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World J Gastroenterol, 2000; 6(3):381-383
World Journal of Gastroenterology
 ISSN 1007-9327

A 12-year cohort study on the efficacy of plasma-derived hepatitis B vaccine in rural newborns

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Subject headings hepatitis B vaccine; HBsAg; vaccination; rural newborn; cohort study

Liu HB, Meng ZD, Ma JC, Han CQ, Zhang YL, Xing ZC, Zhang YW, Liu YZ, Cao HL. A 12-year cohort study on the efficacy of plasma-derived hepatitis B vaccine in rural newborns. ***World J Gastroentero***, 2000;6(3):381-383

Abstract

AIM To understand the anti-HBs persistence and the long-term preventive efficacy in rural newborns after vaccination with plasma-derived he patitis B vaccine.

METHODS In the time of expanded program on immunization (EPI), the newborns were vaccinated with 10 μg × 3 **doses of hepatitis B vaccine and** 762 **newborns who were HBsAg negative after primary immunization were selected for cohort observation from** 1986 **to** 1998**. Their serum samples were detected qualitatively and quantitatively for hepatitis B infecting markers, including HBsAg, anti-HBs and anti-HBc by SPRIA Kits. The annual HBsAg positive conversion rate was counted by life-table method.**

RESULTS ① The anti-HBs positive rate was 94. 44% **for the babies born to HBsAg negative mothers and** 84.21% **for those born to HBsAg positive mothers in the 1st year after immunization, and dropped to** 51.31% **and** 52. 50% **in the** 12**th year respectively. GMT value was dropped from** 31.62 **to** 3.13 **and** 23.99 **to** 3. 65 **in the** 2**nd to the** 12**th year respectively. There was a marked drop in GMT at the** 3**rd to the** 5**th year, and in anti-HBs positive rate at the** 9**th to the** 10**th year. ② In the period of** 12 **years observation, the person-year HBsAg positive conversion rates were** 0.12% **(**5/4150.0**) in newborns born to HBsAg negative mothers and** 0.20% **(**1/508.0**) in those born to HBsAg positive mothers, and none of the HBsAg positive converted children became HBsAg chroni c carriers. Compared with the baseline before immunization, the protective rates were** 97.19% **and** 95.32% **respectively.**

CONCLUSION The protective efficacy of plasma-derived hepatitis B vaccine persisted at least 12 **years, and a booster dose seems not necessarywithin at least** 12 **years after the primary three-doses immunization to newborns born to HBsAg negative mothers.**

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Supported by the National "95" Scientific Foundation, No. 96-906-03-02
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Received 2000-01-18 **Accepted** 2000-01-28

INTRODUCTION

In recent years, many studies on the efficacy of hepatitis B plasma-derived vaccine demonstrated that the anti-HBs antibodies were declined gradually, but the protective rate for children vaccinated with three-doses hepatitis B vacci ne was still more than 80%[1,2]. To understand the anti-HBs persistence and long-term efficacy in newborn, a 1-12 year experimental study on hepatitis B plasma-derived vaccine was carried out among newborns vaccinated with three doses 10 mg/L vaccine in rural area.

MATERIALS AND METHODS

Objects

Newborn infants from one township in Zhengding County, Hebei Province, were vacc inated during 1986-1989. A total of 762 infants who were HBsAg negative after pr imary vaccination were selected for cohort observation, of them 688 born to HBsAg-negative mothers, and 74 to HBsAg carrier mothers. The annual HBsAg positive conversion rate for newborn infants was 4.72% before immunization.

Vaccine and immunization

Hepatitis B plasma-derived vaccine was produced by Beijing Institute of Biologi cal Product. The newborns were immunized with three doses vaccine at 0mo, 1mo and 6mos of age by well-trained

nurses between 1986-1989 under the rural area immunization program launched in 1986. The first dose was vaccina ted at 2.7 mo-0.3 mo (95% CI). The coverage rate of vaccination with a complete course of 3-dose hepatitis B vaccine was 91.5%.

Blood collection and laboratory study

Blood samples were collected from infants by venipuncture at intervals of one or two years. Serum HBsAg, anti-HBs and anti-HBc were tested by RIAs from Beijing Institute of Biological Product. Those who showed HBsAg (S/N value $\geqslant$2.1), anti-HBc (CO/S value $\geqslant$2.0) or both were defined as HBV infection, and anti-HBs (S/N value $\geqslant$2.1) as immunity.

RESULTS

Persistence of anti-HBs after vaccination

The 688 new born babies were born to HBsAg negative mothers, and 74 were born to HBsAg positive mothers. Anti-HBs positive rate was gradually dropped from 94.44% to 51.31% and 84.21% to 52.50% in the 1st-12th year respectively. GMT value was dropped from 31.62 to 3.13 and 23.99 to 3.65 in the 2nd-12th year respectively. There was a marked drop in GMT value at the 3rd-5th year, and in anti-HBs positive rate at the 9th-10th year. Compared with infants born to HBsAg negative mothers, GMT value was lower in infants born to HBsAg positive mothers (Table 1).

