Assessment of monoethylglycinexylidide as measure of liver function for patients with chronic viral hepatitis

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The liver metabolizes lidocaine by oxidative deethyla-
tion to form monoethylglycinexylidide (MEGX), an anal-
alyte proposed as an index of liver function. We deter-
mined MEGX and lidocaine serum concentrations with
the TDx (Abbott Laboratories) at baseline and 15, 30, 60,
and 90 min after the intravenous administration of
lidocaine (1 mg/kg), analyzing specimens from 12 appar-
ently healthy volunteers and 40 patients with chronic
viral hepatitis diagnosed by liver biopsy and serum
tests. The patients were grouped on the basis of the
histology activity index. The following laboratory tests
were performed on serum specimens from all subjects:
albumin (ALB), alanine aminotransferase (ALT), aspar-
tate aminotransferase (AST), alkaline phosphatase, total
bilirubin, and prothrombin time. The results showed no
significant difference among the four groups for the
concentrations of MEGX, lidocaine, and lidocaine/
MEGX at the four time points. However, the concentra-
tions of ALB, ALT, AST, AST/ALT, and prothrombin
time were substantially different among the four
groups. Thus, we conclude that assay of MEGX in our
patients with chronic viral hepatitis did not contribute
to the assessment of liver function when compared with
apparently healthy volunteers and traditional tests of
liver function.

Chronic viral hepatitis, which results from chronic infec-
tion with hepatitis B, hepatitis C, or delta hepatitis, is
often a progressive disease that can lead to cirrhosis and
its attendant complications of liver failure and portal
hypertension. In clinical practice, a liver biopsy in con-
junction with biochemical variables is used to determine
the degree of liver injury and the prognosis related to
these diseases. However, to what extent these variables
estimate the true functional hepatic reserve at any time
is controversial. In addition, evidence of hepatic synthetic
dysfunction, such as decreased serum albumin (ALB)6
concentration and prolonged prothrombin time, occurs
only late in the course of chronic liver disease, when the
hope for improvement from any antiviral therapy is
limited. Thus, a test that measures more subtle degrees
of hepatic dysfunction that are present before the onset of
decompensated cirrhosis may be useful clinically.

Numerous tests of functional hepatic reserve, such as
galactose elimination capacity [1], antipyrine breath test
[2], and indocyanine green clearance [3], that utilize the
role of the liver as an organ for detoxifying xenobiotics via
the cytochrome P-450 mixed-function oxidase system,
have been investigated previously although their clinical
utility has been limited. Lidocaine, a commonly used local
anesthetic and antiarrhythmic agent, is eliminated from
the body primarily by hepatic metabolism to monoethylgly-
cinexylidide (MEGX) [4]. Lidocaine exhibits a first-pass
effect because it is rapidly taken up and metabolized by
the microsomal cytochrome P-450 enzyme system [5].
Patients with chronic liver disease show a reduced plasma
clearance and prolongation of the plasma half-life of
lidocaine [6]. Thus, after the intravenous administra-
tion of lidocaine, the rate of decrease of the serum lidocaine

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concentration or the rate of increase of the major metabolite, MEGX, may serve as a test of liver function. Determination of the formation of MEGX may be useful as a predictor of short-term survival in cirrhotics before transplantation and may predict donor organ viability [7–13]. Recently, the determination of MEGX has been proposed as a quantitative test of liver function in patients with chronic hepatitis and cirrhosis [9–11]. To evaluate the clinical value of this proposed test for liver function, we determined the MEGX concentration in apparently healthy volunteers and patients with chronic viral hepatitis and compared the results with liver biopsies and established clinical laboratory tests of liver disease in patients.

Materials and Methods

Patients
We studied 40 patients with chronic viral hepatitis (mean age 42 years, range 23–62 years, 9 women and 31 men); 23 patients were chronically infected with hepatitis B, 14 with hepatitis C, and 3 with delta hepatitis. The diagnosis of chronic viral hepatitis was based on an increase in the serum alanine aminotransferase (ALT, EC 2.6.1.2) concentration for the previous 6 months and serological testing. Patients with a long history of alcohol use or taking medication that might induce microsomal enzymes were excluded from the study. The control group for the study consisted of 12 apparently healthy volunteers (mean age 31 years, range 18–55 years, 2 women and 10 men). Informed consent was obtained from all patients and apparently healthy volunteers before participation in the study. The protocol for the study was approved by the Institutional Review Board of the National Institute of Diabetes and Digestive and Kidney Diseases.

