INCREASED CARBOHYDRATE-DEFICIENT TRANSFERRIN DURING PREGNANCY: RELATION TO SEX HORMONES

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Abstract — Controversy exists whether carbohydrate-deficient transferrin (CDT) is valuable as a screening tool for fetal alcohol syndrome. We evaluated serum CDT in 60 non-alcohol-abusing women at different stages of normal pregnancy. CDT was weakly related to week of pregnancy and to human placental lactogen. CDT did not correlate with iron, oestradiol or progesterone. By contrast, good correlations were found between transferrin and week of pregnancy or either sex hormone. Using multiple linear regression analysis, only transferrin and week of pregnancy were important predictors of CDT. The diagnostic accuracy of CDT for detecting alcohol abuse may be limited in pregnant women and should be carefully assessed in relation to alcohol consumption.

INTRODUCTION

As it is difficult to detect concealed alcohol abuse, biochemical markers of increased ethanol consumption are needed (Salaspuro, 1986). Recently, carbohydrate-deficient transferrin (CDT) has been established as a sensitive and specific marker of potentially harmful ethanol consumption (Stibler, 1991). Separation of transferrin isoforms by anion exchange chromatography on mini-columns followed by radioimmunoassay of transferrin (Stibler et al., 1986) has allowed the production of commercial kits and the use of this assay on a large scale.

Using this assay, serum CDT has been found to be useful in male alcoholics (Sillanaukee et al., 1993) and also in patients with alcohol-associated medical disorders (Bell et al., 1994). We recently confirmed that the determination of CDT is valuable in patients with liver dysfunction (Stauber et al., 1995a). Most of the studies were performed in predominantly male populations. Studies in women demonstrate only partial diagnostic efficacy of the CDT test (Stibler et al., 1988; Lof et al., 1994; Anton and Moak, 1994). Interestingly, reported normal values of CDT are higher for women (0–26 U/l) than for men (0–20 U/l). Premenopausal women exhibit significantly higher CDT values than postmenopausal women (Stauber et al., 1995b; Gronbaek et al., 1995). Also, increased levels of CDT were found in women taking oral contraceptives (La Grange et al., 1995).

Recently, CDT was determined in 250 pregnant women of different gestational weeks and significant correlations were found between week of pregnancy and both CDT level and total transferrin, the latter exhibiting a larger increase than CDT (Härlin et al., 1994). It was the aim of the present study to establish relationships between the elevated CDT levels during pregnancy and: (1) female sex steroids; (2) iron status in 60 women with normal pregnancy.

MATERIALS AND METHODS

Subjects

A total of 60 pregnant women were enrolled, who attended the obstetric clinic and reported a level of alcohol consumption of <20 g per day. Serum samples were stored at −70°C for later assay of CDT, transferrin, iron, oestradiol, progesterone, and human placental lactogen (hPL).

CDT assay

Serum samples were tested in duplicate using the CDTect radioimmunoassay (Pharmacia Diagnostics, Uppsala, Sweden). Briefly, following iron
Table 1. Serum carbohydrate-deficient transferrin (CDT) in pregnant women

<table>
<thead>
<tr>
<th>Trimester</th>
<th>n</th>
<th>CDT (U/l)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1st</td>
<td>20</td>
<td>16.4 ± 1.0</td>
</tr>
<tr>
<td>2nd</td>
<td>20</td>
<td>17.1 ± 1.0</td>
</tr>
<tr>
<td>3rd</td>
<td>20</td>
<td>19.4 ± 0.6*</td>
</tr>
</tbody>
</table>

Values are means ± SEM. *P < 0.05 by ANOVA (Duncan's range test).

saturation of the serum samples, separation of the transferrin isoforms was accomplished by anion-exchange chromatography on minicolumns. Thereafter, transferrin was quantified in duplicate by double-antibody radioimmunoassay. The lower limit of detection is ~1 U/l.

Other assays

17β-oestradiol was measured by a double-antibody radioimmunoassay (Clinical Assays Estradiol-2, Sorin Biomedica Diagnostics, Saluggia, Italy; assay sensitivity 5 pg/ml). Progesterone was measured by a radioimmunoassay (PROG-CTK-2, Sorin Biomedica Diagnostics, Saluggia, Italy; assay sensitivity 0.05 ng/ml). Human placental lactogen was measured by a double-antibody radioimmunoassay (hPL RIA 100, Pharmacia Diagnostics, Uppsala, Sweden; assay sensitivity 0.02 mg/l); the hPL standard was calibrated against reference preparation 73.545 from WHO. Serum iron and transferrin were determined by routine clinical laboratory procedures.

