Brief Communication

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Chronic Liver Disease Rarely Follows Acute Hepatitis B in Non-Immunocompromised Adults

Summary: The risk of developing a chronic carriage state after acute hepatitis B infection in adults was evaluated. Two hundred and eighty-nine HBV-susceptible heterosexual partners of acute hepatitis B patients were used to investigate the effectiveness of post-exposure immunoprophylaxis; 75 of them received hepatitis B vaccine, 72 hepatitis B hyperimmune globulin (HBIG), 71 vaccine plus HBIG and 71 placebo. Participants were interviewed, clinically examined and serum specimens were taken at 1, 3, 6 and 9 months after their first intervention. Serum samples were tested for ALT and HBV markers (HBsAg, anti-HBc and anti-HBs) using radioimmunoassays. Forty-six (15.9%) of the heterosexual partners examined were infected; the incidence of HBV infections was higher among placebo (18.3%, 13/71) and HBIG (18.1%, 13/72) recipients compared to vaccine (16.0%, 12/75) and HBIG plus vaccine (11.3%, 8/71) recipients, but the differences were not statistically significant. Infections were significantly more often subclinical after immunoprophylaxis (p = 0.03). HBsAg was detected in all eight clinical and in 13 of the 38 subclinical cases. In the remaining 25 subclinical cases HBV infections were diagnosed by the development of anti-HBc and anti-HBs during the follow-up period. Finally, all 46 cases studied cleared the HBsAg.

Introduction

We have repeatedly shown [1,2] that acute clinical hepatitis B in adults very rarely progresses to chronicity. These findings have been supported by other investigators, too [3]. In contrast, previous follow-up studies have shown that as many as 10% of adults with clinical hepatitis B become chronic HBV carriers [4,5]. These results were determined before methods differentiating acute from chronic and past from recent HBV infection were available [6]. We believe that inclusion of exacerbations of chronic HBsAg-positive hepatitis or superinfections of HBsAg carriers by hepatitis D virus or non-A, non-B viruses overestimated the risk of becoming a chronic carrier after acute HBV infection. It has also been suggested that the risk of chronicity is greater after subclinical than clinical infection [7].

Materials and Methods

To investigate the effectiveness of post-exposure immunoprophylaxis in HBV-susceptible heterosexual partners of acute hepatitis B patients, two prospective clinical trials [8,9] were conducted. Six hundred and eighty-two of the heterosexual partners of the 843 studied patients with acute hepatitis B who reported a heterosexual relationship during the last three months before patient admission to the hospital were accepted to participate in the study. Of those partners, 23.6% (154/682) were found to be HBsAg positive and 24.6% (168/682) were immune to HBV. Of those susceptible to HBV, 289 signed the informed consent.

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A. Roumliotou, G. Papaevangelou: Chronic Disease Rare after Acute HBV

Table 1: Incidence of HBV infections in four groups.

<table>
<thead>
<tr>
<th>Type of hepatitis</th>
<th>Placebo n = 71</th>
<th>Vaccine n = 75</th>
<th>HBIG n = 72</th>
<th>HBIG + vaccine n = 71</th>
<th>Total n = 289</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. positive</td>
<td>%</td>
<td>No. positive</td>
<td>%</td>
<td>No. positive</td>
</tr>
<tr>
<td>Clinical</td>
<td>5</td>
<td>7.0</td>
<td>2</td>
<td>2.7</td>
<td>1</td>
</tr>
<tr>
<td>Subclinical</td>
<td>8</td>
<td>11.3</td>
<td>10</td>
<td>13.3</td>
<td>12</td>
</tr>
<tr>
<td>Total</td>
<td>13</td>
<td>18.3</td>
<td>12</td>
<td>16.0</td>
<td>13</td>
</tr>
</tbody>
</table>

