Short communication

Hepatitis B surface antibody response of household contacts of hepatitis B virus carriers in Palestine

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ABSTRACT To evaluate the effectiveness of hepatitis B virus (HBV) vaccination of household contacts of HBV carriers in Tulkarm district, Palestine, quantitative hepatitis B surface (anti-HBs) antibody response in 161 household contacts was measured after vaccination. A seroprotective anti-HBs response (titre ≥ 10 IU/L) was elicited in all vaccinated subjects. Of these 2.5% had titres of 10–99 IU/L, 61.5% 100–999 IU/L and 36.0% ≥ 1000 IU/L. The number of vaccination doses had no effect on the achievement of seroprotection. HBV infection was demonstrated in 13 cases and their anti-HBV titres were in the range 25–350 IU/L.

Réponse en anticorps dirigés contre l’antigène de surface de l’hépatite B des contacts familiaux de porteurs du virus de l’hépatite B en Palestine

RÉSUMÉ Afin d’évaluer l’efficacité de la vaccination contre le virus de l’hépatite B (VHB) des contacts familiaux de porteurs du virus de l’hépatite B dans le district de Tulkarem (Palestine), on a mesuré la réponse quantitative en anticorps dirigés contre l’antigène de surface du virus de l’hépatite B (anti-HBs) chez 161 contacts familiaux après vaccination. Tous les sujets vaccinés présentaient des titres séroprotecteurs (titres d’anti-HBs ≥ 10 UI/L). Parmi ceux-ci, 2,5 % avaient un titre de 10–99 UI/L, 61,5 % de 100–999 UI/L et 36,0 % supérieur ou égal à 1000 UI/L. Le nombre de doses de vaccin reçues n’avait aucun effet sur l’apparition de la séroprotection. Une infection par le VHB a été démontrée dans 13 cas et le titre d’anticorps anti-VHB chez ces derniers était compris entre 25 et 350 UI/L.

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Introduction

The hepatitis B virus (HBV) is one of the most common chronic pathogens in the world. Over 2 billion of the world’s population has been exposed to this virus. About 350 million of these, 5% of the world’s population, are chronic carriers [1–4]. Annually up to 1 million of this population dies due to the consequences of this infection, such as cirrhosis and hepatocellular carcinoma [5]. More than three-quarters of HBV infections occur in Asia, the Middle East and Africa [1].

The risk of HBV infection varies among different groups. Besides medical professionals, drug users and people with multiple sexual partners, other high-risk groups include household contacts of HBV infection carriers [6].

Without ignoring current trends and recommendations for universal vaccination against HBV, the Immunization Practices Advisory Committee (ACIP) of the Centers for Disease Control and Prevention has insisted on the importance of vaccination of all persons belonging to identified risk groups, including household contacts of HBV carriers [7–10].

In Palestine, an area of high endemicity of HBV carriers [1], the Ministry of Health established an obligatory hepatitis B vaccination of household contacts of HBV carriers and of other high-risk groups in 1994. All household contacts of HBV carriers have to be vaccinated against HBV with 3 intramuscular vaccine doses according to the schedule 0 (initial), 1 and 6 months [11]. The objective of this study was to evaluate the hepatitis B surface antibody response to vaccination of household contacts of HBV carriers in northern Palestine.

Methods

The subjects of this study were all household contacts of confirmed HBV chronic carriers (n = 161) of 50 families in Tulkarm district, Palestine. The median age was 23.6 years (range 3 to 55 years). Data was collected from records of the epidemiological service of the Ministry of Health of Palestine about the HBV status of subjects according to 3 markers: hepatitis B surface antigen (HBsAg), antibody to hepatitis B surface antigen (anti-HBs) and antibody to hepatitis B core antigen (anti-HBc). Only those with all 3 HBV markers negative were enrolled in the vaccination programme.

For adults, 20 µg of recombinant, mammalian cell derived HBsAg (Bio-Hep-B™/Sci-B-Vac™, Bio-Technology General, Israel) was administered in the deltoid region at 0, 1 and 6 months. The dose for individuals less than 11 years of age was 10 µg. The subjects who received 3 doses of vaccine, regardless of the between-dose interval, were considered completely vaccinated.

Blood samples were collected from all subjects at 6 months after enrolment in the vaccination programme. The serological anti-HBs antibody titrations using an international standard were carried out at An-Najah National University, Palestine during the period 1999 to 2000 using a commercial kit (Bioelisa, Biokit, Barcelona, Spain). Anti-HBs antibody titres greater than or equal to 10 IU/L were considered to be seroprotective against HBV disease [12–14]. In addition, HBsAg was determined using Auszyme® Monoclonal (Abbott Laboratories, Abbott Park, Illinois) as a marker for recent (< 3 months) or chronic (carrier) infection.
Statistical analysis was performed using the SPSS program. Unpaired Student $t$-test was used to compare mean values between different independent groups. $P < 0.05$ was considered statistically significant.