Statistical analysis

Results are expressed as means ± SEM. Differences between group means were analysed by ANOVA. Relationships between the variables studied were examined by linear regression analysis. To determine which variables are important predictors of CDT, multiple linear regression with stepwise selection of independent variables was performed using the SPSS statistical program on a microcomputer. P values of <0.05 were considered to be statistically significant.

RESULTS

Serum levels of CDT increased with duration of pregnancy. Mean CDT values for the third trimester were significantly higher than for the first and second trimesters (Table 1). Serum CDT correlated weakly with week of pregnancy (Fig. 1), whereas a good correlation was found between total transferrin and week of pregnancy (Fig. 2).

As shown in Table 2, CDT correlated significantly with hPL but not with oestradiol or progesterone. Good correlations were found between transferrin and either sex hormone. No correlation was found between CDT and serum iron.

Table 2. Correlations in pregnant women

<table>
<thead>
<tr>
<th></th>
<th>Week</th>
<th>Oestradiol</th>
<th>Progesterone</th>
<th>hPL</th>
<th>Transferrin</th>
<th>Iron</th>
</tr>
</thead>
<tbody>
<tr>
<td>CDT</td>
<td>0.31*</td>
<td>0.08</td>
<td>0.24</td>
<td>0.28*</td>
<td>0.55**</td>
<td>-0.08</td>
</tr>
<tr>
<td>Transferrin</td>
<td>0.84**</td>
<td>0.44**</td>
<td>0.64**</td>
<td>0.77**</td>
<td>-</td>
<td>-0.12</td>
</tr>
<tr>
<td>Week</td>
<td></td>
<td>0.51**</td>
<td>0.74**</td>
<td>0.88**</td>
<td>0.84**</td>
<td>-0.06</td>
</tr>
</tbody>
</table>

Correlation coefficients (n = 60). *P < 0.05, **P < 0.001.
Week of pregnancy

Fig. 2. Serum transferrin v week of pregnancy. A good correlation was found \( r = 0.84, y = 0.06x + 2.1; n = 60 \).

Multiple linear regression analysis yielded the following equation \( r = 0.61, P < 0.001 \):

\[
\text{CDT} = 4.5 \times \text{transferrin} - 0.17 \times \text{week} + 5.8
\]

Thus only transferrin and week of pregnancy appeared to be important predictors of the CDT level, whereas oestradiol, progesterone, hPL or iron were not selected as independent variables.

**DISCUSSION**

In this study in healthy pregnant women, we demonstrated an increase of CDT with duration of pregnancy. A relation of this increase to alcohol abuse is unlikely since none of the study subjects consumed more than 20 g ethanol per day. Our findings confirm preliminary data of Härlin et al. (1994) who investigated 250 pregnant women and likewise found the CDT level, and more so the total transferrin level, to increase as a function of gestational week.

Transferrin is a steroid-responsive plasma protein and has been shown to correlate both with week of pregnancy and serum oestradiol (Skjöldebrand Sparre et al., 1988). Since CDT is a fraction of total serum transferrin, similar influences of pregnancy or female sex steroids on the CDT level might be expected. However, we were unable to demonstrate close correlations between CDT and sex steroids, while we could confirm such correlations between total transferrin and either of the sex steroids studied. Multiple regression analysis yielded only transferrin and week of pregnancy as predictors of the CDT level in our sample.

A possible relation between CDT and iron status has been suggested by Anton and Moak (1994), as iron deficiency might lead to a compensatory increase in transferrin and thus its subfraction, CDT. In the present study, we were unable to find any relation between serum iron and either week of pregnancy or the CDT level. Thus, we found no evidence for the hypothesis that iron deficiency might increase the CDT level. However, since iron levels did not substantially decrease with the duration of pregnancy, a possible influence of iron deficiency on the CDT level cannot be excluded from the present study.

Besides its value in early detection of heavy drinking among women, the determination of CDT may be useful for detection of occult alcohol abuse among pregnant women and thus possibly for prevention of fetal alcohol syndrome. Our findings, like those of Härlin et al. (1994), suggest a weak influence of pregnancy itself on the CDT level, which should therefore be interpreted with caution, especially at levels near the cut-off value. However, we presume that significant ethanol consumption will increase CDT to a larger extent than the alterations during late pregnancy. In a preliminary report, CDT did not appear to be a useful marker of alcohol abuse during pregnancy (Whitty et al., 1995). Further studies are needed to evaluate the diagnostic accuracy of CDT against self-reported daily ethanol consumption in pregnant women.

In conclusion, pregnant women demonstrate an increase of CDT as a function of gestational week, which is mainly related to the associated increase of total transferrin. Female sex hormones appear to increase total transferrin but less so its carbohydrate-deficient isoforms. Whether CDT is useful for diagnosis of alcohol abuse in pregnancy remains to be investigated.

**REFERENCES**


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