Histological Analysis
All hepatitis patients in the study had a percutaneous liver biopsy within 1 week of MEGX testing. Each biopsy specimen was reviewed and scored by an investigator (M.W.F.) and a pathologist (D.E.K.) with the scoring system established by Knodell et al. [14] and referred to as the histology activity index (HAI): periportal injury, piecemeal necrosis (0–10, PP score), portal inflammation (0–4, P score), lobular injury (0–4, L score), and fibrosis (0–4, F score). The maximum total score is 22 (sum of the maximum four individual scores), but the maximum score found in this study was 18. Patients were grouped on the basis of their HAI score: mild (HAI 0–6, mean age 41 years, range 27–59 years, 1 woman and 4 men), moderate (HAI 7–12, mean age 39 years, range 23–54 years, 6 women and 15 men), and severe (HAI 13–22, mean age 46 years, range 28–62 years, 2 women and 12 men).

MEGX Testing and Laboratory Analyses
MEGX testing was performed on all patients after an overnight fast. Patients in the supine position were given a dose of 1 mg/kg of 20 g/L lidocaine-HCl injected slowly into a peripheral vein over a period of ~1 min. Blood samples anticoagulated with EDTA were obtained just before injection and at 15, 30, 60, and 90 min after lidocaine administration. The plasma lidocaine and MEGX concentrations were measured by fluorescence polarization immunoassay with an Abbott TDx analyzer (Abbott Laboratories). The among-day CV for MEGX at a concentration of 98.7 µg/L (n = 22) was 7.7%; for lidocaine at 730 µg/L it was 2.6%. The concentration of MEGX before injection (background) was undetectable in all individuals.

Before the injection of lidocaine, the following tests were performed on a serum specimen from each patient and apparently healthy volunteer with the Hitachi 736 (Boehringer Mannheim): ALT, aspartate aminotransferase (AST, EC 2.6.1.1), ALB, alkaline phosphatase (EC 3.1.3.1), and total bilirubin. Further, the prothrombin time was determined by photo-optical clot detection with the Coag-A-Mate X2 (Organon Technika).

Statistics
The results for MEGX and lidocaine concentrations and the lidocaine/MEGX ratio are expressed as the mean ± SEM (Table 1). We calculated MEGX and lidocaine indices on the basis of the area under the curve (MEGX or lidocaine concentration at four time points) for each patient and apparently healthy volunteer. Further, analysis of variance (ANOVA) was used to compare four groups with the MEGX and lidocaine concentrations, the lidocaine/MEGX ratio at 15 min, and the indices (Table 1) and with traditional liver function tests (Table 2). Log transformation was used on all chemical tests except ALB and the lidocaine/MEGX ratio to normalize the data. If the ANOVA was significant (P <0.05), we used Duncan Multiple Range Test [15] to determine differences between groups. Groups shown with the same letter are not significantly different from each other (Table 2). We compared the HAI and the four-component biopsy scores comprising the HAI with the MEGX concentration at each time interval and the index by pairwise regression analysis (Table 3). A power analysis also was performed for the experimental design to determine the probability of detecting a difference in the concentration of MEGX, lidocaine, and the ratio at 15 min [16].

Results
There were no significant differences (P >0.05) among the four groups (apparently healthy volunteers and patients with mild, moderate, and severe hepatitis) for the MEGX and lidocaine concentrations and lidocaine/MEGX results at all time intervals and their indices (Table 1). The mean and SEM of the MEGX concentration for the three groups of hepatitis patients and apparently healthy volunteers are shown in Fig. 1. There was a progressive lowering of...
the curve for hepatitis patients, going from mild to severe injury. The curve for apparently healthy volunteers was similar to that for patients with moderate hepatic injury, with all points for mild hepatic injury above and severe hepatic injury below that of apparently healthy volunteers. The power analysis with 80% power to find a difference among groups indicated that a 20% difference in the mean is required for lidocaine, a 50% difference for MEGX, and 70% difference in the ratio for results at 15 min. Four (ALB, ALT, AST, and prothrombin time) of the six traditional laboratory tests to assess liver function and the AST/ALT ratio show a significant difference ($P < 0.01$) among the four groups (Table 2). The best tests were ALB, ALT, AST, and the AST/ALT ratio, which showed no overlap between apparently healthy volunteers and the three groups of hepatic injury. The prothrombin time results for apparently healthy volunteers overlapped with patients with mild and moderate chronic hepatitis but did differ from patients with chronic severe hepatitis. Two of the tests, total bilirubin and alkaline phosphatase, did not differ significantly among the four groups.

