Laboratory Markers of Alcohol Abuse

Pekka Sillanaukee
Alcohol Related Diseases, Pharmacia & Upjohn Diagnostics AB, Sweden, and University of Tampere, Medical School, Finland

Alcohol consumption in many parts of Europe has increased considerably in the past 25 years, and with it alcohol-related problems have risen sharply. Consequently, more patients seen in clinical practice as well as among drunk drivers have an underlying alcohol problem. The need for accurate methods for detection and monitoring of alcohol abuse in different health care settings is huge.

Despite the need there is no exact clinical finding or symptom in a patient history, in an interview or in a clinical status that is sufficiently sensitive and specific to detect alcohol abuse in its early phase. The clinical signs of alcohol abuse are rather minimal in the early phase of alcohol abuse while most of the signs arise later, after several years of excessive drinking. Alcohol consumption is usually under-reported in interviews. Alcohol abusers tend to underestimate their drinking even more than the social drinkers (Poikolainen, 1995). For example, in our study among heavy drinkers who were willing to participate in a brief intervention treatment the typical first self-reported alcohol consumption was only 124 g/week among males and 73 g/week among females (Sillanaukee, 1995). The reliability of personal interviews about alcohol consumption is difficult. This is especially true when the individual is trying to get feedback about his/her excessive drinking.

The reasons for using biological laboratory markers are that they give objective information about alcohol consumption and changes in drinking habits. Consequently, laboratory tests are useful in screening heavy drinking; in decision making about the role of alcohol as an etiologic factor of disease; in follow-up and monitoring changes in alcohol consumption; in motivating patients to change their drinking habits by showing alcohol-induced changes in their bodies; and, finally, in picking up patients who are sensitive for alcohol-induced problems.
Thus, the search for more objective laboratory markers of alcohol abuse has been active. Several laboratory abnormalities based on hematological characteristics, liver enzyme activities, lipids, immune function factors, hormones, neurological factors have been observed to be associated with alcohol abuse (Holt et al, 1981; Cushman et al, 1984; Watson et al, 1986; Salaspuro, 1986 and 1989; Nilssen and Huseby, 1992; Mihas and Tavassoli, 1992; Stibler, 1992; Allen et al, 1994).

Blood, urine or breath ethanol analyses (5HTOL) and creatinine or 5-hydroxyindoleacetic acid (HIAA) in urine have been proposed to be a specific short-term marker for alcohol consumption (Voltaire et al, 1992; Helander et al, 1995). 5HTOL stays elevated 6-20 hours after ethanol disappearance. False positive values have been reported in patients using drugs inhibiting aldehyde dehydrogenase. If the 5HTOL ratio to creatinine (instead of HIAA) is used also serotonine rich food may cause false positive values. The marker seems to be promising, having high sensitivity and specificity for detecting recent alcohol consumption. The measurement is based on GC-MS technique or HPLC with electrochemical detection (Helander, 1992) and thus the problem is the difficulty of routine application today.

Elevated serum levels of membrane-bound enzyme, gamma-glutamyl transferase (GGT) have been widely used as a marker of alcohol abuse. The sensitivity of GGT in detecting alcohol abuse has been reported to vary between 34% and 85%. GGT is not increased after acute alcohol intake but needs probably alcohol consumption of 80-200 g/day for one or several weeks. The half-life of elevated GGT is between two and three weeks. In addition to alcohol abuse increased GGT is frequently found in non-alcoholic liver disease, diabetes, obesity, pancreatitis, hyperlipidemia, heart failure, severe trauma, and in subjects using barbiturates, antiepileptics or anticoagulants. Despite its poor specificity, 50-72% of elevated GGT values can be explained by an excessive alcohol consumption (Kristenson et al, 1980; Penn et al, 1981; Suokas, 1992).

