

Response to hepatitis B virus vaccination in haemodialysis patients with and without hepatitis C infection

H. Sorkhi,¹ M.R.H. Roushan,² G.H. Al Hashemi,³ M.R.E. Dooki⁴ and S. Bai¹

استجابة مرضى الديال الدموي للتلقيح ضد فيروس التهاب الكبد "بي" مع أو بدون العدوى بالتهاب الكبد "سي"

هادي سرخي، محمد رضا حسنجاني روشن، قمر الحسيني الهاشمي، محمد رضا اسمعيلي دوكي، سهيلا باي

الخلاصة: استهدفت هذه الدراسة تحديد مدى نجاعة التلقيح ضد فيروس التهاب الكبد B واستجابة مرضى الديال الدموي للقاح، سواء منهم المصابون وغير المصابين بعدوى فيروس التهاب الكبد C. خلال الفترة من نيسان/أبريل 2000 إلى أيلول/سبتمبر 2003. تلقى جميع مرضى الديال الدموي الذين أحيوا إلى مستشفى بابول، 4 كروغرامات من اللقاح على ثلاث حقن عضلية عند قدومهم وبعد شهر وبعد 6 شهور. وقد كانوا جميعاً سلبين لواسمات العدوى بالتهاب الكبد B (المستضد السطحي للتهاب الكبد B، ضد السطحي للتهاب الكبد B والضد اللي للتهاب الكبد B). ومن بين 62 مريضاً، استجاب 53 (85.5%) للتلقيح، منهم 26 (49.1%) استجابوا استجابة عالية. وقد استجاب جميع المصابين بعدوى فيروس التهاب الكبد C للتلقيح. ولم يكن لطول مدة تلقي الديال الدموي تأثير على الاستجابة للتلقيح.

ABSTRACT The aim of this study was to determine the efficacy of hepatitis B virus (HBV) vaccination and the response to vaccine in individuals on haemodialysis with and without HCV infection. From April 2000 to September 2003 all haemodialysis patients referred to the haemodialysis department in a Babol hospital received 4 µg vaccine intramuscularly at 0, 1, and 6 months. All were negative for HBV infection markers (HBcAb, HBsAg and HBsAb). Of 62 patients, 53 (85.5%) responded to vaccination and 26 (49.1%) were high responders. All individuals with HCV infection responded to vaccination. Duration of haemodialysis had no effect on response to vaccination.

Réponse à la vaccination contre le virus de l'hépatite B chez des patients hémodialysés infectés et non infectés par le virus de l'hépatite C

RÉSUMÉ L'objectif de cette étude était de déterminer l'efficacité de la vaccination contre le virus de l'hépatite B (VHB) et la réponse vaccinale chez des sujets hémodialysés infectés et non infectés par le virus de l'hépatite C (VHC). D'avril 2000 à septembre 2003, tous les patients hémodialysés adressés au service d'hémodialyse d'un hôpital de Babol ont reçu 4 µg de vaccin intramusculaire à 0, 1 et 6 mois. Chez tous ces patients, les marqueurs de l'infection par le VHB – l'antigène (Ag) HBs, les anticorps anti-HBc et les anticorps anti-HBs – étaient négatifs. Tous les sujets infectés par le VHC ont répondu à la vaccination. La durée de l'hémodialyse était sans effet sur la réponse vaccinale.

¹Department of Paediatric Nephrology; ²Department of Infectious Diseases; ⁴Department of Paediatric Gastroenterology, Babol Medical University, Babol, Islamic Republic of Iran (Correspondence to H. Sorkhi: hadisorkhi@yahoo.com).

³Department of Paediatric Nephrology, Shiraz Medical University, Shiraz, Islamic Republic of Iran.

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Introduction

Chronic hepatitis B virus (HBV) infection is one of the most important public health problems in Asia and developing countries [1]. More than 350 million people in the world are suffering from chronic HBV infection [2].

Haemodialysis patients are particularly at risk for developing of HBV infection and are unable to eliminate the virus because of their impaired immune systems. Infected individuals are predisposed to develop chronic liver disease and then renal transplantation problems may occur [3]. So, immunity against HBV infection is essential for all haemodialysis patients [4–7].