consent and were enrolled in the study. They were divided into four groups according to the type of intervention which took place 3 to 7 days after the patient’s admission to the hospital. Seventy-five of them received hepatitis B vaccine, 72 hepatitis B hyperimmune globuline (HBIG), 71 vaccine plus HBIG and 71 placebo (Table 1). None of the included 289 sexual partners admitted intravenous drug use or had any symptoms or signs of such use. Of the 81 male partners included in this study none reported bisexual contacts. All participants were “healthy” without any symptomatic disease, were not diabetics and no evidence for their being immunocompromised was found. Participants were interviewed, clinically examined and serum specimens were taken at 1, 3, 6 and 9 months after their first intervention. Serum samples were tested for ALT as well as for HBV markers (HBsAg, anti-HBc and anti-HBs) using radioimmunoassays (Abbott). Participants with confirmed serologic evidence of HBV infection were excluded from further intervention and received appropriate medical attention. HBV events were classified as acute clinical (icteric or anicteric) and subclinical hepatitis. We were able to detect ALT elevations only in two of our subclinical cases, because of the serosampling schedule. They were diagnosed by the development of anti-HBc with or without HBsAg. In none of the subclinical cases was jaundice or clinical symptoms reported. The 46 heterosexual partners infected during the follow-up period (5 males and 41 females aged 18 to 43 years) were included in this study.

Results

Table 1 shows the overall as well as the separate attack rates in the four study groups. As expected, more subclinical (38/46; 82.6%) than clinical (8/46; 17.4%) HBV infections were diagnosed. The clinical to subclinical ratio ranged from 1:1.6 in placebo recipients to 0:8 in those who received HBIG plus vaccine.

HBsAg was detected in all eight clinical cases during the acute phase of the disease. All of them cleared the HBsAg and developed anti-HBs within six months. HBsAg was detected in 13 of the 38 subclinical cases. All of them cleared the HBsAg and developed anti-HBs within two months. HBsAg was not detected in the remaining 25 subclinical cases, possibly because of the shorter duration of antigenemia or late testing. HBV infection was diagnosed in all of them by the development of anti-HBc and anti-HBs at some time during the follow-up of the study.

Discussion

The development of chronic hepatitis is highly related to age at the time of primary infection. Several studies demonstrated evolution to the carrier state in 90–95% of infected neonates [10], in 20% of infected preschool children [11], but in less than 3% of infected university students [12]. The development of chronic hepatitis is more frequent among infected immunocompromised persons than among “healthy” people. The possibility of becoming an HBV carrier is greater in drug users, homosexual men, persons with Down’s syndrome or AIDS, in hemodialysis patients or patients undergoing immunosuppressive therapy. Thus, the estimation of the rate of development of chronic hepatitis in adults depends mainly on the proportion of homosexuals and IVDUs among the population under study. It is also evident that the HBsAg carrier rate is higher in homosexuals and IVDUs. Reactivation of the antedating hepatitis B chronic infection [13] or superimposed acute viral infection from other non-B hepatitis viruses [14] can be misdiagnosed as acute hepatitis B infection, unless methods differentiating acute from chronic and past from recent HBV infection are used [6].

Several data support our hypothesis that at least in “healthy” non-immunocompromised adults acute hepatitis B very rarely progresses to chronicity. We have shown retrospectively that only one out of 507 “healthy” adult patients with acute hepatitis B developed chronic hepatitis [2]. Seef et al. [3] reported a very low carrier rate (0.26%) among people infected by contaminated vaccine against yellow fever. Rinker et al. [15] did not find one HBsAg carrier among 32 inadvertently infected people. Similar data were also reported by other investigators [16]. The results of the present prospective study among heterosexual partners with clinical infection support the findings that chronic hepatitis rarely develops in “healthy,” non-immunocompromised, infected adults. Because lower immune response is related to chronicity it is believed that subclinical infections may increase the carrier rate among the general population. Data concerning the outcome of subclinical infections among “healthy” adults would be of great importance for those...