

Efficacy of hepatitis B vaccine in susceptible spouses of chronic hepatitis B virus infected individuals at the time of marriage

Mohammad R. Roushan, MD, Hayedeh Samie, MD, Mohammad J.S. Amiri, PhD.

ABSTRACT

Objectives: To evaluate the efficacy of hepatitis B virus (HBV) vaccine in susceptible spouses at the time of marriage.

Methods: From April 2003 to December 2005, 60 cases of susceptible wives of infected husbands and 32 cases of susceptible husbands of the infected wives in Babol north of Iran, received recombinant hepatitis B (HB) vaccine at the time of marriage followed with the second and third doses at 1, and 6 months. Post vaccination tests for hepatitis B surface antigen (HBsAg), anti-HBs and anti-hepatitis B core (HBc) were assessed 2 months of the later dose. The HBs antibody levels of ≥ 10 mIU/ml was considered to be protective. Those with anti-HBs levels of < 10 mIU/l received the second series of HBV vaccination.

Results: The mean age of the infected husbands was 26.4 ± 6 years and for infected wives were 22.7 ± 4.7 years. Seventy (76.1%) cases were HBsAg and anti-hepatitis B e (HBe) positive. Among the recipients of vaccine, the mean age of females was 19 ± 3.8 years and in males was 25.2 ± 4.8 years ($p=0.007$). The HBs antibody levels of ≥ 10 mIU/ml were detected in 79 (85.9%) cases. The HBs antibody levels of > 100 mIU/ml were developed in 76.7% males and in 75% females ($p=0.430$). Twelve (13%) cases were non-responder and among them 11 (91.7%) cases responded to the second course of HBV vaccination. The HBs and HBc antibodies were developed in one case.

Conclusion: This study shows that administration of hepatitis B vaccine at the time of marriage prevents the transmission of hepatitis B virus in susceptible spouses.

Saudi Med J 2007; Vol. 28 (4): 540-543

From the Department of Infectious Diseases (Roushan), Department of Gynecology (Samie), and the Department of Laboratory Medicine (Amiri), Babol Medical University, Babol, Iran.

Received 28th August 2006. Accepted 16th December 2006.

Address correspondence and reprint request to: Dr. Mohammad R. Roushan, Department of Infectious Diseases, Yahyanejad Hospital, Babol Medical University, Babol 4717641367, Iran. Tel. +98 (111) 3234387. Fax. +98 (111) 2227667. E-mail: hagar2q@yahoo.ca

One of the most important routes of transmission of hepatitis B virus (HBV) is by permucosal exposure to infectious body fluids, sexual contact with an infected person.¹⁻² In endemic areas, hepatitis B is an important cause of mortality and is the main cause of cirrhosis and hepatocellular carcinoma. Vaccination against hepatitis B prevents not only the morbidity and mortality due to acute viral disease, but also chronic hepatitis B and its ultimately fatal complications.³ The presence of hepatitis B e antigen (HBeAg) in carriers has been mentioned as a possible factor determining the rate of transmission.⁴⁻⁶ Several studies showed that acute hepatitis B occurred in married cases and transmission between spouse was a predominate route.⁷⁻¹⁰ The transmission of HBV from hepatitis B surface antigen (HBsAg) carrier women to their husbands was supposed to take place shortly after marriage.⁸ For unvaccinated persons sustaining an exposure to HBV, a combination of hepatitis B immune globulin (HBIG) and hepatitis B vaccine is recommended.¹¹⁻¹² In such instances as living with a hepatitis B positive person it is desirable to acquire protection as quickly as possible. This study was designed to evaluate the effectiveness of HBV vaccine and antibody response in susceptible spouses of infected wives or husbands.