The MEGX concentration at the four sampling times and the index was compared with the composite HAI biopsy score and its four components (Table 3). There was a significant correlation ($P < 0.04$) between the composite HAI biopsy score and the MEGX concentration at 15 and 60 min and the index. Four of the five MEGX variables correlated significantly with either fibrosis or periportal injury and piecemeal necrosis. Portal inflammation correlated with the MEGX concentration only at 15 min, and there was no correlation of any of the MEGX variables with lobular injury.

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**Table 1. Comparison of lidocaine and MEGX concentrations and their ratio (mean ± SEM) among three groups with chronic viral hepatitis on the basis of severity and apparently healthy volunteers.**

<table>
<thead>
<tr>
<th>Group*</th>
<th>n</th>
<th>Analyte</th>
<th>15</th>
<th>30</th>
<th>60</th>
<th>90</th>
<th>Index, µg/L per h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apparently healthy volunteers</td>
<td>12</td>
<td>LIDOCaine, µg/L</td>
<td>816.7 ± 50.5</td>
<td>533.3 ± 51.2</td>
<td>383.3 ± 50.5</td>
<td>316.7 ± 57.5</td>
<td>675.0 ± 66.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MEGX, µg/L</td>
<td>69.6 ± 10.6</td>
<td>76.2 ± 6.8</td>
<td>78.7 ± 7.6</td>
<td>77.6 ± 6.9</td>
<td>104.7 ± 10.1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>L/M ratio</td>
<td>16.2 ± 3.5</td>
<td>7.5 ± 0.9</td>
<td>5.3 ± 0.8</td>
<td>4.3 ± 0.8</td>
<td>10.6 ± 1.5</td>
</tr>
<tr>
<td>Mild hepatitis</td>
<td>5</td>
<td>LIDOCaine, µg/L</td>
<td>860.0 ± 24.5</td>
<td>520.0 ± 37.4</td>
<td>380.0 ± 37.4</td>
<td>280.0 ± 49.0</td>
<td>670.0 ± 39.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MEGX, µg/L</td>
<td>88.6 ± 17.4</td>
<td>88.1 ± 14.0</td>
<td>84.8 ± 13.1</td>
<td>87.0 ± 12.7</td>
<td>119.4 ± 18.2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>L/M ratio</td>
<td>11.7 ± 2.7</td>
<td>6.9 ± 1.8</td>
<td>5.2 ± 1.4</td>
<td>4.0 ± 1.6</td>
<td>9.2 ± 2.4</td>
</tr>
<tr>
<td>Moderate hepatitis</td>
<td>21</td>
<td>LIDOCaine, µg/L</td>
<td>828.6 ± 56.5</td>
<td>490.5 ± 25.7</td>
<td>338.1 ± 17.6</td>
<td>252.4 ± 14.8</td>
<td>623.2 ± 32.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MEGX, µg/L</td>
<td>73.5 ± 9.4</td>
<td>78.9 ± 7.2</td>
<td>76.8 ± 5.7</td>
<td>74.7 ± 5.6</td>
<td>105.1 ± 8.7</td>
</tr>
<tr>
<td></td>
<td></td>
<td>L/M ratio</td>
<td>18.5 ± 5.1</td>
<td>10.2 ± 2.9</td>
<td>5.9 ± 1.4</td>
<td>4.7 ± 1.2</td>
<td>12.3 ± 3.4</td>
</tr>
<tr>
<td>Severe hepatitis</td>
<td>14</td>
<td>LIDOCaine, µg/L</td>
<td>664.3 ± 68.4</td>
<td>464.3 ± 45.2</td>
<td>342.9 ± 32.7</td>
<td>300.0 ± 23.4</td>
<td>586.6 ± 52.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>MEGX, µg/L</td>
<td>41.5 ± 9.6</td>
<td>55.5 ± 8.8</td>
<td>56.4 ± 6.1</td>
<td>61.1 ± 5.8</td>
<td>74.7 ± 10.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>L/M ratio</td>
<td>28.3 ± 8.2</td>
<td>11.3 ± 2.2</td>
<td>6.7 ± 0.7</td>
<td>5.4 ± 0.6</td>
<td>16.0 ± 3.2</td>
</tr>
</tbody>
</table>

*Patients were grouped according to their HAI biopsy score: mild (0–6), moderate (7–12), and severe (13–18).

