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## Carbohydrate-deficient transferrin in patients with alcoholic cardiomyopathy

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Carbohydrate-deficient transferrin (CDT) serum concentrations were analysed by a modified radioimmunoassay test in 20 males with alcoholic cardiomyopathy and 30 males with idiopathic dilated cardiomyopathy, and results were compared with reported alcohol intake derived from a structured questionnaire. The test was found to be successful at detecting harmful alcohol intake and alcohol intake above the recommended level.

CDT was compared with other known markers of high alcohol intake, and it was found that CDT was a more sensitive and specific marker than  $\gamma$ -glutamyltransferase (GT), or mean corpuscular haemoglobin (MCV).

These results indicate that CDT is a marker of alcohol intake that can be used to differentiate between alcoholic cardiomyopathy and idiopathic dilated cardiomyopathy in male. *J Clin Bas Cardiol 1998; 1: 34–6.*

**Key words:** Alcohol, cardiomyopathy

**D**ilated cardiomyopathy is defined as a heart muscle disease with systolic pump failure according to the most recent WHO/ISFC classification [1]. Its clinical characteristics are dilatation of cardiac chambers, poor contractile function, associated disturbance of diastolic function, and often a poor prognosis.

Among other things, excessive alcohol consumption often affects the cardiovascular system, including the heart. It can cause alcoholic cardiomyopathy [2–4]. This disease has a broad spectrum from preclinical state [5] to cardiomyopathy [6]. Alcoholic cardiomyopathy shows ventricular dilatation and poor cardiac function, comparable to dilated cardiomyopathy of other cause. Even the histological findings are similar: both diseases show non-specific findings including fibrosis, degeneration, or hypertrophy of myocytes [7–10]. These non-specific findings correlate both with cardiac function and prognosis [11–13].

The prognosis of alcoholic cardiomyopathy differs from other forms of dilated cardiomyopathy: in the case of alcohol abstinence, patients with alcoholic cardiomyopathy have a better prognosis than patients with idiopathic dilated cardiomyopathy [14]. Therefore, a laboratory marker differentiating between both diseases is of great clinical importance. We therefore determined the serum concentration of carbohydrate-deficient transferrin (CDT),  $\gamma$ -glutamyltransferase (GT), and mean corpuscular haemoglobin (MCV) in patients with suspected alcoholic heart disease and dilated cardiomyopathy.

### Methods

50 male patients were examined clinically, with ECG, colour flow doppler, echocardiography, and invasive procedures (coronary angiography, ventriculography and endomyocardial biopsy). Dilated cardiomyopathy was defined by left ventricular dilatation and reduced left ventricular function (ejection fraction < 50 %) without coronary artery disease and endomyocardial biopsy free of relevant inflammatory cells in the endomyocardial biopsy. Patients were classified as having dilated cardiomyopathy if they had no or negligible alcohol

consumption (< 30 g/d). If they had a daily alcohol consumption of 50 g or more in their history, they were assigned to the alcoholic cardiomyopathy group.

Women were excluded from this study as it is known that CDT levels are not correlated with the alcohol consumption in women [15]. The cause is unknown.

The amount of alcohol intake was derived from a structured questionnaire. The participants were asked in multiple choice form if they had a hardly ever/never, monthly, weekly, or daily intake of beer (number of bottles), wine (number of glasses) or spirits (number of drinks). The daily total intake of alcohol was then calculated using common tables of alcohol content [16] in diverse spirits.

We analysed CDT, GT and MCV. Patients with the carbohydrate-deficient glycoprotein syndrome and patients with pancreas, lung and malignant disorders and hypertension were excluded from this study as these diseases influence the CDT-level. Furthermore, patients with iron deficiency and pernicious anaemia were excluded as the MCV is altered by these diseases.

Serum concentration of CDT was determined by a commercially available radio-immunoassay. After *in vitro* iron saturation of serum transferrin and absorption of isotransferrins with a pI < 5.7 at anion exchange microcolumns, isotransferrin with pI > 5.7 (CDT) were determined in the efflux by a competitive double-antibody immunoassay. CDT in the efflux competes with a fixed amount of <sup>125</sup>I-labeled transferrin for the binding sites of the transferrin antibodies. Bound and free transferrin were separated by addition of a second antibody immunoabsorbent, followed by centrifugation. The radioactivity in the pellet is inversely proportional to CDT in the sample. Precision and accuracy of the assay were assessed by analysis of a serum pool and a quantitative control sample (delivered with the test kit) with CDT near the upper reference limit of 20 U/l and 30 U/l in each run. Intra- and interassay variations were 10 % and 17 %. An external quantitative control sample was not available. All measurements were done in duplicate with calculation of the mean.

Serum activity of the  $\gamma$ -GT (EC 2.3.2.2) was measured at 25° C with  $\gamma$ -glutamyl-4-nitroanilid as a substrate, serum

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creatinine was determined kinetically, without prior precipitation of proteins by use of the Jaffé-method, serum glucose was analysed by the hexokinase method with a HITACHI 747-analyzer. Serum transferrin was determined immunonephelometrically. MCV was assessed with a coulter MAXM-Hematology analyser.

## Results

The mean age (51.3 years in alcoholic cardiomyopathy vs. 52.4 in dilated cardiomyopathy), ejection fraction (43.5 % vs. 45.5) and left ventricular end-diastolic diameter (65.9 mm vs. 67.5 mm) was similar in both groups (Table 1). The most popular alcohol was beer, followed by wine and drinks.

12 patients had an alcohol intake of more than 80 g per day. CDT was positive in all these patients. In statistical analysis of these patients CDT had a higher sensitivity and specificity than GT, MCV for alcoholic cardiomyopathy. 8 patients had a moderate alcohol intake (50–60 g per day), 2 of them were CDT-positive. Therefore, in the case of moderate alcohol intake the predictive value of CDT, GT and MCV was low. No patient was false-positive for CDT (Fig. 1).