Methods. From April 2003 to December 2005, chronic hepatitis B virus infected males or females who had counseling for marriage in Babol north of Iran were entered into this study. At the base line, HBsAg, HBeAg, hepatitis B surface antibody (HBsAb) and anti-hepatitis B core (HBc) antibody were assessed in all subjects (HBsAg, from Bio Merieux, the Netherlands; anti HBs from Radim Italy, anti HBc, HBeAg and HBeAb from Dia.Pro Diagnostic BioProbes,

Italy). These tests were also performed in the spouses of these HBV infected individuals. Subjects with HIV infection, diabetes mellitus, chronic renal failure, and those with evidence of previous HBV infection were excluded from this study. All susceptible spouses received the first dose of HBV vaccine (20 microgram recombinant vaccine) exactly at the time of marriage followed with the same dose of HBV vaccine at 1 and 6 months later. No preventive measures were used by these spouses during the vaccination period. Testing for HBsAg, HBsAb and anti-HBc antibody were performed one to 2 months after their later dose. Those with HBsAg and anti-HBc negative but anti-HBs antibody positive were considered as vaccine responder. Those positive for HBs and anti-HBc antibodies were considered resolved HBV infection. Those negative for HBsAg, HBc antibody but positive anti-HBs levels <10 mIU/ml were considered as non-responder. Anti-HBs levels of 10-99 mIU/ml were low and ≥ 100 mIU/ml was considered as well responder. Non-responder cases received the second series of HBV vaccination as described above. Testing for HBsAg, HBsAb and anti-HBc antibody were performed one month after the later dose. The local ethic committee approved the study and all cases gave their informed consent.

Statistical analysis. Categorical variables were tested by the two-tailed chi-square test and Fisher exact test. Poor and well responders either in males or females and HBeAg or anti-HBe status of spouses were compared. Ninety-five percent confidence intervals (CIs) were calculated when appropriate. Statistical significance was taken as $p < 0.05$.

Results. Sixty males and 32 females with chronic hepatitis B virus were studied. The mean age of

males and females was 26.4 ± 6 and 22.7 ± 4.7 years, respectively ($p=0.003$). Among 60 HBV infected males, 46 subjects (76.7%) were anti-HBe and 14 cases were HBeAg positive. Among 32 female cases, 24 (75%) cases were anti-HBe positive ($p=0.526$). Characteristics of the patients are shown in **Table 1**. The mean age of the wives of 60 HBV infected males was 22.5 ± 4.8 years and for husbands of 32 infected females was 25 ± 3.8 years ($p=0.007$). Anti-HBs levels ≥ 10 mIU/ml was developed in 53 (88.3%) wives and in 26 (81.3%) susceptible husbands ($p=0.325$) (**Table 2**). Seven females and 5 males were non-responder and among them, protective levels of anti-HBs were developed in 11 (91.7%) cases after the second series of vaccination. Only one male became anti-HBs and anti HBc antibody positive. Anti-HBs antibody levels ≥ 100 mIU/ml developed in 70 (76.1%) cases. There were no significant differences in the development of protective levels of anti-HBs with regards to gender, HBeAg or anti-HBe positive status of their spouses.

Discussion. In Iran, approximately 22-37% of the general population have previous exposure to HBV as judged by serological markers, such as HBsAg, anti-HBs and anti-HBc and the reported prevalence of HBsAg carriage varies from 1.3-8.7% in the general population.¹³⁻¹⁷ In this country, universal neonatal vaccination against HBV started in 1993 according to the World Health Organization recommendations. At present, it seems that transmission of HBV between spouses is the main route of transmission of HBV. In this study, we found that vaccination of susceptible spouses at the time of marriage produced protective levels of antibody in 79 (85.9%) subjects without any

Table 1 - Characteristics of hepatitis B virus infected spouses at baseline.

Characteristics	n	(%)
Spouse		
Male	60	(65.2)
Female	32	(34.8)
HBV markers		
HBsAg and anti HBe ⁺	70	(76.0)
HBsAg and HBeAg ⁺	22	(24.0)
Anti HBe⁺ spouse		
Male	46	(76.7)
Female	24	(34.3)
HBeAg⁺ spouse		
Male	14	(63.6)
Female	8	(36.4)

HBV - hepatitis B virus, HBsAg -hepatitis B surface antigen, HBe⁺ - anti-hepatitis B e positive, HBeAg⁺ - anti-hepatitis B e antigen positive

Table 2 - Levels of anti-hepatitis B surface (HBs) antibody after hepatitis B virus vaccination in susceptible spouses.

