Should One Vaccinate Patients with Chronic Liver Disease for Hepatitis A Virus in India?

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Abstract

Background: Hepatitis A virus (HAV) vaccination is recommended worldwide for patients with chronic liver disease to prevent decompensation due to superinfection with HAV. India being endemic for HAV, the prevalence of pre-existing antibodies against HAV due to subclinical exposure to the virus in childhood among patients with chronic liver disease may be high and, therefore, vaccination may not be needed. However, little data are available on the prevalence of HAV antibody among patients with chronic liver disease in India.

Methods: All patients with chronic liver disease seen at Gastroenterology Center, Army Hospital R and R, New Delhi during the year 2002 and diagnosed to have either chronic liver disease were tested for the presence of IgG anti-HAV antibody in their sera (using a commercial ELISA kit). All patients with acute exacerbation or rapid deterioration of a preexisting chronic liver disease were separately studied for presence of IgM anti-HAV. In addition, a matched number of patients who attended the center due to diseases other than liver disease were also studied as controls.

Results: One hundred and eighty seven patients of chronic liver disease and 89 controls were studied. Mean age of these two groups was 38.6 and 42.1 years and 153 (81.8%) and 78 (87.6%) of them were males respectively. Etiology of chronic liver disease was HBV infection in 91 (48.7%), HCV infection in 62 (33.2%), autoimmune chronic hepatitis in 3 (1.6%), PBC in seven (3.7%) and cryptogenic 24 (12.8%). Of these 179 (95.7%) patients tested positive for IgG anti-HAV. A total of 37 hospitalisations in 29 patients were noted during the study period due to acute exacerbation of pre-existing chronic liver disease. None of these were positive for IgM anti-HAV, while 28 were positive for IgG anti-HAV. Among the controls, 87 controls (94.6%) were positive IgG anti-HAV. The prevalence of anti-HAV positivity was similar among patients with various etiologies.

Conclusion: Vaccination against HAV is not routinely required among patients with chronic liver disease in India as there is a very high prevalence of pre-existing antibodies in these patients. HAV superinfection as a cause of acute exacerbation of chronic liver disease was not seen in this.

INTRODUCTION

Hepatitis A virus (HAV) vaccine has become commercially available in India and is being routinely recommended for patients with chronic liver disease on the basis of studies carried out in other countries. Such recommendations are based on studies that suggest that acute HAV superinfection in patients with chronic liver disease is associated with an increase in the severity of the disease and a high mortality.

While the ability of this vaccine to safely induce high levels of immunity even in patients with chronic liver disease has been demonstrated, its usefulness in Indian settings is suspect due to high prevalence of anti-HAV among Indian Patients. Several recent reports from various parts of the world have documented a decreasing prevalence of protective antibodies against HAV in the general population, presumably due to an improvement in hygiene and sanitation in these countries. Similar trend has not however, been found in India and HAV prevalence in India has been reported to vary between 85% and 95%. Available studies report an anti-HAV antibody prevalence of 5.3-97.6% among patients with chronic liver disease. HAV vaccine is expensive and may add to the cost of medical care for such patients. Therefore, we evaluated the prevalence of anti-HAV antibody among...
patients with chronic liver disease in India.

**MATERIAL AND METHODS**

The study population consisted of (a) a cohort of patients with chronic hepatitis and cirrhosis who are being followed up at the a tertiary care center and Armed Forces Chronic Hepatitis Registry during the year 2002 and (b) additional studies were carried out in patients with chronic liver disease who presented with acute exacerbation of disease.

Chronic liver disease patients included those with chronic hepatitis and cirrhosis. The diagnosis of chronic hepatitis was based on the clinical profile, liver function tests (LFT), viral and other serological studies and liver biopsy. All patients with cirrhosis were also investigated as above and also underwent upper gastrointestinal endoscopy, imaging (ultrasound/CT scan) and whenever possible liver biopsy. Hepatitis B was diagnosed when the hepatitis B surface antigen (HBsAg) was positive and hepatitis C was diagnosed when HCV RNA was positive. Sera of all the patients included in the study were tested for antibodies against the hepatitis A virus (IgG anti-HAV) and HBsAg using a commercially available kit for the enzyme-linked immunosorbent assay (ELISA; Organon Teknika, Amsterdam, The Netherlands) while HCV RNA was tested by the reverse transcriptase polymerase chain reaction (RT-PCR). Acute exacerbation of chronic liver disease was defined as clinical deterioration such as new development or significant worsening of ascites, jaundice or encephalopathy, or biochemical deterioration such as rapid rise in bilirubin (>5 mg/dl) from previous value or development of coagulopathy with over two point rise in INR from previous value over a few days. Sera of all such patients were also tested for IgM anti-HAV in addition to all the tests mentioned above. Data from patients and the control group was compared by unpaired t test and chi square test as applicable.