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**Table 2. Comparison of traditional liver tests among three groups with chronic active hepatitis on the basis of severity and apparently healthy volunteers.**

<table>
<thead>
<tr>
<th>Test</th>
<th>Units</th>
<th>$P$ value</th>
<th>Healthy</th>
<th>Mild</th>
<th>Moderate</th>
<th>Severe</th>
<th>Hepatic injury</th>
</tr>
</thead>
<tbody>
<tr>
<td>ALB</td>
<td>(g/L)</td>
<td>&lt;0.0001</td>
<td>47.4 (1.1)</td>
<td>42.4 (1.0)</td>
<td>40.4 (0.7)</td>
<td>38.3 (1.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Duncan group</td>
<td>A</td>
<td>B</td>
<td>B/C</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>ALT</td>
<td>(U/L)</td>
<td>&lt;0.0001</td>
<td>20.0 (1.9)</td>
<td>69.8 (14.1)</td>
<td>126.7 (19.2)</td>
<td>137.6 (20.1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Duncan group</td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>AST</td>
<td>(U/L)</td>
<td>&lt;0.0001</td>
<td>24.3 (2.2)</td>
<td>42.9 (5.8)</td>
<td>84.1 (12.1)</td>
<td>120.4 (16.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Duncan group</td>
<td>A</td>
<td>B</td>
<td>C</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>AST/ALT</td>
<td></td>
<td>&lt;0.0001</td>
<td>1.29 (0.11)</td>
<td>0.66 (0.06)</td>
<td>0.74 (0.08)</td>
<td>0.91 (0.06)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Duncan group</td>
<td>A</td>
<td>B</td>
<td>B/C</td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>TB</td>
<td>(mg/L)</td>
<td>&gt;0.05</td>
<td>5.7 (0.5)</td>
<td>5.3 (1.0)</td>
<td>8.4 (1.6)</td>
<td>9.4 (1.1)</td>
<td></td>
</tr>
<tr>
<td>ALK</td>
<td>(U/L)</td>
<td>&gt;0.9</td>
<td>84.2 (10.3)</td>
<td>88.0 (23.6)</td>
<td>84.5 (6.2)</td>
<td>91.0 (11.4)</td>
<td></td>
</tr>
<tr>
<td>PT</td>
<td>(s)</td>
<td>&lt;0.01</td>
<td>11.7 (0.2)</td>
<td>11.2 (0.3)</td>
<td>12.1 (0.2)</td>
<td>12.6 (0.3)</td>
<td></td>
</tr>
</tbody>
</table>

This table shows the mean value (± SEM) of each traditional liver test for the three groups of patients and apparently healthy volunteers and the $P$ value of the ANOVA comparing these four groups. The Duncan test was used to assess significant difference between groups if that is what the ANOVA showed. Log transformation was used on all chemical tests except ALB to normalize the data. Means with the same letter have no significant difference between them. Patients were grouped according to HAI: mild (0–6), moderate (7–12), and severe (13–18). TB, total bilirubin; ALK, alkaline phosphatase; PT, prothrombin time.
For 70 years, the metabolism and excretion of several xenobiotics have been used as a measurement of liver function with limited success. One of the most widely used xenobiotics in the past, bromsulfophthalein, is not used today because of the risk of fatal hypersensitivity reactions. Several other xenobiotics (aminopyrine, antipyrene, caffeine, galactose, indocyanine green, etc.) have been evaluated but proven not to be superior to conventional clinical laboratory tests. One of the more recent xenobiotics proposed to assess liver function is lidocaine and its metabolite MEGX. Do the properties of lidocaine and MEGX differ from these other xenobiotics in such a way that the metabolism and excretion of this compound by the liver will provide useful clinical information about the function of this organ?

The use of lidocaine and MEGX to assess liver function was first proposed by Oellerich et al. in 1987. These authors reported that the MEGX concentration obtained 15 min after lidocaine injection was substantially lower in patients with liver cirrhosis and correctly predicted success or failure of transplanted livers in the majority of cases. Since that report, several studies, which had inconsistent findings, have assessed the value of this test in determining the suitability of the donor liver for transplantation.