**Results**

Of the 161 participants, 90 (55.9%) were male and 71 (44.1%) were female. The mean age of the study group was 23.6 years (range 3–55 years).

Two-thirds of the participants (67.1%) completed the vaccination series (3 doses of the vaccine), 31.1% received 2 doses and 1.9% received 1 dose (Table 1). Regardless of the dosing schedule, all the subjects achieved seroprotection.

Of the participants, 2.5% presented anti-HBV titres of 10–99 IU/L, 61.5% 100–999 IU/L and 36.0% ≥1000 IU/L. The mean (standard deviation) value of anti-HBV titres were higher in the group receiving 3 doses [1843 (585) IU/L] than in the group receiving 1 or 2 doses [1455 (415) IU/L]. However, no statistically significant difference was observed between the groups completing and not completing the vaccination schedules ($P > 0.05$).

Testing of the study group for the presence of HBsAg revealed that 13 (8.1%) of the 161 subjects had HBV infection. None of these subjects was haemophiliac or had a history of blood transfusion or haemodialysis. Of them, 4 had anti-HBV titres in the range 25–99 IU/L and the remaining subjects had anti-HBV titres in the range 110–350 IU/L.

**Discussion**

Systematic vaccination of individuals at risk of exposure to the virus has been the main method of controlling the morbidity and mortality associated with hepatitis B.

All studies of the antibody response to currently licensed hepatitis B vaccines have shown that between 5% and 10% or more of healthy immunocompetent subjects do not mount an antibody response to the surface antigen component present in these preparations (non-responders) or that they respond poorly (hyporesponders) [12].

The minimal protective titre has been assumed almost universally to be 10 IU/L, and immunological memory is thought to ensure protection even after circulating antibody becomes undetectable [12–14]. In the United Kingdom, a healthy vaccinee who develops an anti-HBs titre of <100 IU/mL is considered to be unprotected and at risk of HBV [15].

In our study, regardless of dosing schedule, protective anti-HBs were observed in all vaccinated subjects. Despite the extremely high rate of response among the subjects, which is higher than reported in numerous studies [12–14], HBV infection was demonstrated in 13 (8.1%) of the studied group. Of these, 4 subjects were

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Serological data for 161 household contacts of hepatitis B virus (HBV) carriers</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Variable</strong></td>
<td><strong>No.</strong></td>
</tr>
<tr>
<td>No. of vaccinations</td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>50</td>
</tr>
<tr>
<td>3</td>
<td>108</td>
</tr>
<tr>
<td>Anti-HBV (IU/L)$^a$</td>
<td></td>
</tr>
<tr>
<td>10–99</td>
<td>4</td>
</tr>
<tr>
<td>100–999</td>
<td>99</td>
</tr>
<tr>
<td>&gt;1000</td>
<td>58</td>
</tr>
<tr>
<td>HBV infection</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>13</td>
</tr>
<tr>
<td>No</td>
<td>148</td>
</tr>
</tbody>
</table>

$^a$Titres ≥ 10 IU/L were considered seroprotective.
hyporesponders. The remaining subjects had anti-HBs titres in the range 110–350 IU/L. It is worth noting that only 3 of the 13 subjects with verified HBV infection did not complete the vaccination series. This finding is consistent with the fact that no empirical data are available for the hepatitis B surface antibody titre required for protection against particular routes of infection or the size of the infectious inoculum at the time of exposure.

Our study also looked at the effect of the number of vaccination doses, and found that this variable had no effect on the achievement of seroprotection.

We conclude that people at risk of a poor response should be tested after completion of HBV vaccination and, if necessary, offered additional doses of vaccine.

References

Hepatitis B surface antigen Assays: operational characteristics. Phase I. Report 2

In 1998, the World Health Organization, Blood Safety and Clinical Technology Department, conscious of the need to advise Member States on laboratory aspects associated with Hepatitis B and Hepatitis C testing for blood transfusion safety, initiated a project to provide objective assessments of commercially available assays for detection of Hepatitis B surface antigen (HBsAg) and Hepatitis C (HCV) antibodies, similar to that which has existed for HIV since 1988. This second report presents the findings of the Phase I evaluations of 5 HBsAg assays conducted between September 2001 and January 2004. The HBsAg assays evaluated included:

- Enzygnost HBsAg 5.0 (Dade Behring Inc)
- Equipar HBsAg One Step (Equipar Diagnostici)
- Genedia HBsAg ELISA 3.0 (Green Cross Life Science Corp)
- HEPALISA (J Mitra & Co)
- Murex HBsAg Version 3 (Abbott-Murex).

Copies of these reports are available on request from the Department of Essential Health Technologies (EHT), World Health Organization, 1211 Geneva 27, Switzerland.