Clinical Study

Rapid Immunization Scheme for Spouses of Individuals Established as Hepatitis B Carriers during Premarital Tests

Selma Tosun,1 Murat Yüçeturk,2 Aydın Bilal Dönmez,2 and Turan Gündüz3

1 Department of Clinical Microbiology and Infectious Diseases, Manisa State Hospital, Manisa, Turkey
2 Primary Health Care Clinic No. 2, Turgutlu, Manisa, Turkey
3 Department of Microbiology, Vocational School of Health Services, Celal Bayar University, Manisa, Turkey

Correspondence should be addressed to Turan Gündüz, drtle@turch.gov.tr

Received 13 October 2012; Revised 27 November 2012; Accepted 28 November 2012

Academic Editor: Mario Clerici

Background. The aim of this study was to monitor the cases identified as hepatitis B carriers during premarital tests, to vaccinate their prospective spouses with a rapid vaccination scheme, and to compare the anti-HBs responses with the traditional vaccination scheme. Methods. Blood samples of 1250 couple spouses were tested for HBsAg and anti-HBs. HBsAg positive cases’ fiancées which were found HBV negative were administered a rapid three-dose vaccination scheme on days 0, 7, and 21. Forty controls with similar age and gender were also administered three doses of the same vaccine. Results. Out of 1250 cases (625 couples), 46 (3.6%) were HBsAg positive, and 40 of them aged between 18 and 39 were admitted to the rapid vaccination program. Conclusion. Upon determination of HBsAg positivity in premarital tests, a rapid vaccination program provides early protection, but the 6th and 12th month vaccinations are also required. Anti-HBs response should be monitored.

1. Introduction

As sexual intercourse is an important route of transmission for HBV, in case of the determination of a carrier status during premarital testing, protection of the prospective spouse by early vaccination is imperative [1]. Since both vertical and horizontal transmission is possible in HBV and children of HBsAg-positive mothers predominantly infected during delivery, the testing of pregnant women during pregnancy or even prior to marriage for carrier status is critical [2, 3].

The civil law in effect as of 2002 suggests testing for HBV, HCV, and HIV as a component of the premarital health certificate [4]. In the current situation, when HBV infection still presents a serious health issue, this procedure creates an opportunity both to determine and further evaluate and monitor carrier cases, and to prevent the infection of their spouses and future children with the virus and the emergence of new carrier cases. The aim of this study was to test couples applying to a primary healthcare clinic for premarital testing for HBsAg and anti-HBs, and in case of HBsAg positivity, to introduce the prospective spouse with negative HBV markers into a rapid vaccination program on days 0, 7, and 21.

We also aimed to compare the anti-HBs responses with the traditional vaccination scheme.

2. Materials and Methods

Blood samples were obtained for premarital testing for HBsAg and anti-HBs, and individuals sensitive to HBV whose future spouses were HBsAg positive were administered a three-dose rapid vaccination scheme on the 0th, 7th, and 21st days with the vaccine provided by the Ministry of Health (Euvax B). Blood samples were obtained at the 1st, 6th, and the 12th months after the last vaccination to check anti-HBs titers. All cases were also administered a booster dose at the 12th month. On the 13th and 14th months of vaccination, at least one month after the last dose of vaccine, one more blood sample was tested for anti-HBs titers. As the control group, 40 healthy volunteers, with similar age and gender who were negative for HBV markers, were administered three doses of the same vaccine at months 0, 1, and 6; control blood samples were obtained on the 45th day, and also 6 months and 5 years later. Statistical analysis was performed by Statcalc epi-info.
the control group showed anti-HBs titers above 10 IU/mL after the completion of three doses of vaccine, seroprotective anti-HBs titers were 70% in the study group, while 17 persons in the control group had anti-HBs responses above the seroprotective level (10 mIU/mL). Blood tests at the 12th month showed anti-HBs titers below the seroprotective level in one subject in the study group, while 17 persons in the control group had protective anti-HBs responses above 10 IU/mL.

The subject in the study group with an anti-HBs response below protective level was considered to be at high risk and administered a single booster dose vaccine, and blood tests performed one month after this vaccine showed a high anti-HBs titer (>100 mIU/mL). Blood tests at the 12th month demonstrated that 19 individuals in the study group and all subjects in the control group had anti-HBs responses above the protective level; blood samples tested one month after the last vaccine dose on month 12 in individuals in the study group showed high anti-HBs titers in all cases (Table 1). In the study group, anti-HBs responses above 10IU/mL were statistically higher on the 45th day and in the 6th month when compared with the control group ($P < 0.05$). However this response was lower than the control group in the 12th month ($P < 0.05$). At the 5th-year control, both the study and the control group showed anti-HBs titers above 10 IU/mL.

### 3. Results

Totally 1250 (625 couples) subjects were tested and 46 (3.6%) were found as HBsAg positive. 25 couples were already living together and had at least one child, in one of these households, both spouses were carriers. In terms of exposure to HBV of the spouses of other carrier cases, four had previously been exposed to HBV and immunized. Consequently, the remaining 40 subjects were admitted into the rapid vaccination program. The age range of the study group was 18 to 36, 22 were males and 18 females. The control group consisted of 20 male and 20 female individuals whose ages ranged between 18 and 38.

