HEPATITIS A VACCINATION IN CHRONIC LIVER DISEASE: IS IT REALLY REQUIRED IN A TROPICAL COUNTRY LIKE INDIA?

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Abstract

Vaccination against hepatitis A virus (HAV) has been recommended in patients with chronic liver disease to prevent any decompensation due to superinfection. This may not hold good in high endemic areas for hepatitis A like India. The aim of this study was to find out the seroprevalence of anti-HAV antibodies in patients with chronic liver disease and to justify the need for vaccination against hepatitis A virus in these patients. One hundred and thirty three consecutive patients with cirrhosis of liver attending Gastroenterology department of our Institute between June 2004 and June 2005 were enrolled. Seventy-five healthy persons were taken as controls. The diagnosis of cirrhosis was based on clinical profile, biochemical, radiological (ultrasound abdomen) and endoscopic findings. The etiology of cirrhosis was based on presence of viral markers, history of significant alcohol consumption, autoimmune and metabolic workup. All patients and controls were tested for anti-HAV (total) antibodies using commercially available enzyme-linked immunosorbent assay kits. Data from patients and control group were compared by unpaired ‘t’ test and Chi square test. All subjects were in the age group 11 to 75 years. Etiology of chronic liver disease was as follows: HBV- 29.3%, HCV - 14.28%, HBV+HCV dual -1.5%, alcohol- 21.8%, Cryptogenic -23.3%, Wilson’s Disease -1.5% and Budd chiari -1.5%. The prevalence of HAV was 93.2% in patients with cirrhosis of liver and 94.6% in controls. The prevalence was almost similar irrespective of the etiology. In view of high seroprevalence of HAV antibodies among cirrhotic patients in our study and the high cost of the vaccine, the hepatitis A vaccination may not be routinely required in this part of the world.

Key words: Chronic liver disease, hepatitis A virus, vaccine

Hepatitis A virus (HAV) is an enterically transmitted virus, endemic in many countries. Infection by HAV is often sub clinical and asymptomatic particularly in preschool and early school age. With increasing age symptomatic acute infections are more common.1,2

During the past few years several reports from S. Asia, Latin America and Europe have documented a decreasing seroprevalence of protective anti-HAV IgG antibodies. One of the important factors for this decrease could be attributed to the improvement in living conditions, hygiene and sanitation in these countries. This may result in decreased exposure of the children to HAV resulting in higher incidence of acute HAV infection in adults. HAV infection in nonexposed adults causes more severe and prolonged disease.1,3

It is also suggested that superinfection with HAV in patients with underlying chronic hepatitis or cirrhosis of liver may result in further decompensation,4 therefore in the West, vaccination against HAV is recommended in all patients with cirrhosis of the liver. Safe and highly immunogenic HAV vaccines are commercially available in India.5 The inhibitory cost of vaccine is an important factor in implementing this. The usefulness of this vaccine is also controversial as HAV is endemic in India and needs to be justified by doing seroprevalence studies in India. There are scanty reports on the seroprevalence of HAV in chronic liver disease in our part of the country, hence the present study was undertaken to study the seroprevalence of anti-HAV antibodies (total) in patients of chronic liver diseases and to determine the need for HAV vaccination in these patients.

Materials and Methods

This prospective study included 133 patients with cirrhosis of liver and chronic liver diseases attending a tertiary care hospital. The study also included 75 age and sex matched healthy controls. The diagnosis of chronic liver disease was based on clinical examination, biochemical investigations, ultrasound abdomen and upper gastrointestinal endoscopy. The etiology of liver disease was based on history of significant alcohol consumption, presence of viral markers (HBsAg, HCV), HBV DNA, HCV RNA autoimmune markers and metabolic workup.

The serum samples of both patients and controls were tested using commercially available enzyme-linked immunosorbent assay kits for HBsAg (Hepanostica, Biomerieux, Netherlands), anti HCV (HEPAVASE-A-96, General Biologicals, Taiwan) and total anti-HAV antibodies (SP-NANBASE C-96, General Biologicals, Taiwan).

Data from patients and the control groups were compared using unpaired “t” test.
Results

One hundred and thirty three chronic liver diseases and seventy-five healthy controls in the age group 11-75 years were included. The mean age in patient and control group was 45.7 ±14.0 and 44.3 ± years respectively. The most common cause of chronic liver disease was HBV (29.3%), followed by alcohol (21.1%), HCV (14.2%), HBV HCV dual infection in 1.5% and cryptogenic cirrhosis (23.3%). The remaining cases were Budd chiari (2%), autoimmune (1%), Wilson’s (2%) and acute on chronic liver disease (2%).

Among the total 133 chronic liver diseases 124 (93.2%) patients were found to be positive for antiHAV (total) antibodies. Among the healthy controls 71/75 (94.6%) had antiHAV antibodies.

