SENSITIVITY OF CARBOHYDRATE-DEFICIENT TRANSFERRIN (CDT) IN RELATION TO AGE AND DURATION OF ABSTINENCE

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Abstract — Carbohydrate-deficient transferrin (CDT) serum concentrations were prospectively determined in 162 subjects (alcoholics n = 62, controls n=100) using three different methods of detection (IEF, CDTect™, Axis%CDT™). Repeated testing in alcoholics after 3 and 5 days of abstinence demonstrated a significantly higher sensitivity of CDT in patients above 40 years of age compared to younger patients.

INTRODUCTION

In recent years, carbohydrate-deficient transferrin (CDT) has been recognized as a reliable state marker of high alcohol consumption (Stibler, 1991). Recent data suggest CDT to be helpful in monitoring alcoholics during periods of alcohol abstinence in order to detect relapses (Helander et al., 1996; Schmidt et al., 1997). Whereas the high specificity of CDT is widely accepted (Stibler, 1991), its sensitivity is still a contentious issue; the data range from 22% to 83% (Nystrom et al., 1992; Spies et al., 1995). To investigate the influence of age and duration of abstinence on CDT sensitivity, we prospectively determined the serum CDT concentrations in 62 alcohol-dependent in-patients on the first, third and fifth days of abstinence and compared the sensitivities of CDT in different age subgroups.

SUBJECTS AND METHODS

Sixty-two alcoholics diagnosed according to DSM-III-R criteria (American Psychiatric Association, 1987) (patients with polytoxico-mania were excluded), who were admitted to our hospital and asked to withdraw from alcohol, underwent a detailed addiction history including the Munich Alcoholism Test (MALT) questionnaire (Feuerlein et al., 1977) and information on drinking behaviour (frequency and extent of daily alcohol intake). All had a daily alcohol consumption of more than 80 g over the previous 3 months (range: 85–210 g/day). Routine laboratory testing on the first, third, and fifth days after admission as well as a general medical and neurological examination were performed in all cases. None of the patients had clinical evidence of liver cirrhosis or alcohol related polynuropathy. For further analysis, patients were divided into two subgroups according to their age: group I ≤40 years (n = 20, median 36 years, range: 28–40 years); group II >40 years (n = 42, median 50 years, range: 41–69 years).

Fasting blood samples were taken from the cubital vein after minimal stasis between 07:30 and 08:30. Determinations of CDT serum concentrations were performed using three different techniques: (1) isoelectric focusing (IEF) followed by immunofixation applied to the Pharmacia Phast System™ according to the method of van Noort and van Eijk (1992) with a cut-off of 20 U/l for men and 24 U/l for women; (2) anion-exchange chromatography followed by double antibody radioimmunoassay (Kabi Pharmacia Diagnostics, CDTect™) with a cut-off of 20 U/l for men and 26 U/l for women; (3) anion-exchange chromato-
Table 1. Sensitivity of carbohydrate-deficient transferrin (CDT) during a 5-day period of alcohol abstinence in 62 alcoholics of different age subgroups

<table>
<thead>
<tr>
<th>Groups and gender CDT determination:</th>
<th>Frequency of CDT values above the cut-off level (n) and sensitivity of CDT (%)</th>
<th></th>
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<tbody>
<tr>
<td></td>
<td>IEF</td>
<td>CDTect™</td>
</tr>
<tr>
<td></td>
<td>1st</td>
<td>3rd</td>
</tr>
<tr>
<td>Group I (&lt;40 years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n = 20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (n = 13)</td>
<td>11 (55)</td>
<td>8 (40)</td>
</tr>
<tr>
<td>Female (n = 7)</td>
<td>3 (43)</td>
<td>2 (29)</td>
</tr>
<tr>
<td>Group II (&gt;40 years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n = 42</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male (n = 25)</td>
<td>34 (81)</td>
<td>33 (79)</td>
</tr>
<tr>
<td>Female (n = 17)</td>
<td>13 (76)</td>
<td>12 (71)</td>
</tr>
</tbody>
</table>

Abbreviation: IEF, iso-electric focusing.

graphy of transferrin antibody complexes (Axis Biochemicals AS, Axis%CDTAssay™) with a cut-off of 2.5% for both sexes.

Cut-off levels for all individual methods were committed to the 95th percentile of CDT data obtained from 100 well-matched healthy volunteers (mean age 36.7 years, male/female ratio was 61/39) with a daily alcohol intake of less than 20 g. For comparison of numeric variables (categorical variables) across groups, the Mann–Whitney test ($\chi^2$-test for a $2 \times 2$ plan; group I vs II, absolute frequency of CDT values above vs below the cut-off level). Interestingly, measuring CDT with the three different techniques (at least one value above the cut-off level) led to a substantial increase of CDT sensitivity only for patients over the age of 40 years. In that group, we found a sensitivity of 81% even after 5 days of abstinence (the maximum sensitivity obtained for any of these procedures alone was only 64%), whereas in group I, there was a 5% increase of CDT sensitivity only (fifth day: 35%).

