LABORATORY MARKERS OF ALCOHOL ABUSE

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Abstract — A number of routine laboratory markers provide objective information about alcohol use and abuse. The usefulness of these markers is discussed. One such marker recently developed is serum carbohydrate-deficient transferrin (CDT), which has a greater overall marker potential than other existing tests. The use of CDT in combination with some of the other markers is likely to enhance the detection of alcohol abuse or heavy consumption.

INTRODUCTION

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 clearly considerable.

Despite such a need, there is no exact clinical finding or symptom in a patient history, in an interview or in a clinical setting 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 this process while most of the signs arise later after several years of excessive drinking. Also alcohol consumption is usually under-reported in interviews; alcohol abusers tend to underestimate their drinking even more than the social drinkers (Poikolainen, 1985). For example in our study among heavy drinkers, who were willing to participate in 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.

USE OF LABORATORY MARKERS

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 aetiological 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 body; and finally in detecting patients who are sensitive for alcohol-induced problems. The search for more objective laboratory markers of alcohol abuse has therefore been active. Several laboratory abnormalities based on haematological characteristics, liver enzyme activities, lipids, immune factors, hormones and 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, 1989; Stibler, 1991; Nilssen et al., 1992; Mihas and Tavassoli, 1992; Allen et al., 1994). The following is a brief description of the most frequently used short- and long-term markers for alcohol consumption.

ETHANOL

Blood, urine or breath ethanol analyses provide no information about the severity of alcohol drinking, but the presence of an increased tolerance can be identified. Blood or breath alcohol levels > 1.5% (35 mmol/l) without gross evidence of intoxication or > 3% (69 mmol/l) at any time has been reported to be the first-level criterion of alcoholism (National Council of Alcoholism, 1972). Due to the short half-life of ethanol and the fact that alcohol drinking does not necessarily mean alcohol abuse, its value...
Table 1. Comparisons of markers of alcohol use and abuse

<table>
<thead>
<tr>
<th>Marker</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>Half-life/elimination</th>
</tr>
</thead>
<tbody>
<tr>
<td>ETOH</td>
<td>0-100</td>
<td>100</td>
<td>1 g/kg/h</td>
</tr>
<tr>
<td>5-HTOL/5-HIAA</td>
<td>0-90</td>
<td>&gt;90</td>
<td>5-20 h after ETOH disappearance</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>
</table>

ETOH = ethanol; 5-HTOL/5-HIAA = 5-hydroxytryptophol/5-hydroxyindol-3-ylacetic acid ratio, GGT = γ-glutamyl transferase; MCV = mean corpuscular volume, ASAT = aspartate aminotransferase; ALAT = alanine aminotransferase; CDT = carbohydrate-deficient transferrin.

as a marker of alcohol abuse is limited.

5-HYDROXYTRYPTOPHOL

The ratio of the serotonin metabolite 5-hydroxytryptophol (5-HTOL) to creatinine or to 5-hydroxyindol-3-ylacetic acid (5-HIAA) in urine has been proposed to be a specific short-term marker for alcohol consumption (Voltaire et al., 1992; Helander et al., 1992a,b). 5-HTOL stays elevated 6-20 h after ethanol disappearance. False-positive values have been reported in patients using drugs inhibiting aldehyde dehydrogenase. If the 5-HTOL ratio to creatinine (instead of 5-HIAA) is used, serotonin-rich foods may also 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 high-performance liquid chromatography with electrochemical detection (Helander et al., 1992a) and thus the problem is the difficulty of routine application today.

GAMMA-GLUTAMYL TRANSFERASE

An elevated serum level of membrane-bound enzyme, gamma-glutamyl transferase (GGT) has 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 2 and 3 weeks. In addition to alcohol abuse, increased GGT is frequently found in non-alcoholic liver disease, diabetes, obesity, pancreatitis, hyperlipidaemia, 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

Mean corpuscular volume (MCV) is an index of red blood cell size. Increased MCV values have been observed in 34-89% of alcohol abusers (Unger and Johnson, 1974; Wu et al., 1974; Chick, 1981). Increased MCV values are also found in cases of vitamin B₁₂ and folic acid deficiency, liver diseases, several haematological disorders, 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 3 months of abstinence (Morgan et al., 1981).

SERUM AMINOTRANSFERASES

Other widely used markers are serum aspartate aminotransferase (ASAT) and alanine aminotransferase (ALAT). These enzymes are more indicative of liver damage than of alcohol abuse. The pooled sensitivity of ASAT has been estimated to be 35% as a marker of alcohol abuse (Rosman and Lieber, 1992). The sensitivity for ALAT may be even poorer. Increased values are also found in non-alcoholic liver diseases (ASAT, ALAT), in
CARBOHYDRATE-DEFICIENT TRANSFERRIN

One of the recently developed routine laboratory tests for alcohol abuse is serum carbohydrate-deficient transferrin (CDT). The marker consists of the asialo, monosialo and disialo isoforms of transferrin that are deficient in their terminal trisaccharides. In a recent review by Stibler (1991), summarizing 2500 individuals in different studies, a total clinical sensitivity of 82% and specificity of 97% were estimated. False-positives have been reported in patients with severe liver diseases (mainly in primary biliary cirrhosis, chronic hepatitis C, hepatic malignancies), 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 specificity of >90% among males who drank >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 monosialo-transferrin. CDT has now been shown to have a 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 a level of 50–80 g ethanol per day. It also has 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 for monitoring either abstinence or relapse during treatment. Additionally, following relative changes in CDT and GGT from each individual’s baseline values, rather than using the conventional population-based cut-offs, may improve the detection of relapses in a monitoring situation (Borg et al., 1995; Helander et al., 1996). In one study, CDT indicated relapses even before self-report among male subjects (Rosman et al., 1995).

CONCLUSION AND COMMENTS

Table 1 summarizes the sensitivities, specificities and half-lives of different laboratory markers of alcohol abuse. Due to the limited sensitivity of any single laboratory marker, the parallel measurement of CDT with traditional alcohol markers may enhance the ability to detect alcohol abuse. Recent studies indicate that the combined measurement of CDT and GGT or of CDT and MCV could achieve such an enhancement (Allen et al., 1994; Anton and Moak, 1994; Yersin et al., 1995; Helander et al., 1996).

REFERENCES