Study population	No. of patients (%)			
	Anti HBs <10 mIU/ml	Anti HBs levels 10-99 mIU/ml	Anti HBs ≥ 100 mIU/ml	Total
Female	7 (11.7)	7 (11.7)	46 (76.6)	60 (100)
Male	5 (15.6)	2 (6.3)	*25 (78.1)	32 (100)
Total	12 (13.0)	9 (9.8)	71 (77.2)	92 (100)

*One case with anti-HBs and anti-hepatitis B core positive after vaccination included in this group. There were no significant differences between anti-HBs levels and HBeAg or anti-HBe positive status of their spouses.

difference between males and females. Although post-exposure efficacy of hepatitis B vaccine was evaluated in susceptible spouses of acute hepatitis B patients in Greece,¹⁸ they reported that vaccinated (16%) and unvaccinated spouses (18.3%) showed similar attack rates for infection. They also showed that the vaccine group had fewer clinical infections (2.7% against 7.0%) and fewer infections occurring more than one month after the first vaccination (8.7% against 14.7%). They recommended hepatitis B vaccination with hepatitis B immunoglobulin to protect this high-risk group. The high rate of occurrence of acute hepatitis B in vaccine recipients of susceptible spouses of patients with acute hepatitis B may be due to long duration of exposure with index sources and higher viral load of acute disease. Experience with hepatitis B vaccination at the time of marriage in susceptible spouses is limited in the medical literature. In the present study, there were no evidence seen on HBV transmission in the vaccine recipients of wives of 14 HBeAg positive husbands and 8 husbands of HBeAg positive females. The prevalence of HBeAg in HBsAg positive adult cases in our region is low and the most HBV infected individuals are anti-HBe positive.⁴ As we showed in **Table 2**, there were no significant differences for production of antibody regarding sex, HBeAg and anti-HBe status of the spouses. Other studies reported anti-HBs levels ≥ 10 mIU/ml in 12.4 - 30% of vaccinees, 30 days after administration of the first dose.¹⁹⁻²⁰ With administration of 2 doses one month apart, anti-HBs levels ≥ 10 mIU/ml was developed in 73 - 98.8% of the vaccine recipients.²⁰⁻²² With complete immunization seroprotection rate has been determined as 95-99%.²²⁻²³ In Iran, due to a particular cultural and religious background, homosexuality is not known as a common phenomenon compared to the western countries. For the same reasons, it is very unlikely for an individual to have sexual contact (especially in the form of intercourse) with his/her would be spouse. Orsolini et al²⁴ and Goldfarb et al²⁵ reported more rapid and comparatively high seroprotection rates with the conventional schedule in neonates.²⁴⁻²⁵ With administration of 2 doses of hepatitis B vaccine in homosexual men one month apart, showed high levels of anti-HBs in 77% of the vaccinated persons. This rate increased to 96% after the later dose. Hepatitis B or subclinical infection developed in only 1.4-3.4% of the vaccine recipients as compared with 18-27% of placebo recipients.³ In the present study, subclinical hepatitis B occurred only in one case with development of anti-HBs and anti-HBc. These observations suggest that the vaccine may be efficacious even when given after exposure. In the present study, 12 (13%) cases were non-responder and were susceptible to be infected with HBV. With the second series of HBV vaccination in these groups of patient, anti-HBs levels ≥ 10 mIU/ml

developed in 11 (91.7%) of the non-responder cases. Other studies reported sufficient levels of anti-HBs in 68 to 100% of non-responder cases with the second series of vaccination.²⁶⁻²⁷ With one additional dose of HBV vaccine, several studies reported seroprotection rate between 25-100%.²⁷⁻³¹ One month after the second doses of HBV vaccine, sufficient levels of anti-HBs developed in 58% cases.²⁷ Whether one or 2 additional doses of hepatitis B vaccine are sufficient for non-responder susceptible spouse to hepatitis B virus should be clarified. In summary, although the combination of HBIG and hepatitis B vaccine is recommended for spouses with acute hepatitis B cases, hepatitis B vaccine at the time of marriage can prevent the transmission of HBV between spouses. This vaccination schedule seems to be cost saving and is recommended for health policy in Iran and those countries with similar demographic conditions and cultural background.

Acknowledgment. We are indebted to the technicians from the Clinical Virology of Razi Laboratory in Babol, Iran. This study was supported financially by Babol Medical University.

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