RESULTS

Between the subgroups created here (groups I and II), no significant differences emerged in relation to the following alcohol-related variables: mean (± SD) MALT total score (28.9 ± 6.0 vs 29.5 ± 7.4), mean daily alcohol consumption (137.8 ± 38.0 vs 141.4 ± 42.7 g/day) and mean duration of the last period of abuse (24.6 ± 13.0 vs 21.5 ± 11.4 weeks). As expected, patients in group II had a significantly longer history of alcohol dependency compared to younger patients (9.2 ± 3.1 vs 4.1 ± 3.5 years, Mann–Whitney test $P < 0.05$).

Table 1 compares the CDT sensitivity of each individual method concerning age and gender differences. At all times of examination, we found a higher sensitivity of CDT in men compared to women. In male as well as female patients, the sensitivity of CDT in detecting alcoholism was obviously higher in subjects over 40 years of age compared to younger subjects. In both groups, the sensitivity of CDT decreased as abstinence continued. On the third and fifth days of abstinence, there was a significantly higher sensitivity of CDT in group II compared to group I ($P < 0.05$, $\chi^2$-test for a $2 \times 2$ plan; group I vs II, absolute frequency of CDT values above vs below the cut-off level). Interestingly, measuring CDT with the three different techniques (at least one value above the cut-off level) led to a substantial increase of CDT sensitivity only for patients over the age of 40 years. In that group, we found a sensitivity of 81% even after 5 days of abstinence (the maximum sensitivity obtained for any of these procedures alone was only 64%), whereas in group I, there was a 5% increase of CDT sensitivity only (fifth day: 35%).

DISCUSSION

Our data demonstrate a significantly higher sensitivity of CDT as a marker of chronic alcohol consumption in alcoholics over 40 years of age, compared to younger subjects. This may reflect that younger individuals have a shorter history of heavy alcohol consumption or that they may recover more quickly after alcohol intake (Allen et al., 1994). Particularly low rates of sensitivity have often been found in young populations (Nystrom et al., 1992; Bisson and Milford-Ward, 1994). Our data are in accordance with these findings. On the other hand, Yersin et al. (1995)
found the highest CDT sensitivity in 20- to 40-year-old patients and the lowest in a subgroup over 60 years of age. Since our data were obtained from a more homogeneous group of strictly selected alcohol-dependent in-patients, whose socioeconomic backgrounds were quite similar and who were all hospitalized in a psychiatric unit of a large urban hospital, this disagreement may probably be due to the fact that different populations were studied. Other factors known to influence the sensitivity of CDT are gender differences (Anton and Moak, 1994) and the amount of daily alcohol intake (Bell et al., 1994). However, in the age subgroups created here, these variables were not significantly different and thus probably may not account for the differences in CDT sensitivity we found. Nevertheless, the total period of alcohol dependency was significantly longer in group II patients. Yamauchi et al. (1993) suggested CDT to be a useful marker only for alcohol-related liver diseases, but not for alcohol consumption. On the basis of these findings, a possible relationship between the reduced sensitivity of CDT in young alcoholics and a lower prevalence of subclinical liver damage, a lower cumulative consumption of alcohol or a shorter half-life of CDT in that population should be investigated in further studies. Confirming the data of other study groups (Lesch et al., 1996), our results point to a decrease in CDT sensitivity as abstinence continues. Altogether, a sensitivity of at least 60% was found in the group of patients above 40 years of age at all times of examination. Thus, in this age group, the sensitivity of CDT is at least equivalent to or higher than those obtained for other, commonly used markers of increased alcohol consumption, such as gamma-glutamyl transferase, aspartate aminotransferase, or mean corpuscular volume (Bell et al., 1994). In contrast, in younger patients a sufficiently high sensitivity of CDT was found on the first day of abstinence only.

The combined use of different methods of CDT detection on the one hand led to a considerable increase of CDT sensitivity after 5 days of abstinence, particularly in patients above 40 years of age (81%). On the other hand, this resulted in a decrease in the specificity of CDT. Since CDT is a highly specific marker (specificity of about 90%), we believe that in exceptional cases, such as in older patients who during the course of alcohol-withdrawal therapy suffer relapse while persistently denying the fact, multiple determinations would be justified, since this could provide definitive evidence for such a relapse even after a few days of abstinence. By contrast, this procedure may not be appropriate in younger alcoholics, because there is minor benefit only and the laboratory costs are high.

REFERENCES


