Antibody response to Salmonella typhi O and H antigens was evaluated in 24 individuals with either hepatointestinal or hepatosplenic schistosomiasis mansoni before and after typhoid vaccination, and compared with that of non-infected controls. Before vaccination, Schistosoma-infected patients showed a higher frequency of positive antibody to O antigen and the same frequency to H antigen when compared with that of healthy individuals. However, those with hepatosplenic schistosomiasis showed higher titres of antibody to H antigen than those with hepatointestinal disease or healthy individuals. Infected subjects, particularly those with hepatointestinal disease, showed a decreased response after typhoid vaccine. This diminished ability to mount an immune response towards typhoid antigens during schistosomiasis may interfere with the clearance of the bacteria from blood stream and, therefore, play a role in the prolonged survival of salmonella as observed in some patients with chronic salmonellosis associated with schistosomiasis.


Comprised 16 individuals with the hepatointestinal, and 10 with the hepatosplenic schistosomiasis, characterized according to the criteria defined by Prata2. Their clinical and nutritional status were satisfactory. Eggs of Schistosoma mansoni in faeces were quantified by the Kato-Katz method8. The control group comprised nine healthy individuals of both sexes, 20 to 50 years old (mean ± SD = 29 ± 9), 70% being Caucasians.

The Salmonella typhi vaccine, prepared with 10⁶ formol-treated bacteria strain Ty2 by the Instituto Oswaldo Cruz, was intradermally administered in a single dose, as indicated by the manufacturer. Before vaccination and 30 days after serum antibodies to O and H antigens were detected using a Widal agglutination test29 provided by Laborclin. Titres > 20 were considered as positive.

The results were statistically analysed by the Chi-square test and Fisher’s exact test, at a level of 5% of significance (p < 0.05).

**RESULTS**

Antibodies to O antigen of Salmonella typhi were detected in 3 out of the 26 Schistosoma-infected patients (11.5%) before the application of typhoid vaccine and in none of the normal controls (Table 1). In the positive individuals, the antibodies titres were 40, 80 and 160, and they presented 96, 672 and 984 eggs of Schistosoma mansoni per gram of faeces, respectively. The frequency of pre-vaccination positive titres to H antigen was the same in infected and healthy individuals (Table 1). However, the highest titres of antibody to H antigen were found in the hepatosplenic patients and no difference was detected between the hepatointestinal and control groups (Table 2).

<p>| Table 1 - Frequency of pre-vaccination positivity of antibody to Salmonella typhi O and H antigens in hepatointestinal (HI) and hepatosplenic (HS) Schistosoma mansoni-infected patients and healthy individuals. |
|---------------------------------|---------------------------------|---------------------------------|---------------------------------|</p>
<table>
<thead>
<tr>
<th>Group</th>
<th>Antibodies to</th>
<th>O antigen n²</th>
<th>%</th>
<th>H antigen n²</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>0/9</td>
<td>0.0</td>
<td>4/9</td>
<td>44.4</td>
<td></td>
</tr>
<tr>
<td>HI</td>
<td>1/16</td>
<td>6.3</td>
<td>8/16</td>
<td>50.0</td>
<td></td>
</tr>
<tr>
<td>HS</td>
<td>2/10</td>
<td>20.0</td>
<td>5/10</td>
<td>50.0</td>
<td></td>
</tr>
</tbody>
</table>

*p > 0.05 for both antigens by Chi-square test (5 x 2 table) and Fisher’s exact test (2 x 2 table: HI x Normal, HS x Normal, HI x HS).

Thirty days after vaccination, 20.8% of Schistosoma-infected patients and 55.5% of normal controls presented antibodies to salmonella O antigen. Within the group of infected individuals a difference in the frequency of positivity was found between the hepatointestinal (12.5%), hepatosplenic (37.5%) and normal (55.5%) subjects (Table 3). An antibody response to H antigen was also less frequently found in the hepatointestinal (50%) than in hepatosplenic (75%) or normal individuals (100%) (p<0.05) (Table 3).

