Revised cutoff values of serum aminotransferase in detecting viral hepatitis among CAPD patients: experience from Taiwan, an endemic area for hepatitis B

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Abstract

Background. To determine the best cutoff values of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) in detecting viral hepatitis C infection among patients of continuous ambulatory peritoneal dialysis (CAPD).

Methods. 90 (44 male and 46 female) CAPD patients and 526 adult controls (266 male, 260 female) were enrolled. Serum AST and ALT were measured by an auto-analyser monthly. Serum HBsAg was examined using a RIA method and anti-HCV by a second-generation EIA method. The best cutoff values of AST and ALT for detecting viral hepatitis were obtained from the ROC (receiver-operating characteristic) curve.

Results. The prevalence of anti-HCV(+) was significantly higher in CAPD patients (16.7%) than in normal controls (4.9%), while that of HBsAg(+) was similar in both groups. CAPD patients had significantly lower levels of serum aminotransferases compared to normal controls. Mean AST were 23.8 IU/l in normal control and 18.8 IU/l in the CAPD patients (P < 0.001). Mean ALT were 21.9 IU/l in normal controls and 15.3 IU/l in the CAPD patients (P < 0.001). CAPD patients with HCV infection had higher serum AST and ALT levels than those without. However, HBV infection did not cause significant serum aminotransferase elevation in patients. The conventional cutoff values of AST (40 IU/l) and ALT (40 IU/l) for detecting viral hepatitis yielded only a sensitivity of 27.3 and 18.2% respectively; on the contrary, our revised cutoff values of AST (24 IU/l) and ALT (17 IU/l) had better sensitivities (AST, 72.7%; ALT, 63.6%). For serial aminotransferase values, the sensitivity of AST and ALT for detecting HCV were 36.4 and 27.3% by conventional criteria, and were both 81.8%, by our newly revised criteria.

Conclusions. Serum aminotransferase cutoff values should be modified for screening viral hepatitis in a CAPD population. Our new cutoff criteria had important clinical implications in providing benefits of earlier detection and possible prevention from chronic hepatic deteriorations.

Key words: serum aminotransferase; viral hepatitis; CAPD

Introduction

Virus hepatitis is highly prevalent in the dialysis population [1–5]. Taiwan is one of the endemic areas with a high prevalence rate of virus hepatitis [6,7]. In our previous work, we have demonstrated a relatively higher prevalence rate, compared with other countries, of hepatitis B virus (HBV) and hepatitis C virus (HCV) infection in our hemodialysis (HD) patients [8].

Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) are used for screening liver disease both in general population [9], and in HD patients [3,4]. It had been reported that serum aminotransferases were decreased in HD patients [10,11] and the cutoff value of AST and ALT in detecting viral hepatitis should be set at lower levels in such population [11]. However, to our knowledge, they had never been studied in patients on continuous ambulatory peritoneal dialysis (CAPD). The aim of this study is to build up a newly revised cutoff values of AST and ALT for better screening of viral hepatitis infection in the CAPD population.

Subjects and methods

Patients

Ninety patients on regular CAPD were enrolled. Forty-four patients were men (48.9%) and forty-six (51.1%) women. Patients with habitual chronic alcoholism were excluded. The mean age of the patients was 45.4 ± 2.5 years (range 18–73...
Serum aminotransferase for detecting viral hepatitis in CAPD

Results of ROC plotting curve. Specificity 90.6%) and 17 IU/l (Sensitivity 63.6%, specificity, which is the point nearest the top left-hand corner.

Statistical analysis

Results were expressed as mean ± SEM. Serum aminotransferases were then logarithmically transformed for statistical tests. Student's t-test was used to evaluate the differences of continuous variables between two groups. The chi-square test with Yates' correction was used to determine the statistical differences between proportions entered in 2 × 2 contingency tables. Differences were considered significant when P was less than 0.05.

The best cutoff values of AST and ALT for screening viral hepatitis were obtained from the ROC (receiver-operating characteristic) curve [11–13], on the assumption that the false-positive cost/false-negative cost ratio was 1/1. The best cutoff is that which maximizes the sum of the sensitivity and specificity, which is the point nearest the top left-hand corner of ROC plotting curve.