One month after the completion of three vaccine doses, all cases in the study group had anti-HBs responses above the seroprotective level (10 mIU/mL). Of the control group of 20 individuals, only five cases showed protective anti-HBs response. Tests performed at the 6th month showed anti-HBs titers below the seroprotective level in one subject in the study group, while 17 persons in the control group had anti-HBs responses above the seroprotective level.

The subject in the study group with an anti-HBs response below protective level was considered to be at high risk and administered a single booster dose vaccine, and blood tests performed one month after this vaccine showed a high anti-HBs titer (>100 mIU/mL). Blood tests at the 12th month demonstrated that 19 individuals in the study group and all subjects in the control group had anti-HBs responses above the protective level; blood samples tested one month after the last vaccine dose on month 12 in individuals in the study group showed high anti-HBs titers in all cases (Table 1). In the study group, anti-HBs responses above 10IU/mL were statistically higher on the 45th day and in the 6th month when compared with the control group ($P < 0.05$). However this response was lower than the control group in the 12th month ($P < 0.05$). At the 5th-year control, both the study and the control group showed anti-HBs titers above 10 IU/mL.

### 4. Discussion

Hepatitis B vaccinations have been in use for approximately 20 years, produce high-titer antibody responses in adults and children, and are generally well tolerated [5–12]. Traditional vaccination scheme is three doses administered on the 0-1-6th months or four doses administered on the 0-1-2-12th months. Nevertheless, recent studies have investigated administration of three doses on days 0-7-21 or 0-10-21 with a booster dose in 12 months to subjects traveling to HBV endemic regions, those with an irregular former vaccine scheme, and subjects who need a rapid antibody response with positive results [13–15]. Bock et al. used three different vaccine schemes: 0-1-2nd day (group A), 0-14-28th day (group B), and 0-7-21st day (group C). Blood samples on day 28 showed that groups B and C had similar results, but significantly higher anti-HBs titers than group A; one month after the completion of three doses of vaccine, seroprotective anti-HBs titers in groups A, B, and C were 89%, 78.5%, and 76.4%, and on month 13, 95.8%, 98.9%, and 98.6%, respectively [16].

Marchou et al. vaccinated an adult group on days 0, 10, and 21 and found seroprotective anti-HBs responses of 40% on days 21, 91% on day 82, and 90% at the end of year 1 [17]. Another study by the same author investigated a scheme of vaccination on days 0-10-21 (group A) and months 0-1-2 (group B), with revaccination on month 12 in adults. In blood samples obtained one month after the completion of three doses, seroprotective anti-HBs responses were 70% in group A and 92% in group B; on month 12 prior to the administration of the booster dose, responses were 93% and 95%, respectively, and blood testing one month after the booster dose showed that seroprotection was provided in all cases [18].

Various studies concluded that a rapid vaccination scheme gave similar results with a traditional vaccination scheme, and anti-HBs response was maintained for at least 1 year [19, 20]. In our study, all cases administered a rapid vaccination scheme had developed a protective anti-HBs response at the end of month 1, while only five subjects in the group administered a traditional vaccination scheme had developed a protective anti-HBs response at the end of month 1. As subjects in the study group were couples applying for premarital testing and generally do not use condoms, an early anti-HBs response is important in this group. In the 6th month control, one subject in the study group had an anti-HBs response below the seroprotective level, while in the control group, 32 subjects had protective

### Table 1: Anti-HBs titers after the vaccination scheme in the study group and the control group.

|                | 45th day | 6th month | 12th month | 5th year |
|----------------|----------|-----------|------------|----------|
|               | 10 IU/mL | 10 IU/mL  | 10 IU/mL   | 10 IU/mL |
| Study group n = 40 | 40 (%100) | 1 (%2.5)  | 21 (%52.5)| 40 (%100) |
| Control group n = 40 | 35 (%87.5) | 5 (%12.5) | 8 (%20)   | 40 (%40)  |
| Chi-square value | 62.22     | 0.028     | 28.47      | Na       |
| P value         | 0.000     | 0.028*    | 0.000      | Na       |

*Fisher exact test result.

In the study group, anti-HBs responses above 10 IU/mL were statistically higher on the 45th day and in the 6th month when compared with the control group. In the control group, anti-HBs responses above 10 IU/mL were statistically higher in the 12th month when compared with the study group.

Na: Not available.
anti-HBs responses. On the 12th month, 19 subjects in the study group and all subjects in the control group had seroprotective anti-HBs responses, and one month after the 12th month vaccine administered to the study group, all cases had quite high anti-HBs titer. Although the number of cases included in the study group is not high, the rapid vaccination scheme can be favored in order to provide an early anti-HBs response in cases where premarital tests reveal HBsAg positivity in the prospective spouse. However, anti-HBs titer gradually diminish with this scheme of vaccination, and thus these subjects need to be closely monitored and revaccinated on month 12. The investigation of larger groups and the surveillance of subjects administered a rapid vaccination scheme in terms of anti-HBs titer in later years will provide further direction about the feasibility of this method.

