Isolated Presence of Antibody to Hepatitis B Core Antigen in Injection Drug Users: Do They Need to Be Vaccinated?

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In a study of 497 injection drug users who had isolated presence of antibody to hepatitis B core antigen (anti-HBc) at the time of enrollment, 404 (81%) retained this condition after a mean of 49 months of follow-up, during which no new hepatitis B surface antigen marker was detected. These findings support the hypothesis that patients with isolated presence of anti-HBc have strong resistance to re-infection and do not need vaccination.

Although isolated presence of antibody to hepatitis B core antigen (anti-HBc) is uncommon among members of low risk populations (prevalence, 0.1%–2%) [1, 2], the condition is much more common among members of high-risk groups, such as injection drug users (IDUs), among whom the prevalence can be >30% [3, 4]. We investigated whether patients with isolated presence of anti-HBc are susceptible to new hepatitis B virus (HBV) infection. The results will help us draw conclusions about whether these subjects should be vaccinated; research on this topic is scarce.

The data presented in this study were collected prospectively from 1 January 1985 through 31 December 1998 at 7 Public Centers for Drug Users in Italy, all of which belong to the Scientific Intercenters Collaborative Drug Users Group. Eligible participants for the study included injection heroin users, some of whom may have been users of other drugs as well. We recruited only those IDUs who had isolated presence of anti-HBc and for whom 2 successive tests for HBV markers (HBsAg, anti-HBs [titer ≥10 mUI/mL], and anti-HBc) had positive results. In other words, if a subject had initial test results that were positive for anti-HBc and also for other markers of HBV infection, the subject became eligible for the study only when test results were negative for all HBV markers other than anti-HBc.

Using this condition of eligibility as the baseline, we analyzed the variations over time for each subject, with particular regard to the possible appearance of HBsAg, a marker of re-infection. All subjects who had been vaccinated against HBV were excluded from the study. The data recorded for each subject were as follows: sex; the period of time during which monthly observations were made, from the first test result that showed the subject had isolated presence of anti-HBc until the last test for HBV markers; the number of tests performed; and HIV status. Serological testing for HBsAg, anti-HBs, and anti-HBc was performed at 7 different laboratories. All laboratories used EIA test kits (Abbott Laboratories), according to the manufacturer’s instructions.

A total of 497 subjects (80% were male and 20% were female) who had isolated presence of anti-HBc were included in the study. They were followed for a mean duration (±SE) of 47.3 ± 1.65 months. The mean number of blood tests they underwent (±SE) was 4.3 ± 0.13. One hundred fifty-three subjects (31%) were HIV-positive. Of the 497 subjects who had isolated presence of anti-HBc, 404 (81%) maintained that original condition. They were followed for a mean duration (±SE) of 49 ± 1.9 months, and they underwent 4.3 ± 0.16 blood tests. Ninety-three subjects (19%) who had isolated presence of anti-HBc showed modifications in that original condition. They were followed for a mean (±SE) of 40 ± 3 months, and they underwent 4.1 ± 0.26 blood tests (table 1).

In none of these subjects was it possible to document the presence of HBsAg, which is one of the markers of HBV infection. The only variation observed in the patients who had isolated presence of anti-HBc was the appearance of anti-HBs at a titer ≥10 mUI/mL. Subjects with this variation can be considered to have a “natural booster”; that is, they had a history of hepatitis and showed a reduction of anti-HBs titer to <10 mUI/mL, probably because of new exposure to HBV.

There are various hypotheses to explain isolated anti-HBc seropositivity [5, 6]. (1) It may indicate a “window” phase that follows acute HBV infection—a period after HBsAg has dis-
Table 1. Duration of follow-up, number of blood tests, and HIV status of injection drug users who had isolated presence of antibody to hepatitis B core antigen (isolated anti-HBc).

<table>
<thead>
<tr>
<th>Patient variable</th>
<th>No. (%) of patients</th>
<th>Duration of follow-up, mean mo ± SE</th>
<th>No. of blood tests performed, mean ± SE</th>
<th>No. (%) of patients infected with HIV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enrolled</td>
<td>497</td>
<td>47.3 ± 1.65</td>
<td>4.3 ± 0.13</td>
<td>153 (31)</td>
</tr>
<tr>
<td>Persistence of isolated anti-HBc</td>
<td>404 (81)</td>
<td>49 ± 1.1</td>
<td>4.3 ± 0.16</td>
<td>130 (32)</td>
</tr>
<tr>
<td>Modifications in isolated anti-HBc</td>
<td>93 (19)</td>
<td>40 ± 3</td>
<td>4.1 ± 0.26</td>
<td>23 (25)</td>
</tr>
</tbody>
</table>

appeared from the bloodstream and before anti-HBs has appeared. (2) It may indicate a chronic HBV carrier state, in which HBsAg levels are below the detection limit of routine assays. (3) It may indicate that anti-HBc persists longer than HBsAg in persons who have had HBV infection. (4) It may be a false-positive test result, perhaps caused by cross-reacting antibodies.

We enrolled only subjects who were found to have isolated presence of anti-HBc by means of at least 2 successive tests, to reduce the possibility of laboratory errors, which are not uncommon in this kind of analysis [6]. It should be noted that, in the geographic area where the study was conducted and during the years of the study, the incidence of HBV seroconversion among HBV-negative IDUs was 11% [7].

The evaluation of our data supports the hypothesis that IDUs with isolated presence of anti-HBc have resistance to HBV re-infection and do not need vaccination. This finding is remarkable, considering that >30% of the subjects who were examined were HIV-positive, a condition associated with immunity dysfunction, and, therefore, these subjects were at risk for reactivation or reinfection with HBV [8, 9].

References