The prevalence of antibodies was similar irrespective of etiology of chronic liver disease (Table). The three cases of acute on chronic were negative for IgM antiHAV antibodies.

The total anti HAV antibodies were stratified according to age group and it was observed that 87% of controls and 75% of patients in age group 10-20 years had protective antibodies while subjects above 20 years in both groups had antiHAV in the range of 90-100% in different age groups (Figure).

Discussion

HAV is a globally distributed and faeco-orally transmitted virus. The epidemiology of the virus varies and depends on standards of sanitation and hygiene. The infection in preschool and school age children is generally mild, subclinical and acute symptomatic in adolescents and young adults.1,2 In high endemic areas like India most adults are immune to HAV infection. Recently some of the developing countries have observed a shift from high endemicity to intermediate endemicity. This may be because of improved hygiene and sanitation in these countries. This has resulted in a decreased exposure of the children to water and food contaminated with HAV that has led to higher incidence of HAV infection among adults. HAV in adults causes more severe and prolonged disease.4 Over the past few years in India, improvement in living standards has resulted in change in epidemiology of HAV from hyper endemic to that of intermediate endemicity.6 This might leave a proportion of adolescents and adults unexposed to HAV infection. This large multicentric study has also shown that seropositive rates increased with age from 52.2% to 80.8% in group under five years and in 16 years and above respectively. The seroprevalence from five cities varied from 3% to 85.4% (mean 77%).

In spite of change in epidemiology, another study from North India has found that majority of school children (96-98%) have protective antiHAV antibodies, hence vaccination may not be necessary.7 Retrospective seroprevalence study by Arankalle et al from Pune has revealed a clear shift in the epidemiological profile to HAV especially in urban population.8 Another study from Delhi also found a very low prevalence of 5.3%.9

In the Western countries, mortality due to acute HAV infection is high in chronic liver diseases. Hence, Hepatitis A vaccination is recommended worldwide for patients with chronic liver disease to prevent decompensation due to super infection with HAV.10 Studies with HAV vaccine have shown seroconversion rates up to 98% in patients with compensated cirrhosis and 65.7% in decompensated cirrhosis.10,11 Whether this strategy is justified in India needs to be evaluated.

In this study we have found a seroprevalence of 92% in controls and 93.2% in the patient group. The higher prevalence is probably due to older age groups (mean age 45.7 ±14.0 years). In a study from New Delhi 97.6% of cirrhotics (248/288) were found to be HAV IgG positive.12 Study from Chandigarh revealed 99% seroprevalence among 55 patients of cirrhosis.13 One of the studies from south India has shown 51 out of 52 patients with cirrhosis of the liver (mean age 57.1 ± 11 years) and all controls (mean age 52±54 years) were positive for antibodies to HAV.14 Our results are in agreement with other reports from our country. These studies have also

Table: Prevalence of antiHAV antibodies in control subjects and patients with chronic liver diseases

<table>
<thead>
<tr>
<th>Etiology</th>
<th>n</th>
<th>No. positive (%)</th>
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<tbody>
<tr>
<td>Healthy controls</td>
<td>75</td>
<td>71 (94.6)</td>
</tr>
<tr>
<td>HBV related</td>
<td>39</td>
<td>36 (92.3)</td>
</tr>
<tr>
<td>HCV related</td>
<td>19</td>
<td>84 (94.7)</td>
</tr>
<tr>
<td>HBV+HCV</td>
<td>2</td>
<td>1 (50)</td>
</tr>
<tr>
<td>Alcoholic</td>
<td>29</td>
<td>27 (93.1)</td>
</tr>
<tr>
<td>Cryptogenic</td>
<td>31</td>
<td>30 (96.7)</td>
</tr>
<tr>
<td>Acute on chronic</td>
<td>3</td>
<td>3 (100)</td>
</tr>
<tr>
<td>Autoimmune</td>
<td>5</td>
<td>4 (80)</td>
</tr>
<tr>
<td>Wilson’s</td>
<td>3</td>
<td>3 (100)</td>
</tr>
<tr>
<td>Budd Chiari</td>
<td>2</td>
<td>2 (100)</td>
</tr>
<tr>
<td>Total</td>
<td>133</td>
<td>124 (93.2)</td>
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</tbody>
</table>

Figure: Prevalence of anti HAV antibody in different age groups in control subjects and patients with chronic liver disease (CLD)
recommended that vaccination against HAV is not required in Indian patients.

Vaccination against HAV would have been justified if there was a decreased seroprevalence of antiHAV IgG or increased prevalence of acute hepatitis A in liver cirrhosis. Das et al have shown in a small number of cases that HAV induced decompensation is not common.9

Thus, in view of high prevalence of HAV antibodies in cirrhosis of liver, HAV vaccine is not routinely required in chronic liver disease. Prior screening for HAV may be more cost effective than vaccination.

References


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