Results

Prevalences of viral hepatitis and serum aminotransferase levels

As shown in Table 1, no significant difference of the seropositive rate of HBsAg arose between controls (14.4%) and CAPD patients (13.3%) (P = 0.46). However, the prevalence of anti-HCV(+) was significantly higher in the CAPD patients (control 4.9%) vs. CAPD patients (16.7%), (P < 0.001). Mean AST were 23.8 ± 1.8 (22–25.6) IU/l in normal controls and 18.8 ± 1.8 (17–20.6) IU/l in the CAPD patients respectively (P < 0.001). Mean ALT were 21.9 ± 1.6 (20.3–23.5) IU/l in normal controls and 15.3 ± 1.2 (14.1–16.4) IU/l in the CAPD patients (P < 0.001). CAPD patients had significantly lower levels of serum aminotransferases compared to normal controls.

For studying the impact of hepatitis B or C infection on serum aminotransferase levels, we divided the CAPD patients into four subgroups, i.e. HBV(+)&HCV(−), HBV(−)&HCV(+), HBV(+)&HCV(+), and HBV(−)&HCV(−) (Table 2). In the Table, number of patients, gender, mean age, aminotransferase levels, and status of viral hepatitis among each subgroup were shown. There was no statistically significant difference in serum aminotransferase levels between subgroups 1 and 2, nor between subgroups 3 and 4. Therefore the status of HBV infection (i.e. HBsAg(+) vs HBsAg(−)) had no impact on serum aminotransferase levels. On the contrary, individuals with anti-HCV antibody (subgroups 1 and 2) always had higher mean AST and ALT values than those without anti-HCV antibody (subgroups 3 and 4) (P < 0.001).

Cutoff values of serum aminotransferase from ROC analysis

As shown in Figure 1, the areas under the curve of AST and ALT were similar in CAPD patients and normal populations. The calculated cutoff values of AST and ALT for detecting HCV infection in our CAPD population were 24 IU/l (sensitivity 72.7%, specificity 90.6%) and 17 IU/l (sensitivity 63.6%, specificity 88.7%) respectively. On the contrary, conventional cutoff values for AST (40 IU/l) and ALT (40 IU/l) yielded only a sensitivity (specificity) of 27.3% (92.4%) and 18.2% (96.2%) respectively.

Old vs new criteria for sensitivity and specificity

For evaluating whether the new criteria are better than conventional ones in detecting HCV during serial examinations, serial monthly serum aminotransferase levels in the range of 6–14 months were reviewed retrospectively from 64 individuals of the 90 CAPD patients. The aminotransferase patterns were defined as ‘normal’, if all of the aminotransferase values were within normal limits by conventional or new cutoff criteria; and ‘abnormal’, if alternatively normal and abnormal values were found. Only the ‘normal’ pattern was considered as ‘normal’ in calculating sensitivity and specificity. The sensitivity/specificity for detecting HCV infection by conventional criteria were 36.4%/92.4% and 27.3%/90.6% for AST and ALT respectively. However, according to our new criteria (AST = 24 IU/l, ALT = 17 IU/l), the sensitivity/specificity for HCV(+) and HBV(−)&HCV(−) were 24.2% (96.2%) and 18.2% (96.2%) respectively.

Table 1. The clinical characteristics and seroprevalences of viral hepatitis in the CAPD population and normal controls.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control (n = 526)</th>
<th>CAPD (n = 90)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>45 ± 2.3</td>
<td>45.4 ± 2.5</td>
<td>0.82</td>
</tr>
<tr>
<td>Age range (years)</td>
<td>20–79</td>
<td>18–73</td>
<td></td>
</tr>
<tr>
<td>Sex (M:F)</td>
<td>266:260</td>
<td>44:46</td>
<td>0.34</td>
</tr>
<tr>
<td>AST (IU/l)*</td>
<td>23.8 ± 1.8</td>
<td>18.8 ± 1.8</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>ALT (IU/l)*</td>
<td>21.9 ± 1.6</td>
<td>15.3 ± 1.2</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>HBsAg(+)</td>
<td>76 (14.4%)</td>
<td>12 (13.3%)</td>
<td>0.46</td>
</tr>
<tr>
<td>anti-HCV(+)</td>
<td>26 (4.9%)</td>
<td>15 (16.7%)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

*Mean ± SEM; n case numbers.
Table 2. Clinical and biochemical findings in subgroups of CAPD patients with different viral hepatitis markers