The results of studies vary for the use of the MEGX test for the assessment of liver function. Several studies of patients with cirrhosis and viral hepatitis and children with liver disease have found some value in the MEGX test for assessing liver function. On the other hand, a study by Meyer-Wyss et al. concluded that the MEGX test “quantitates a very particular enzymatic reaction which may not be representative for the functional reserve of the entire organ.” The results of the current study would support this statement because we

<p>| Table 3. Correlation of MEGX results with HAI biopsy scores for patients with chronic viral hepatitis. |</p>
<table>
<thead>
<tr>
<th>MEGX</th>
<th>HAI F score</th>
<th>PP score</th>
<th>P score</th>
<th>L score</th>
</tr>
</thead>
<tbody>
<tr>
<td>15 min</td>
<td>&lt;0.04</td>
<td>&gt;0.1</td>
<td>&lt;0.02</td>
<td>&lt;0.04</td>
</tr>
<tr>
<td></td>
<td>(-0.33)</td>
<td>(-0.25)</td>
<td>(-0.39)</td>
<td>(-0.33)</td>
</tr>
<tr>
<td>30 min</td>
<td>&gt;0.05</td>
<td>&lt;0.04</td>
<td>&lt;0.02</td>
<td>&gt;0.3</td>
</tr>
<tr>
<td></td>
<td>(-0.29)</td>
<td>(-0.34)</td>
<td>(-0.38)</td>
<td>(-0.16)</td>
</tr>
<tr>
<td>60 min</td>
<td>&lt;0.03</td>
<td>&lt;0.003</td>
<td>&lt;0.03</td>
<td>&gt;0.5</td>
</tr>
<tr>
<td></td>
<td>(-0.35)</td>
<td>(-0.45)</td>
<td>(-0.36)</td>
<td>(-0.09)</td>
</tr>
<tr>
<td>90 min</td>
<td>&gt;0.05</td>
<td>&lt;0.02</td>
<td>&gt;0.05</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td></td>
<td>(-0.31)</td>
<td>(-0.40)</td>
<td>(-0.27)</td>
<td>(-0.04)</td>
</tr>
<tr>
<td>Index</td>
<td>&lt;0.04</td>
<td>&lt;0.02</td>
<td>&lt;0.02</td>
<td>&gt;0.1</td>
</tr>
<tr>
<td></td>
<td>(-0.33)</td>
<td>(-0.38)</td>
<td>(-0.38)</td>
<td>(-0.17)</td>
</tr>
</tbody>
</table>

This table shows the P values for the ANOVA and the correlation coefficient (r value, in parentheses) comparing MEGX with the biopsy scores. Significant P values (<0.05) are shown in bold type. The components of the HAI biopsy scores are F, fibrosis; PP, periportal injury and piecemeal necrosis; P, portal inflammation; L, lobular injury.

Discussion

For 70 years, the metabolism and excretion of several xenobiotics have been used as a measurement of liver function with limited success. One of the most widely used xenobiotics in the past, bromsulfophthalein, is not used today because of the risk of fatal hypersensitivity reactions. Several other xenobiotics (aminopyrine, antipyrene, caffeine, galactose, indocyanine green, etc.) have been evaluated but proven not to be superior to conventional clinical laboratory tests. One of the more recent xenobiotics proposed to assess liver function is lidocaine and its metabolite MEGX. Do the properties of lidocaine and MEGX differ from these other xenobiotics in such a way that the metabolism and excretion of this compound by the liver will provide useful clinical information about the function of this organ?

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The results of studies vary for the use of the MEGX test for the assessment of liver function. Several studies of patients with cirrhosis and viral hepatitis and children with liver disease have found some value in the MEGX test for assessing liver function. On the one hand, a study by Meyer-Wyss et al. concluded that the MEGX test “quantitates a very particular enzymatic reaction which may not be representative for the functional reserve of the entire organ.” The results of the current study would support this statement because we
found no significant differences in MEGX and lidocaine concentrations and lidocaine/MEGX ratio among the three groups with progressive hepatitis based on the HAI and apparently healthy individuals.