References

[1] A. S. F. Lok and B. J. McMahon, "Chronic hepatitis B. AASLD Practice Guidelines," *Hepatology*, vol. 45, no. 2, pp. 507–539, 2007.

[2] D. Lavanchy, “Viral hepatitis: global goals for vaccination,” *Journal of Clinical Virology*, vol. 55, no. 4, pp. 296–302, 2012.

[3] F. André, “Hepatitis B epidemiology in Asia, the Middle East and Africa,” *Vaccine*, vol. 18, no. 1, pp. S20–S22, 2000.

[4] E. E. Mast, M. C. Weinbaum, E. A. Fiore et al., “Comprehensive immunization strategy to eliminate transmission of hepatitis B virus infection in the United States recommendations of the advisory committee on immunization practices (ACIP) part II,” *MMWR Morbidity and Mortality Weekly Report Recommendations and Reports*, vol. 55, no. 16, pp. 1–25, 2006.

[5] D. Lavanchy, “Hepatitis B virus epidemiology, disease burden, treatment, and current and emerging prevention and control measures,” *Journal of Viral Hepatitis*, vol. 11, no. 2, pp. 97–107, 2004.

[6] R. A. Gunn, P. J. Murray, M. L. Ackers, W. G. M. Hardison, and H. S. Margolis, “Screening for chronic hepatitis B and C virus infections in an urban sexually transmitted disease clinic: rationale for integrating services,” *Sexually Transmitted Diseases*, vol. 28, no. 3, pp. 166–170, 2001.

[7] S. M. Lemon and D. L. Thomas, “Vaccines to prevent viral hepatitis,” *The New England Journal of Medicine*, vol. 336, no. 3, pp. 196–204, 1997.

[8] R. J. Burnett, A. Kramvis, C. Dochez, and A. Meheus, “An update after 16 years of hepatitis B vaccination in South Africa,” *Vaccine*, vol. 7, no. 30, pp. 45–51, 2012.

[9] J. H. Liang, M. Wang, J. H. Liu, Y. S. Cai, and J. X. Xu, “Study on the immunization coverage and effects of hepatitis B vaccine in the 20-59 years-old population in Guangzhou city,” *Zhonghua Liu Xing Bing Xue Za Zhi*, vol. 31, no. 12, pp. 1336–1339, 2010.

[10] W. Magdzik and M. P. Czarkowski, “Coverage of vaccination against Hepatitis B in Poland in 2004,” *Przegląd Epidemiologiczny*, vol. 60, no. 2, pp. 185–192, 2006.

[11] H. Pham, S. A. Geraci, and M. J. Burton, “Adult immunizations: update on recommendations,” *American Journal of Medicine*, vol. 124, no. 8, pp. 698–701, 2011.

[12] Y. Poovorawan, V. Chongsrisawat, A. Theamboonlers, H. L. Bock, M. Leyssen, and J. M. Jacquet, “Persistence of antibodies and immune memory to hepatitis B vaccine 20 years after infant vaccination in Thailand,” *Vaccine*, vol. 28, no. 3, pp. 730–736, 2010.

[13] A. A. Z. Asli, M. Moghadami, N. Zamiri et al., “Vaccination against hepatitis B among prisoners in Iran: accelerated versus classic vaccination,” *Health Policy*, vol. 100, no. 2-3, pp. 297–304, 2011.

[14] L. Y. Hwang, C. Z. Grimes, T. Q. Tran et al., “Accelerated Hepatitis B vaccination schedule among drug users: a randomized controlled trial,” *Journal of Infectious Diseases*, vol. 202, no. 10, pp. 1500–1509, 2010.

[15] G. M. Keating, S. Noble, F. M. Averhoff et al., “Recombinant hepatitis B vaccine (Engerix-B): a review of its immunogenicity and protective efficacy against hepatitis B,” *Drugs*, vol. 63, no. 10, pp. 1021–1051, 2003.

[16] H. L. Bock, T. Loscher, N. Scheiermann et al., “Accelerated schedule for hepatitis B immunization,” *Journal of Travel Medicine*, vol. 2, no. 4, pp. 213–217, 1995.

[17] B. Marchou, N. Picot, P. Chavanet et al., “Three-week hepatitis B vaccination provides protective immunity,” *Vaccine*, vol. 11, no. 14, pp. 1383–1385, 1993.

[18] B. Marchou, J. L. Excler, C. Bourderioux et al., “A 3-week hepatitis B vaccination schedule provides rapid and persistent protective immunity: a multicenter, randomized trial comparing accelerated and classic vaccination schedules,” *Journal of Infectious Diseases*, vol. 172, no. 1, pp. 258–260, 1995.

[19] C. Belloni, A. Pistorio, C. Tinelli et al., “Early immunisation with hepatitis B vaccine: a five-year study,” *Vaccine*, vol. 18, no. 14, pp. 1307–1311, 2000.

[20] S. E. Wilkinson, M. Morath, M. A. Burgess, and D. Isaacs, “Accelerated schedule of hepatitis B vaccination in high-risk youth,” *Journal of Paediatrics and Child Health*, vol. 32, no. 1, pp. 60–62, 1996.