The response rates to HBV vaccine in this group of patients differ in several studies [6,8–13]. Haemodialysis patients have poor immunity, so the response to HBV vaccine is much lower than in healthy people [5,14]. After HBV vaccination, specific antibody is produced via activation of B-cells by class II (CD4 + T-helper) and class I-restricted (CD8 + CTL-cytotoxic T-cells) T-cell responses. Insufficient T- and B-cells responses can cause chronic liver disease in 30% of HBV infected haemodialysis patients [15,16]. Second-generation recombinant vaccine (expressing the “s” gene) is safer and more immunogenic than plasma-derived vaccines [4,11,17]. In addition, some studies have shown a low response rate to HBV vaccine in haemodialysis patients infected with hepatitis C virus (HCV) and some authors could not find the effective conversion rate of HCV infection on response to HBV vaccine [14,18–22].

The purpose of this study was to assess the efficacy of HBV vaccine in a group of haemodialysis patients and HCV-infected individuals in Babol city, Islamic Republic of Iran.

Methods

From April 2000 through September 2003, all haemodialysis patients referred to the haemodialysis department of Shahid Beheshti Hospital, Babol Medical University were enrolled in this study. The department serves all haemodialysis patients living in Babol city and the villages around it. Haemodialysis patients who were positive for hepatitis B virus surface antigen (HBsAg), antibody to hepatitis B surface antigen (anti-HBs) and antibody to hepatitis B core antigen (anti-HBc) were excluded.

All patients received 2 cm³ Engerix-B vaccine (40 µg) HBsAg (Herberbiovac HB, Cuba) intramuscularly in the deltoid muscle in 3 doses (at 0, 1 and 6 months). One month after the last dose of vaccine, the HBsAb (anti-HBs) titre was determined using an enzyme-linked immunosorbent assay (ELISA) method, and antibody titres > 10 mIU/mL were considered as seroprotective. HCVAb, HBcAb, HBsAg and HBsAb were assayed with ELISA methods (Randox, England). Antibody levels between 10–99 mIU/mL were defined as responder and > 100 mIU/mL as high responder.

The local ethics committee approved the study and informed consent was obtained from all patients.

Statistical analysis was performed using *SPSS*, version 10. Chi-squared and Fisher exact tests were used to compare the antibody levels by age, sex, duration of haemodialysis and concurrent HCV infection. *P*-values < 0.05 were considered as significant.

Results

During this study 62 patients (28 males and 34 females) were evaluated (16 patients

were excluded due to early transplantation, elevated liver enzyme tests or death). The mean age of the patients was 50.95 (SD 17.82) years, range 10 to 79 years. Eleven (17.7%) patients were < 30 years, 14 (22.6%) were 30–49 years and 37 (59.7%) were 50+ years (Table 1). The duration of haemodialysis was 2 years in 45 (72.6%) patients, 2–4 years in 13 (21.0%) and > 5 years in 4 (6.5%).

Fifty-three (85.5%) of the patients had an antibody response to HBV vaccine: 25 (89.2%) males and 28 (82.4%) females ($P > 0.05$). Almost half of them (26, 49.1%) were high responders.

There was no significant difference in antibody response by age ($P > 0.05$). All (100%) of the 11 patients who were < 30 years old responded to HBV vaccine, 12 (85.7%) of the patients 30–49 years and 30 (81.1%) of the patients 50+ years old. There was also no significant difference in response by duration of haemodialysis ($P > 0.05$); 80.0% with duration < 2 years responded compared with 100% of those with longer durations (Table 1).

HCV infection was also detected in 19 (30.6%) patients. All of the HCV-infected individuals responded to HBV vaccine and 8 of them were high responders.

Discussion

Haemodialysis patients have impaired immunologic function and are predisposed to development of infections. In the United States of America (USA), complications of HBV infection are the second cause of death in these patients [23]. They have high risk for HBV infection, and recombinant HBV vaccine has been recommended for all patients undergoing haemodialysis since 1980. However, the success rate of vaccination is lower than in the general population [5,14,24].