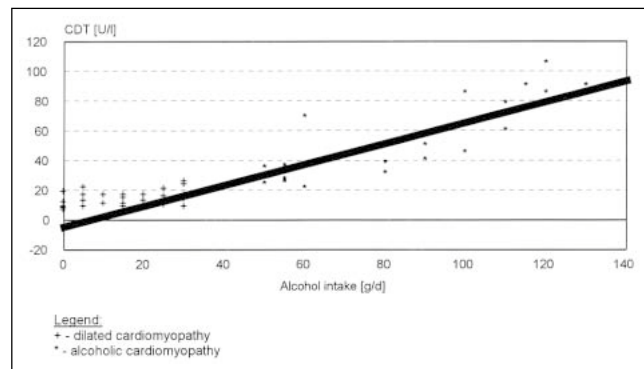
These results indicate that CDT is useful in the diagnosis of alcoholic cardiomyopathy but it is not acceptable for detection of moderate alcohol intake.

In histologic analysis 5 patients with alcoholic cardiomyopathy and 4 patients with dilated cardiomyopathy had focal lymphocytic infiltrates. Therefore, CDT levels did not differentiate between infiltrate-positive and infiltrate-negative patients.

## Discussion

The direct cardiotoxic effect of alcohol and its metabolite acetaldehyde has been demonstrated both in laboratory animals and in humans. The risk of developing alcoholic cardiomyopathy is related to both the mean daily alcohol intake and the duration of drinking, but there is much individual susceptibility to the toxic effect of alcohol [17]. Most patients, in whom alcoholic cardiomyopathy develops, have been drinking over 80 g/d for more than 5 years [17]. The clinical diagnosis of alcoholic cardiomyopathy reflects the coexistence of global myocardial dysfunction in a heavy drinker in whom no other cause for myocardial disease was found.

As in case of alcohol abstinence patients with alcoholic cardiomyopathy have a better prognosis than patients with idiopathic dilated cardiomyopathy [14], there is the need for a laboratory marker differentiating between both diseases. In comparison with  $\gamma$ -GT and MCV, CDT shows, however, the best overall specificity (> 90 %) for alcohol abuse [18–20]. Some cases with elevated CDT in the absence of alcohol abuse were reported in disease of the pancreas and lung, malignant disorders and hypertension [21–24]. The majority of false positive results with regard to chronic alcohol abuse can be ascribed to patients with the rare carbohydrate-deficient



**Figure 1.** CDT and Alcohol Intake. Comment: The dispersion is high in patients with high alcohol intake. The reason could be that these patients are not able to estimate their alcohol consumption.

glycoprotein syndrome [20, 25–27], with primary biliary cirrhosis [20, 24, 28, 29] and to healthy persons with genetic transferrin-D variants [20, 28]. Excluding these subjects, CDT measurement is now used for clinical decisions in forensic and employmental medicine, alcohol-related problems in traffic, and in screening analysis for alcohol abuse as an exclusion criterion in patients with liver cirrhosis subjected to liver transplantation [30–33].

As CDT has this superior diagnostic sensitivity to commonly used parameters of alcohol abuse in man [14, 20, 34–36], we tested the parameter to differentiate between idiopathic dilated cardiomyopathy and alcoholic cardiomyopathy. We found that CDT is an acceptable parameter for detection of harmful alcohol consumption in man. This result is of great clinical interest because alcoholic cardiomyopathy has a much better prognosis in cases of alcohol abstinence than idiopathic dilated cardiomyopathy. Therefore, the therapy for alcoholic cardiomyopathy must be alcohol withdrawal. In patients with alcohol abuse and myocarditis the immune functioning appears to be compromised. Several studies suggest that heavy drinking alters both lymphocyte and granulocyte production and function. Alcohol consumption *per se* might harm the immune system. Furthermore, the myocardial damage due to alcohol consumption could initiate autoreactive mechanisms comparable with those in viral or idiopathic myocarditis [37]. In our study, CDT-positive patients had no higher risk of myocarditis than DCM patients. CDT was not adequate to differentiate between infiltrate-positive and infiltrate-negative patients.

For the management of patients with alcohol abuse the prevention of further alcohol intake is mandatory to reverse the myocardial damage and the unfavourable predisposition for infection. Specific treatment of myocarditis is the second important option, and treatment of heart failure by reducing the size of the dilated heart and alleviating the signs and symptoms of heart failure is a logical third step [37].

**Table 1:** Results

Disease	Patients [n =]	Age [years]	Alcohol [g]	Ejection Fraction [%]	LVEDD [mm]	CDT [U/l]	MCV [fl]	$\gamma$ -GT [U/l]
ACM+DCM	50	51.4 ± 15.0	41.5 ± 44	44.6 ± 17.7	66.2 ± 9.2	23.9 ± 27.7*	90.3 ± 6.8*	78.2 ± 208.7
ACM	20	51.3 ± 16.1	82.4 ± 41.2	43.5 ± 18.2	65.9 ± 9.3	40.5 ± 37.6*	92.7 ± 8.4	147.4 ± 315.4
DCM	30	52.4 ± 16.7	15.8 ± 20.9	45.5 ± 17.0	67.5 ± 10.9	15.1 ± 16.1*	89.0 ± 5.5	32.1 ± 27.2*

ACM, alcoholic cardiomyopathy; DCM, idiopathic dilated cardiomyopathy; LVEDD, left ventricular end-diastolic diameter; \*significantly correlated with alcohol intake ( $p < 0.05$ ).

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