<table>
<thead>
<tr>
<th>Subgroup Status</th>
<th>1 (HBV(+) &amp; HCV(+))</th>
<th>2 (HBV(−) &amp; HCV(+))</th>
<th>3 (HBV(+) &amp; HCV(−))</th>
<th>4 (HBV(−) &amp; HCV(−))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numbers</td>
<td>4</td>
<td>11</td>
<td>8</td>
<td>67</td>
</tr>
<tr>
<td>M:F</td>
<td>2:2</td>
<td>7:4</td>
<td>5:3</td>
<td>30:37</td>
</tr>
<tr>
<td>Age</td>
<td>44.8 ± 2.1</td>
<td>44.3 ± 1.9</td>
<td>43.8 ± 1.6</td>
<td>45.2 ± 2.5</td>
</tr>
<tr>
<td>AST</td>
<td>25.0 ± 2.1</td>
<td>29.8 ± 3.1</td>
<td>13.6 ± 2.0</td>
<td>17.1 ± 1.4</td>
</tr>
<tr>
<td>ALT</td>
<td>24.9 ± 2.8</td>
<td>31.1 ± 4.8</td>
<td>9.8 ± 1.6</td>
<td>11.4 ± 1.0</td>
</tr>
</tbody>
</table>

HBV (+); HBsAg (+), HCV (+); anti-HCV (+), age: mean ± SEM; *P = NS, compared with subgroup 2; **P < 0.001, compared with subgroup 3; †P < 0.001, compared with subgroup 4; ‡P = NS, compared with subgroup 4.

Fig. 1. ROC plots of serum aminotransferase for detecting HCV infection in normal control and CAPD patients. The areas under the curve of AST were similar in normal controls (0.713 ± 0.038) and in CAPD patients (0.732 ± 0.08). The areas under the curve of AST were similar in normal controls (0.709 ± 0.041) and in CAPD patients (0.721 ± 0.082). (*P = NS).

Sensitivity were 81.8%/90.6% and 81.8%/86.7% for AST and ALT respectively.

Discussion

High prevalences of HBV carrier rate (13.3%) and HCV infection (16.7%) in CAPD patients were demonstrated in this work (Table 1). The prevalence of HBsAg (+) in CAPD patients (13.3%) was similar to that of the normal controls (14.4%) and general populations (15–20%) [6]. This may be attributed to Taiwan’s high endemic state for HBV infection and reflect acquisition prior to the initiation of maintenance dialysis therapy [6,8]. However, the prevalence rate of HCV infection in CAPD patients (16.7%) was higher than the observations from Western countries (1.8–8.9%) [14,15]. Besides, in this work we have demonstrated that status of HBV infection had no impact on the mean AST and ALT levels in CAPD subgroups while HCV infection did (Table 2). This implied that AST and ALT were more useful in detecting HCV than HBV infections in our CAPD population, although such results may be preliminary because of limitations in cases enrolled. In Taiwan, an area hyperendemic for HBV infection, HCV has become the primary cause of liver diseases in dialysis patients, and early detection of HCV infection is noteworthy and mandatory.

The exact mechanism of decreased serum aminotransferase levels in dialysis patients remained uncertain, though some had postulated that pyridoxine deficiency might be the leading cause. As shown in Table 1, mean AST and ALT levels were both significantly lower in our CAPD patients. This meant that most of the CAPD patients with HCV infection and abnormally ‘elevated’ serum aminotransferase levels may be masked by ‘depressed’ baseline AST and ALT values, and thus would be regarded as ‘normal’ and miss the benefits of earlier diagnosis. If we apply the conventional cutoff values of serum transaminase (AST = 40 IU/l, ALT = 40 IU/l) to screen HCV infec-
tion in CAPD patients, the sensitivity will be unacceptably low (18.2–27.3%). On the contrary, our revised AST and ALT cutoff criteria can greatly improve the sensitivities to 72.7% and 63.6% for AST and ALT, respectively, in detecting HCV infection in CAPD population. Since the cost of false-positive cases was only that for surveying viral hepatitis markers, while the cost of false-negative cases was the missed benefit of early detection and potential prevention from chronic hepatic decompensation [16]; our new criteria of serum aminotransferase cutoff values, albeit slightly less specific, may provide more good than harm to CAPD patients in screening viral hepatitis.

Viral hepatitis may cause fluctuations of aminotransferase levels. There remained one question of whether the new cutoff values, based on ‘spot observations’, could be applicable to those on serial evaluations. In 64 of the 90 CAPD patients, serial monthly AST and ALT values were available for analysis. By conventional criteria, 63.6% (by AST = 40 IU/l) and 72.7% (by ALT = 40 IU/l) of patients infected with HCV would be missed and misjudged as ‘normal’. However, such missed rate can be reduced to 18.2% by our new AST and ALT cutoff criteria. Thus the new cutoff values deduced from ‘spot observation’ and ROC analysis can also be applied to serial examinations.

In conclusion, the revised new cutoff criteria can greatly improve the sensitivities and is well applicable to serial examinations. Our revised new cutoff criteria had important clinical implications in providing benefits of earlier detection and possible prevention [16] from chronic hepatic deterioration among CAPD patients.

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References


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