**RESULTS**

One hundred and eighty seven patients of chronic liver disease and 89 controls were studied. Mean age of these two groups was 38.6 and 42.1 years respectively. One hundred fifty three (81.8%) patients with chronic liver disease and 78 (87.6%) of controls were males. Thirty one controls and 22 patients with chronic liver disease were class officers or their families. Etiology of chronic liver disease was HBV infection in 91(48.7%), HCV infection in 62 (33.2%), primary biliary cirrhosis in three (1.6%), PBC in seven (3.7%) and cryptogenic cirrhosis in 24 (12.8%). Of these 179 (95.7%) patients tested positive for IgG anti-HAV. The prevalence of anti-HAV positivity was similar among patients with various etiologies. (Table 1) Two out of 22 officers and their families, 6/165 persons below officer rank (PBOR) and thier families with chronic liver disease and 1/31 officers and 1/58 PBOR and their families in the control group were IgG anti-HAV negative. In addition, a total of 37 hospitalisations in 29 patients were noted during the study period due to acute exacerbation of pre-existing chronic liver disease. None of these were positive for IgM anti-HAV, while 28 were positive for IgG anti-HAV. Among the controls, 87 (94.6%) were positive IgG anti-HAV. During the same period 23 patients were also hospitalized for acute liver failure and five of these were found to be IgM anti-HAV positive.

**DISCUSSION**

We found that about 95% patients with or without chronic liver disease in our set up have antibodies against HAV. The prevalence was similar irrespective of the aetiology and type of chronic liver disease.

HAV infection in India occurs at an early age. In one study from Lucknow, 68% children from 0-5 years age group, 91% from 6-10 years and 96% from 11-18 years age group were found to have anti-HAV positive.12 Another study from Delhi evaluated 276 male and 224 female school children aged 10-17 years for anti-HAV antibodies. The prevalence of these antibodies in the age group 10-12, 13-14 and 15-17 years was found to be 98.6 per cent, 94.8 per cent and 98.3 per cent respectively.13 Need for vaccination against HAV in India is under scrutiny even for general population.

The prevalence of anti-HAV antibody reported among the general population from various parts of India also ranges between 85% and 98%,5,13-15 One study from India has reported an anti-HAV antibody prevalence of only 5.3% among 94 patients with chronic liver disease. Another study conducted with an adequate sample size with appropriate diagnostic criteria for the underlying disease, showed the IgG anti-HAV prevalence to be 97.6% using highly sensitive ELISA method of assessment.3 It is difficult to explain such a large discrepancy in the prevalence of anti-HAV antibody in a similar population. Our results suggest that HAV vaccination among patients with chronic liver disease in India is not routinely required.

5-15% of adult population in India is negative for IgG anti-HAV.5,13-15 These could be persons belonging to the affluent sections of society who may not have had subclinical exposure to HAV in their early life.3 However in our control population, officers and their families did not have significantly lower IgG anti-HAV positive results as compared to PBOR and their families.

Since the number of IgG anti-HAV patients is small and it

<table>
<thead>
<tr>
<th>Group of patients</th>
<th>Number</th>
<th>Positive for IgG anti HAV</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>89</td>
<td>87</td>
<td>94.6</td>
</tr>
<tr>
<td>HBV related chronic liver disease</td>
<td>91</td>
<td>89</td>
<td>97.8*</td>
</tr>
<tr>
<td>HCV related chronic liver disease</td>
<td>62</td>
<td>58</td>
<td>93.5*</td>
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<tr>
<td>Primary biliary cirrhosis</td>
<td>7</td>
<td>6</td>
<td>85.7*</td>
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<tr>
<td>Autoimmune chronic hepatitis</td>
<td>3</td>
<td>3</td>
<td>100*</td>
</tr>
<tr>
<td>Cryptogenic cirrhosis</td>
<td>24</td>
<td>23</td>
<td>95.8*</td>
</tr>
<tr>
<td>Total</td>
<td>187</td>
<td>179</td>
<td>95.7*</td>
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</tbody>
</table>

Note: * =Difference from controls not significant

Table 1 : IgG anti HAV positivity amongst patients with chronic liver disease
will be more cost-effective to perform HAV serology prior to vaccinating them (the cost per test for IgG anti-HAV is Rs 250 whereas the cost for one dose of HAV vaccine is Rs 1600). Therefore, our results support the contention that the high prevalence of HAV antibodies in patients with chronic liver disease makes the routine vaccination of such patients against HAV infection an exercise in futility.

REFERENCES