<table>
<thead>
<tr>
<th>Table 2 - Frequency of high titres of antibody to salmonella H antigen in hepatointestinal (HI) and hepatosplenic (HS) Schistosoma mansoni-infected patients and healthy individuals before typhoid vaccination.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group</td>
</tr>
<tr>
<td>--------------------------------</td>
</tr>
<tr>
<td>Normal</td>
</tr>
<tr>
<td>HI</td>
</tr>
<tr>
<td>HS</td>
</tr>
</tbody>
</table>

*p > 0.05 by Fisher’s exact test (2 x 2 table: HI x Normal, HS x Normal, HI x HS).

DISCUSSION

Before vaccination, 11.5% of Schistosoma-infected patients showed positive antibody response to salmonella O antigen as compared to no response of healthy controls. However, the basal frequency of reactivity to salmonella H antigen in our infected group was similar to that of the controls. This same frequency of antibodies to salmonella was previously shown by Shikanai-Yasuda et al15 in hepatosplenic patients and by Milhomen and Suassuna14 in healthy individuals.

The antibody to salmonella O antigen, found before vaccination of Schistosoma-infected patients, is an IgM22 and its presence...

indicates recent infection by this bacteria\textsuperscript{1,10}. However, since our patients had neither a history nor any clinical evidence of overt salmonellosis, it is possible that anti-O agglutinins were originated from subclinical salmonella bacteremias. Our finding of increased levels of anti-H antibodies in subjects with hepatosplenic schistosomiasis supports this hypothesis. Another possibility which cannot be ruled out is the occurrence of cross antigens between salmonella and schistosome\textsuperscript{7}.

In our study, schistosome-infected patients, particularly those with the hepatointestinal disease, showed an inadequate antibody response to salmonella O and H antigens after a single dose of typhoid vaccine. The immune response of hepatosplenic subjects appears to be less impaired, as previously shown after three doses of the vaccine\textsuperscript{6} in those with this form of the disease. The finding that suppressor T lymphocytes (CD8\textsuperscript{+}) are increased in hepatointestinal patients and decreased in those with hepatosplenic schistosomiasis\textsuperscript{28}, may help understanding these results. Alternatively, the better antibody response of hepatosplenic individuals may be due to previous contact with salmonella, made easier by the porto-systemic shunts found in these patients. The increased pre-vaccination levels of anti-salmonella antibodies in this group favors this possibility.

It has been recognized that both the functions of T lymphocytes\textsuperscript{15,17} and macrophages\textsuperscript{16} are altered in Schistosoma-infected patients. Our data demonstrate that the ability to produce antibodies to unrelated antigens is also impaired in schistosomiasis. The fact that increasing the antigenic stimulus may induce antibody production in infected subjects\textsuperscript{29} may be interpreted as antigenic competition\textsuperscript{12} between schistosome\textsuperscript{2} and salmonella\textsuperscript{7} antigens present in the serum of these individuals.

The decreased ability of schistosome-infected individuals to mount an adequate immune response to salmonella may very well contribute to the establishment and prolonged survival of this bacteria in subjects suffering from schistosomiasis.

RESUMO

A resposta de anticorpos para os antígenos O e H da Salmonella typhi foi avaliada em 24 indivíduos com esquistossomose hepatointestinal ou hepatoesplênica antes e após vacinação antitifoídica, e comparada com a resposta de indivíduos controles normais. Antes da vacinação, pacientes esquistossomáticos mostraram uma maior frequência de anticorpos positivos para o antígeno O e a mesma frequência de anticorpos positivos para o antígeno H quando comparada com aquela de indivíduos controles normais. Porém, aqueles com esquistossomose hepatoespêlnica mostraram títulos maiores de anticorpos para o antígeno H do que aqueles com a forma hepatointestinal da doença ou os indivíduos controles normais. Pacientes esquistossomáticos, particularmente aqueles com a forma hepatointestinal, mostraram uma menor resposta após a vacinação antitifoídica. Esta menor capacidade para apresentar uma resposta imune para antígenos de salmonela pode interferir com a retirada da bactéria da corrente sanguínea e, portanto, contribuir como um dos determinantes de sua prolongada sobrevivência como observada em pacientes com esquistossomose septicêmica prolongada associada à esquistossomose.

Palavras-chave: Esquistosomose mansoni, Salmonella typhi, Antígenos O e H, Salmonelose septicêmica prolongada associada à esquistossomose.

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REFERENCES