HBsAg annual positive conversion rate for vaccinated children

In the period of 12 years follow-up, 5 children born to HBsAg-negative mother s became HBsAg positively conversed. Two of them occurred at the 5th year and the rest occurred at the 9th-10th year. The person-year HBsAg positive conversi on rate was 0.12% (5/4150.0). One child born to HBsAg positive mothers becam e HBsAg positively conversed, and it occurred at the 5th year. The person-year HBsAg positive conversion rate was 0.20% (1/508.0). None of 6 HBsAg po sitive converted children became HBsAg chronic carriers (Table 2). Compared with the baseline before immunization, the protective rates were 97.19% and 95.32% respectively (Table 3).

Table 1 Dynamic change of anti-HBs positive rate and GMT after vac cination

Years vaccinated	Mothers HBsAg (-)			Mothers HBsAg (+)		
	No.tested	Positive rate (%)	GMT (S/N)	No.tested	Positive rate (%)	GMT (S/N)
1	18	94.44	26.30	19	84.21	15.14
2	134	89.55	31.62	48	95.83	23.99
3	232	89.22	26.30	51	92.16	22.91
4	344	85.17	18.62	51	73.33	6.46
6	296	79.39	9.77	54	79.63	8.71
7	608	80.76	9.33	58	86.21	7.78
8	599	78.30	6.17	56	75.00	5.25
9	517	57.79	4.17	48	60.24	3.47
10	412	50.24	3.09	23	34.78	2.51
11	173	51.80	2.86	30	56.00	2.91
12	424	51.30	3.13	20	52.50	3.65
χ^2m-h		226.12			338.58	
P value		*P*<0.001			*P*<0.001	

Table 2 HBsAg person-year positive conversion for immunized children

Follow-up (year)	Mother HBsAg (-)			Mother HBsAg (+)		
	No. person year	No. positively converted	Annual positive conversion rate	No. person year	No. positively converted	Annual positive conversion rate
1	9.0	0	0.00	9.5	0	0.00
2	76.0	0	0.00	33.5	0	0.00
3	183.0	0	0.00	49.5	0	0.00
4	288.0	0	0.00	51.0	0	0.00
5	454.0	2	0.44	55.5	1	1.80
6	428.0	0	0.00	57.0	0	0.00
7	450.0	0	0.00	56.0	0	0.00
8	602.0	0	0.00	57.0	0	0.00
9	482.0	2	0.34	52.0	0	0.00
10	486.0	1	0.20	35.5	0	0.00
11	292.5	0	0.00	26.5	0	0.00
12	298.5	0	0.00	25.0	0	0.00
Total	4150.0	5	0.12	508.0	1	0.20

Table 3 Protective rate to vaccinated neonates

Mother HBsAg	Observed numbers	Person year numbers	HBsAg positive conversion numbers	Annual Positive conversion rate	Effec tive protective rate
Negative(-)	688	4150.0	5	0.12	97.19
Positive (+)	74	508.0	1	0.20	95.32
Total	762	4658.0	6	0.13	96.96
Baseline	562	1124.0	48	4.27	

DISCUSSION

The ultimate strategy for newborn vaccination with hepatitis B vaccine is contr olling and eliminating hepatitis B. Many specialists think that newborns should be vaccinated within 24 hours which is more effective for preventing HBV mother -infant transmission. In recent studies, some reports say that the risk of HBV infection should increase with the decline of anti-HBs positive rate and GMT value after vaccination of hepatitis B vaccine[2,3]. Thus, a booster of hepatitis B vaccine should be given. In this study, anti-HBs positive rate declined with age, so was GMT value. The anti-HBs positive rate declined markedly from the 9th to the 10th year, and maintained 50% or so at the 10th-12th year. GMT value declined markedly from the 3rd to the 5th year. Therefore, if we only analyze anti-HBs positive rate and GMT value, it is the best schedule to revaccinate at 3-5 years of age after the primary 3-doses regimen.

With the long-term observation of hepatitis B vaccine, more and more scholars think that the protective efficacy for immune responder could persist several years, even if anti-HBs may have declined to undetectable levels. This may be due to the good memory response to hepatitis B vaccination. The higher anti-HBs level after booster immunization dropped quickly with time, and at the end of 3-5 years dropped to the level of children who had not received booster immunization[4,5]. The evaluation of the immune efficacy of hepatitis B vaccine should induce antibody level, but the dynamic of HBsAg and the chronic carrier rate during ten years of immunization. Cao *et al*[6] reported that anti-HBs level declined with years after vaccination and HBsAg positive conversion had not been detected among children born to HBsAg negative mothers in Hunan. Our study indicated that none of children born to HBsAg negative mother became HBsAg chronic carrier within 12 years after vaccination with hepatitis B vaccine, although a few children were infected with HBV and positive for HBsAg. The protective rate to those newborns born to HBsAg negative mother was still more than 95% within 12 years. We believed that long-term efficacy of hepatitis B vaccine was better and the children would have benefited from life-long hepatitis B vaccine. A booster dose seems unnecessary for children born to HBsAg negative mothers within 12 years after primary 3-dose regimen. It was reported by Cao *et al*[7] that HBsAg positive conversion children born to HBsAg carrier mothers may become HBsAg chronic carriers after vaccination with hepatitis B vaccine, and most of them occurred at 2-3 years of age. In our study, only 1 of 74 children born to HBsAg carrier mother became HBsAg positively conversed, but did not become HBsAg chronic carrier within 12 years after vaccination. In order to improve the immune efficacy for those children born to HBsAg positive mothers, the dynamic of HBsAg carrier rate should be observed further in vaccinated children on a large scale.

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Edited by You DY
proofread by Sun SM