were selected at random to be subjected to tests for hepatitis B serological markers. Of those, 105 were male, 75 female, 120 were residents of Hat Yai district, the additional 60 lived in the other districts of Songkhla Province.

Songkhla Province is one of the southernmost provinces of Thailand at a distance of approximately 950km from Bangkok, bordering on the Gulf of Siam in the east and on Malaysia in the south, with Hat Yai as its provincial capital. Economically, the province almost entirely depends on the income garnered from its vast rubber plantations and from fishery and hence, the majority of its population resides in rural areas.

After having obtained informed consent from their parents as to the objective of the study, blood samples were obtained, the sera separated and kept at -20°C until further tested.

Laboratory tests

The presence of HBsAg, anti-HBs and anti-HBc, respectively, was determined by using a commercially available ELISA kit (Human Gesellschaft für Biochemica und Diagnostica, Wiesbaden, Germany). The results were divided into positive and negative according to the cut-off value provided by the manufacturer's instructions.

Data analysis

Upon analysis, the data were depicted as per cent among the different age groups.

RESULTS

Of the 180 children subjected to the test, 129 (71.7 %) had completed the entire course of hepatitis B vaccination consisting of three doses, 18 (10 %) had not received all three doses, and 33 (18.3 %) had altogether not been vaccinated. The details pertaining to children born before and after HB vaccine's inclusion into the EPI are shown in Table 1.

Of the 180 children tested, there was only one case (0.5 %) at the age of 12 years that showed evidence of persistent HBV infection with subsequent asymptomatic carriage in that the serum was found positive for HBsAg. One hundred and six had developed anti-HBs antibody, 5 showed evidence of previous infection by the presence of anti-HBc antibody, one at the age of 2 months harbored

Table 1

Coverage of hepatitis B vaccination before and after its inclusion into EPI.

Hepatitis B vaccination	Birth of children			
	before EPI		after EPI	
	No.	%	No.	%
Complete course	31	47.7	98	85.2
Incomplete course	7	10.8	11	9.6
No vaccination	27	41.5	6	5.2
Total	65	100	115	100

passive anti-HBc antibody received from the mother and 4 had been infected but had developed anti-HBs antibody thus clearing the virus. The prevalence of serological markers for hepatitis B is shown in Table 2 and Fig 1.

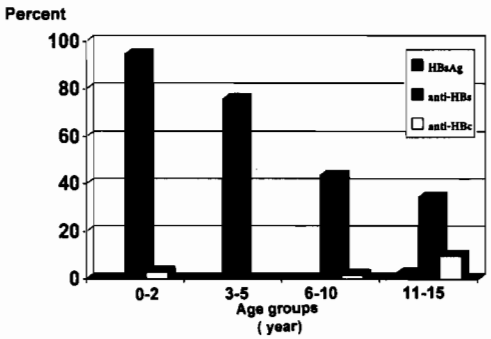

Fig 1–Seroprevalence of hepatitis B markers in relation to age groups.

1989). The remaining five children having contracted the virus belonged to the age groups of 6-10 years (1) and 11-15 years (4), respectively. In other words, it can be assumed that they were born before hepatitis B vaccine had been included as an integrated part of the EPI. Four of those had developed protective anti-HBs whereas one had become an asymptomatic carrier still exhibiting HBsAg.

In total, anti-HBs amounted to 58.9 % among all subjects tested with the highest value (94.4 %) obtained with the age group of between 0-2 years, which gradually declined over 75.6 % with the age group of 3-5 years, then dropping sharply to 43.5 % with the age group of 6-10 years until reaching its minimum of 34.1 % with the age group of 11-15 years. Hence, the present data are comparable to those having been reported after conclusion of the pilot project (Chunsuttiwat *et al,* 1997) conducted at Chon Buri and Chiang Mai provinces between 1988 to 1993. The results of that study showed the protective efficacy at 83.07 %.

Table 2

Prevalence of serological markers for HBV among different age groups.

Age group	No.	HBsAg		anti-HBs		anti-HBc	
(years)		No.+ve (%)		No.+ve (%)		No.+ve (%)	
0 - 2	36	0	(0)	34	(94.4)	1	(2.8)
3 - 5	41	0	(0)	31	(75.6)	0	(0)
6 - 10	62	0	(0)	27	(43.5)	1	(1.6)
11 - 15	41	1	(2.4)	14	(34.1)	4	(9.8)
Total	180	1	(0.55)	106	(58.9)	6	(3.3)

DISCUSSION

The present data clearly demonstrate the protective efficacy of the hepatitis B vaccine mass immunization program in that the carrier rate could be reduced to 0.5 % among children of the age group between 2 months and 15 years. Six children had detectable anti-HBc antibody one of who was only two months old and thus was still expressing anti-HBc he had passively received from his mother. This passive antibody remains detectable in babies up to the age of 13 months (Poovorawan *et al,*

Again, as with anti-HBc, yet inversely related, a clear dependence on the respective age group can be detected indicating the presence of protective anti-HBs to be much more prevalent among the age groups of 0-2 and 3-5 years, respectively, that is, after hepatitis B vaccine had become an integrated part of the EPI.

After the results of the present study the final set of data has been obtained in order to fully evaluate the impact of hepatitis B vaccine administered within the framework of a mass vaccination program in Thailand. As previously reported, the

vaccine has been shown to be safe, immunogenic and highly efficient among the group of children tested (Poovorawan *et al,* 1989).

With the exception of one child who became a chronic carrier, all vaccinated children had produced high titers of anti-HBs, which they retained after administration of the booster dose at month 12. Therefore, protection of these children might well be extended for a period of several years. In fact, as our group has established in a separate study, after completion of three doses of hepatitis B vaccine protection can be guaranteed for a period exceeding 10 years without the necessity of an additional booster dose (Poovorawan *et al,* 1997)

As regards the true impact of hepatitis B mass vaccination, it probably for the first time offers the opportunity to efficiently reduce the number of infected newborns, thus the rate of chronic carriers and on the long run, as has been reported from Taiwan (Chang *et al,* 1997), the number of children, as well as adults diagnosed with hepatocellular carcinoma. Moreover, with the availability of hepatitis B vaccine and its inclusion in the EPI on a nation-wide scale, hepatitis B virus might eventually be eradicated in Thailand, an area hyper-endemic for this agent and the fatal sequelae infection which it draws in its wake.

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