Table 1 Response to hepatitis B virus vaccination in 62 haemodialysis patients by age and duration of haemodialysis

Variable	Responder	Non-responder	Total
<i>Sex</i>			
Male	25	3	28
Female	28	6	34
<i>Age (years)</i>			
< 30	11	0	11
30–49	12	2	14
50+	30	7	37
<i>Duration of dialysis (years)</i>			
< 2	36	9	45
2–4	13	0	13
≥ 5	4	0	4
<i>Total</i>	53	9	62

$P > 0.05$ for all variables.

It is noteworthy that 85.5% of our patients responded with had an anti-HBS titre > 10 mIU/mL. The reason for this high rate of response is not clear. In our study there was no significant difference in the antibody response comparing age groups < 30, 30–50 and 50+ years of old. Elderly haemodialysis patients have been found to have a lower antibody titre to HBV vaccine [25–28]. In Mitwalli's report the rate of seroconversion was higher in younger patients (< 30 years) than in elderly patients (> 50 years) [13]. Chin reported a better response rate to HBV vaccine in patients with a mean age of 51 years compared with 59 years of age [28]. Vlassopoulos et al. used intradermal vaccination and reported that age and sex had no influence on the immune response [29].

Peces et al. used 4 doses of vaccine and did not find any difference in response rate regarding sex, duration of haemodialysis, malnutrition status and haemoglobin level, but the response rate was better in patients < 40 years old [20]. Also, Navarro et al. did

not report any difference in the response rate with regard to age, duration of haemodialysis and serum albumin. They also showed that females had a better response than males [22]. In our study, sex and duration of haemodialysis had no significant effect on response to vaccination ($P > 0.05$).

Some authors have shown a decreased immune response to HBV vaccine in patients with HCV infection. They reported very low antibody titres in these patients and suggested a possible genetic basis for the low response rate to both viruses [14, 19–22]. Navarro et al. reported a low response to HBV vaccination in HCV-infected haemodialysis patients in 2 studies. In the first study, the effective immunization rate (antibody titre ≥ 100 mIU/mL) was lower in HCV infected patients (33.3% versus 70.3%, $P < 0.05$) [19]. In another study they evaluated seroconversion of HBV vaccine in 56 haemodialysis patients for 1 year. They showed that HCV infection influenced the level of immunity; 27 out of 43 HCV-negative patients (62.8%) versus 3 out of 13 HCV-infected subjects (23.1%) had anti-HBs titre > 100 mIU/mL ($P < 0.01$). They suggested that HCV infection may reduce the effectiveness of HBV vaccination in haemodialysis patients [22].

Peces et al., however, reported 80 vaccinated seronegative haemodialysis patients. They used 4 vaccine doses (0, 1, 2 and 6 months) and 77.5% of patients had a high response. There was no difference between responder and nonresponder patients concerning HCV infection [20]. Cheng et al. used 5 vaccine doses and the effective conversion rates of the anti-HCV(+) and anti-HCV(–) groups were 75.0% and 77.3% respectively ($P = 0.867$) [21]. We also found that all cases of HCV infection had a good response to vaccination and 42% of them had a high response. So further large-scale studies are needed to confirm the response to HBV vaccination in HCV-infected haemodialysis patients.

In conclusion, sex, age, duration of haemodialysis and HCV had no association with low response to HBV vaccine, and vaccination can induce sufficient response.

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International travel and health, 2008 edition

International travel can pose various risks to health, depending on the characteristics of both the traveller and the travel. Travellers may encounter sudden and significant changes in altitude, humidity, microbes and temperature, which can result in ill-health. In addition, serious health risks may arise in areas where accommodation is of poor quality, hygiene and sanitation are inadequate, medical services are not well developed and clean water is unavailable. All those planning travel should become informed about the potential hazards of the countries they are travelling to and learn how to minimize any risk to their health.

This report provides information on the main health risks for travellers. It can be ordered or downloaded at: <http://www.who.int/ith/en/>