Why should the results of the current study and that by Meyer-Wyss et al. [10] differ from several other studies? The important factors that relate to this difference are the metabolism of lidocaine and the classification and extent of liver impairment. The rate of conversion of lidocaine to MEGX is related directly to the mass of cytochrome P-450 in the liver. However, the mass of cytochrome P-450 varies among individuals on the basis of genetic heterogeneity [21]. Also several medications are known to induce the cytochrome P-450 system, which will increase the rate of MEGX production [21, 22]. Gender is also a factor; women have a lower concentration of MEGX at 15 min than men [23, 24]. Woman taking oral contraceptives have a further reduction of their MEGX production [23]. The individual variables given above for the metabolism of lidocaine to MEGX are the major factors relating to the broad range for the MEGX concentration at 15 min in apparently healthy individuals found in the current study, 18–137 µg/L (Fig. 1). However, our findings were similar to those of Oellerich et al. [7], who found that the MEGX concentration in apparently healthy individuals at 15 min varied between 15 and 130 µg/L [7]. Many factors independent of the disease process affect the rate of conversion of lidocaine to MEGX by the liver. These nondisease factors erode the accuracy and precision of this test to assess impaired liver function.

The calibrator for comparison of MEGX results varies among the studies in the literature. Six of the studies [4, 5, 9–11, 20] use the Child–Pugh score [25] to grade the extent of the liver disease (cirrhosis) for comparison with MEGX results. This classification is based on a clinical component (ascites and encephalopathy) and a laboratory component (total bilirubin, ALB, and prothrombin time) and is used primarily in patients with cirrhosis. The study by Gremse et al. [20, 26] used a classification for pediatric patients based on a history of ascites and laboratory tests (cholesterol, indirect bilirubin, and partial thromboplastin time). Four of the studies [7, 10, 11, 20] documented the liver disease with a liver biopsy, but only the study by Shiffman et al. [11] used the HAI for comparison with MEGX results. However, these authors found that a given 15-min MEGX concentration predicted the hepatic histology with the HAI, with a sensitivity of only 55–60% and a specificity of only 18–46% [11, 27]. Thus, different variables (clinical evaluation, laboratory tests, or liver biopsy) have been used as calibrators to compare MEGX results. Few studies have used liver histology to assess MEGX results; only one study used the HAI and found poor detectability and specificity.

The type and extent of liver impairment are factors that affect the clinical application of the MEGX test. Steatosis, the degree of hepatic inflammation, and fibrosis may affect MEGX production independently [27]. The mean MEGX concentration in our patients with severe hepatitis was 41.5 µg/L. In the study by Meyer-Wyss et al. [10] with results similar to the current study, patients were grouped on the basis of the Child–Pugh grading system into five categories of increasing clinical severity of liver disease. For the first three groups, the mean MEGX concentration was >40 µg/L, and the last two groups had mean MEGX concentrations ~20 µg/L. However, several of the other studies that found value in the MEGX test had groups with severe liver disease in which the mean MEGX concentration was <20 µg/L [4, 5, 9, 11]. Shiffman et al. [11] found that severe life-threatening complications of cirrhosis were observed only in patients with a MEGX concentration <20 µg/L; at concentrations <10 µg/L, the 1-year survival rate was only 50%. In our study five of our seven tests of traditional liver function were able to discriminate between apparently healthy volunteers and one or more of the three categories of patients with hepatic injury when the MEGX test showed no difference. Thus, the MEGX test may have value in the assessment of liver function in patients with cirrhosis, but it is of little value in quantifying liver function in patients who do not have end-stage liver disease.

The MEGX test at some time points does correlate with the HAI and components of the HAI in our patients with chronic viral hepatitis. The MEGX concentration at 15 min shows a significant inverse correlation with the composite HAI and two of the components, portal inflammation and periporal injury and piecemeal necrosis. Interestingly, the fibrosis score did not show a correlation with the MEGX concentration at 15 min (the usual time point for this test), but did at all other time points. It may be that the lack of correlation with the fibrosis score at 15 min was a result of nondisease factors in view of the relatively mild degree of liver impairment of our patients. Schifffman et al. [11] found a significant inverse correlation (r = −0.72, P < 0.005) for the change in the 15-min MEGX concentration and the change in the HAI in 35 patients studied before and after treatment. However, about half of their patient population had cirrhosis with a mean MEGX concentration of ~20 µg/L. Thus, the MEGX concentration may relate to the HAI in patients with advanced liver disease.

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References