Mean corpuscular volume (MCV) is an index of red blood cell size. Increased MCV values have been observed in 34-89% of alcohol abusers (Wu et al, 1974; Unger and Johnson, 1974; Chick et al, 1981). Increased MCV values are also found in vitamin B12 and folic acid deficiency, liver diseases, several hematological diseases, hypothyroidism, reticulocytosis, in users of antiepileptics, as well as among smokers. Alcohol abuse has been found to explain
increased MCV values in 89% of men and 56% of women in general practice (Seppä et al., 1991). MCV responds slowly to abstinence and up to 40% may have an elevated MCV value even after three months of abstinence (Morgan et al., 1981).

Other widely used markers are serum *aspartate aminotransferase* (ASAT) and *alanine aminotransferase* (ALAT). The intracellular enzymes are more indicative for liver damage than for alcohol abuse. The pooled sensitivity of ASAT has been estimated to be 35% as a marker of alcohol abuse (Rosman and Lieber, 1991). The sensitivity for ALAT may be even poorer. Increased values are also found in non-alcoholic liver diseases (ASAT, ALAT), in muscle disorders (ASAT), and in myocardial infarction (ASAT).

One of the recently developed routine laboratory tests for alcohol abuse is serum *carbohydrate-deficient transferrin* (CDT). The marker consists of α-, mono-, and disialoisoforms of transferrin that are deficient in their terminal trisaccharide. In a recent review by Helena Stibler (1992) summarizing 2500 individuals in different studies, a total clinical sensitivity was 82% and specificity 97%. False positives have been reported in patients with severe liver diseases (mainly in primary biliary chirrosis, chronic hepatitis C, hepatic malignities), in patients with genetic D-variant of transferrin, and in patients with an inborn error of glycoprotein metabolism. In a more recent study Anton and Moak (1994) reported a sensitivity of 79% and a specificity of >90% among males who drank more than 60 g/day before admission. During abstinence the CDT values normalize with a mean half-life of 14-17 days. Females have higher normal values of CDT than males, possibly due to asialo- and monosialotransferrin.

CDT has now been shown to have high specificity and a sensitivity that is at least equal to that of the conventional laboratory markers. CDT values seem to increase after 10 days of drinking at 50-80 grams of ethanol per day. It has also a relatively good correlation with self-reported alcohol consumption but not with conventional markers. This combination makes it suitable for routine work in the detection of alcohol abuse and monitoring either abstinence or relapse during treatment. Additionally, by following relative changes in CDT and GGT from each individual’s baseline values, rather than using the conventional population-based cut-offs, one may improve the detection of relapses in a monitoring situation (Borg et al, 1995;
Helander et al, 1996). In one study CDT detected relapses even before self-report among male subjects (Rosman et al, 1995).

The summary table below gives an estimation of the sensitivity, specificity and half-life of different laboratory markers of alcohol abuse. Due to the limited sensitivity of a single laboratory marker the parallel measurement of CDT with traditional alcohol markers may increase the possibility to detect alcohol abuse. Recent studies indicate that the combined measurement of CDT and GGT or CDT and MCV will increase the possibility to detect alcohol abuse (Allen et al, 1994; Anton and Moak, 1994; Yersin et al, 1995; Helander et al, 1996).

<table>
<thead>
<tr>
<th>Marker</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Half-life/elimination</th>
</tr>
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<tbody>
<tr>
<td>ETOH</td>
<td>0-100</td>
<td>100</td>
<td>1 g/kg/h</td>
</tr>
<tr>
<td>5HTOL/HIAA</td>
<td>0-90</td>
<td>&gt;90</td>
<td>5-20 h after ETOH</td>
</tr>
<tr>
<td>GGT</td>
<td>34-85</td>
<td>11-85</td>
<td>2-3 weeks</td>
</tr>
<tr>
<td>MCV</td>
<td>34-89</td>
<td>26-91</td>
<td>~3 months</td>
</tr>
<tr>
<td>ASAT</td>
<td>15-69</td>
<td>low</td>
<td>2-3 weeks</td>
</tr>
<tr>
<td>ALAT</td>
<td>26-58</td>
<td>low</td>
<td>2-3 weeks</td>
</tr>
<tr>
<td>CDT</td>
<td>39-94</td>
<td>82-100</td>
<td>2 weeks</td>
</tr>
</tbody>
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RÉFÉRENCES


