EFFECT OF HGV-INFECTION ON CLINICAL COURSE OF HEPATITIS C AND THE POSSIBLE ROLE OF ENDOGENOUS INTERFERON

Light form of disease flow was observed in 69.3% (9/13) among the patients with acute hepatitis C, and in 77.8% (7/9) among the patients with non verified hepatitis. Detectability of RNA-HGV consists of 77.8% (7/9) and 42.8% (3/7) correspondingly among the patients' groups with light form of disease. All HGV RNA positive patients had 2 times lower content of total bilirubin and ALT in the blood comparing to RNA-HGV negative patients. HGV showed an active (4.7 EA) ability to induce the interferon formation. The C + G hepatitis patients had interferon titer equal to 3.7 EA, which apparently provides relief of hepatitis C clinical picture.

Keywords: C-hepatitis, clinical course, co-infection, HCV + HGV, induction of interferon HGV

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Introduction

HGV is spread widely and unevenly over the world. The frequency of RNK-HGV detectability varies from 1.4% before to 22% all over the world (Muerhoff, Simons, and Leary, 1996; Novikov and Mohonov, 2001; Chams, Fournier-Wirth, Chabanel et al., 2003). RNK-HGV is detected in blood serum of patients with acute and chronic hepatitis. However it is necessary to note that HGV-infection in combination with the other hepatitis (B, C and D) and HIV-infection occurs more frequently (from 9.7% to 37%) than mono infection (Lau, Miller, Detmer et al., 1999). It is shown that co-infection HGV with HBV aggravates the defeat a liver affection, whereas in combination with HIV-infection have a beneficial effect on its clinical current (Chams et al., 2003; Lau et al., 1999; Muerhoff, Tillmann et al., 2003). According to some data HGV does not influence on the other hepatitis development (Enomoto, Shuhei et al., 1998; Kiyosawa and Tanaka, 1999). At the same time another group of Japanese researchers showed that current of hepatitis C in combination with HGV-infection has a mild form (Tanaka, Alter et al. 1996; Karayiannis, Hadziannis et al., 1997).

This work is dedicated to attempt to ascertain the nature of HGV influence on hepatitis C course and the possible role of endogenous interferon, which induces patients’ HGV.

Materials and methods

Serum of patients with acute viral hepatitis was investigated by ELISA for the presence of anti-HDV IgM, anti-HBc IgM, HBsAg, anti-HCV IgM, total anti-HCV, anti-HDV IgM, anti-E2HGV using the test kits produced by “Vector Best” CJSC (Novosibirsk, Russia).

RNA-HCV-and RNA-HGV were detected by PCR using the test kits of “AmplisSens-100” and “Poligep G” (“Litech”, Moscow).

ELISA results were taken into account with the help of reader “Teken” (Austria), PCR results - with the help of “Bio Rad Laboratories equipment” (USA).

Determination of interferon activity was made using the micromethod (Novohatskiy, Cherkashkina, and Ershov, 1978) in some modification (Aspetov, Zhumatov, Zhansarina, 2003).
Results and discussion

During the research of acute viral hepatitis serum of 161 patients for diagnostic markers the following data was identified: hepatitis A at 96 (59.6±3.85%), hepatitis B - 26 patients (16.1±2.89%), hepatitis C - 17 (10.5±2.41%), hepatitis D - 2 (2.5%) and there were no markers of hepatitis A, B, C, D and E at 18 (11.2±2.48%).

It should be noted that each group of patients with hepatitis B included both mono and mixed variants of the corresponding nosological forms of viral hepatitis.

To study the nature of the clinical current of hepatitis C, the total bilirubin (TB) indicators and ALT levels as a function of HGV co-infection, we selected 13 patients with mono hepatitis C and 9 patients with non verified hepatitis. A severity of the clinical course, values of total bilirubin, ALT and RNA-HGV were identified at all selected patients. The research results are shown in the table.

<table>
<thead>
<tr>
<th>Examined patients</th>
<th>The clinical course</th>
<th>The number of patients, including positive (+) RNA-HGV</th>
<th>Indicators</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>total bilirubin (µ mol/l)</td>
</tr>
<tr>
<td>Acute hepatitis C (n = 13)</td>
<td>Lung</td>
<td>9</td>
<td>7 RNA-HGV (+)</td>
</tr>
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<td></td>
<td></td>
<td></td>
<td>2 RNA-HGV (-)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>4</td>
<td>2 RNA-HGV (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>2 RNA-HGV (-)</td>
</tr>
<tr>
<td>Non verified hepatitis (n = 9)</td>
<td>Lung</td>
<td>7</td>
<td>3 RNA-HGV (+)</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>4 RNA-HGV (-)</td>
</tr>
<tr>
<td></td>
<td>Moderate</td>
<td>2</td>
<td>2 RNA-HGV (-)</td>
</tr>
</tbody>
</table>

As it is seen in Table 1, the presence of RNA-HGV was revealed at 7 (77.8±13.85%) among the 9 patients with light form of hepatitis C. The content of total bilirubin and ALT levels were almost two times lower the levels at similar patients but without HGV in the blood. Analogous proportions of TB and ALT are observed among patients with average burden of hepatitis C in case of presence of RNK-HGV in their blood.

Among the patients with non verified hepatitis 7 patients had a light clinical current, three of them had RNA-HGV. It is obvious that they can be taken for mono hepatitis G. Their mean value of TB bilirubin was 19.8±7.6 µkmol/l and the mean value of ALT - 9.2±1.9 µmol/liter.

Thus, our research also showed that HGV-hepatitis is characterized by mild clinical course with minor onset of liver affection. The clinical course of acute hepatitis C combined with HGV-infection basically had a mild nature with minimal onset of liver cells cytolysis and disorders of pigment metabolism.

Japanese authors have suggested that the mild course of hepatitis C in combination with HGV-infection may be associated with patients’ HGV induction of endogenous interferon. In this connection, sera of 13 patients with acute hepatitis C, 9 patients with HCV-mixed hepatitis (C+G), 5 patients with mono-G hepatitis (RNA-HGV positive) and as a control sera of 9 donors were examined. All respondents were comparable by age and sex.

The data obtained by determining the interferon concentration (in units of activity in 100 ml of serum) in serum samples is summarized in the following Figure 1.
As can be seen from the Figure 2, the blood serum of healthy individuals (donors) when HGV is absent contains the interferon equal to 1.3 activity units (EA). The patients with hepatitis C have a weak interferon output (2.3 EA). The patients with mixed-hepatitis C + G have interferon production equal to 3.7 EA, which is higher than interferon production of patients with mono C hepatitis. The highest IF production was found at patients with HGV-infection (4.7 EA).

Thus, it is shown that HGV has the most pronounced interferon-inducing activity. Patients with combination of hepatitis C and HGV-co-infection have higher interferon production than those without HGV.

These data allows concluding with more certainty that the above mentioned facts about milder clinical course of hepatitis C combined with HGV co-infection with weak signs of liver cells destruction and pigment metabolism disorders are associated with high IF-inducing activity of HGV.

Absence of consensus on the nature of the HGV effect on clinical course of viral hepatitis (Enomoto et al., 1998; Kiyosawa and Tanaka, 1999; Tanaka et al., 1996; Karayiannis et al., 1997), is probably due to different attitude to the interferon functioning of individual HGV genotypes.

References

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Novikov, V., Mohonov, V., 2001. “GB virus C (GBV-C/HGV),” World of Viral Hepatitis [Mir virusnyh hepatitov], in Russian, No.2, pp.2-4
