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UPDATE ON ALCOHOLIC DILATED CARDIOMYOPATHY

A causal relationship between alcohol and dilated cardiomyopathy (DCM) was suggested some time ago and confirmed in recent studies.^{1,2} Among the forms of DCM, the alcoholic form is defined³ as: (1) the results of chronic abuse (more than 5 years) of alcohol (>40 g/day in women and >80 g/day in men); (2) subject to remission, sometimes complete, with abstinence from alcohol intake, an adequate diet, and possibly thiamine supplementation. Alcoholic DCM has been reported to account for up to 40% of all cases of DCM.² Women appear to be more susceptible to the development of cardiac damage. Prolonged abuse of alcohol is associated with symptoms of heart failure in one third of cases; two thirds of alcoholics without symptoms have an abnormal echocardiogram; in about 10%, there is a picture of DCM.⁴

The clinical evaluation of alcohol abuse is not easy. The CAGE questionnaire (Table I) has a sensitivity of 80% to 90% and a specificity of 77% to 89% in discriminating between alcoholics and nonalcoholics.⁵ Table II lists the biochemical markers of alcohol consumption that can be used in clinical practice.⁴ Blood values of γ -glutamyl transferase (γ -GT) and mean corpuscular volume (MCV) have a negative predictive value of 86% and 84%, respectively. The blood chemistry marker nowadays considered most sensitive and specific is an increase in carbohydrate-deficient transferrin (CDT), which is a result of reduced hepatic synthesis of the sialintransferase enzyme involved in the process of protein glycosylation. Used in association with γ -GT, the sensitivity of detecting alcoholism can reach 90%. Nevertheless, the use of this marker is still controversial.

Alcohol is a proarrhythmic, negative inotrope and can cause histological alterations in the myocardium in the short term. The toxic effect is dose-related and the toxins implicated include ethanol and acetaldehyde. The latter is a metabolite of ethanol and inhibits myocardial protein synthesis, sequesters calcium in the sarcoplasmic reticulum, causes changes in mitochondrial respiration, and disrupts actin-myosin interactions. Ethanol can cause oxidative damage by peroxidation of cell membrane lipids, transformation of xanthine dehydrogenase into xanthine oxidase (an enzyme involved in the generation of superoxide anions), and an increase in the activity of the peroxisomal acyl-CoA catalases and oxidases. Changes in magnesium and phosphate homeostasis have also been suggested as cofactors involved in the development of alcoholic cardiomyopathy. No simple linear relationship exists between myocardial damage and alcohol abuse. There is probably hereditary susceptibility to its toxic effects. Moreover, an autoimmune etiology cannot be excluded: the toxic effect of alcohol causes cell necrosis which could set off an autoimmune process.

Table I. Questionnaire.

- Have you ever felt you need to stop drinking?
- Does it bother you if someone criticizes you because you drink?
- Have you ever felt bad or guilty because you drink?
- Have you ever drunk alcohol early in the morning to relax yourself or to get through a hangover?

Adapted from ref 5

The differential diagnosis between alcoholic DCM and DCM in an alcoholic is not easy. The pathological picture of the heart in alcoholic cardiomyopathy is neither diagnostic nor specific. Interstitial fibrosis tends to be more common in the hypertrophic forms of alcoholic cardiomyopathy; electron microscopy reveals more intense and widespread edema of the sarcoplasmic reticulum. Even the coexistence of alcoholic myopathy is not sufficient to label a DCM as alcoholic. The only criterion that can be used is the remission of the disease after cessation of drinking and introduction of an adequate dietary intake.

Alcohol can also be a precipitating factor in hemodynamic destabilization. It is well known that acute and chronic intake of alcohol has negative inotropic effects, even in normal subjects. Even the withdrawal of alcohol has potentially harmful effects and can provoke an episode of destabilization. Indeed, signs of sympathetic hyperstimulation can develop

and the fluid-electrolyte balance may be altered (because of hyperventilation, fever, diarrhea, vomiting, sweating). These withdrawal symptoms appear about 7 to 8 hours after the last intake of alcohol. The extent and duration of the alcohol abuse influence the severity of these signs.

The treatment of the heart failure is essentially the traditional management, although it is important to remember that liver dysfunction in the alcoholic can decrease the biotransformation of some drugs into their active metabolites. Generally speaking, a sober alcoholic metabolizes drugs more quickly than normal, while an intoxicated one metabolizes them more slowly. In fact, chronic consumption of alcohol increases the activity of some enzymes, such as the hepatic microsomal oxidase system, which metabolize drugs. Alcohol can also interfere with the absorption of drugs from the gastrointestinal tract and affect their protein binding. The administration of anticoagulants becomes more hazardous, since alcohol can have a synergistic effect with these drugs as well as depressing the hepatic synthesis of some coagulation factors.

Table II. Biochemical markers of alcohol abuse.

Adapted from ref 4

Abstinence from alcohol frequently allows cardiac function to recover,

MARKERS	DEFINITION	COMMENTS
Gamma-glutamyl-transferase (γ -GT)	Involved in the transport of amino acids across the blood-brain barrier	Increases in many hepatic, pancreatic, cardiac, renal, and neurological diseases and also in diabetes. Its levels can rise 12-24 hours after intake of a substantial quantity of alcohol and remain high for 2-3 weeks after stopping alcohol assumption.
Mean corpuscular volume (MCV)	An index of red cell volume.	Secondary to dietary and vitamin deficiencies, particularly deficiency of vitamin B ₁₂ , which is necessary for erythropoiesis. A lack of vitamin B ₁₂ causes macrocytic anemia
Alkaline phosphatase	Ubiquitous lysosomal enzyme.	Increase can be caused by intrahepatic obstruction of bile or liver cell damage
Amino-aspartate transferase	Involved in the transfer of amine groups in the synthesis of amino acids	Increased due to liver cell damage. Can increase by 10-fold in cirrhosis
Uric acid	A byproduct of purine metabolism	Raised levels because of increased degradation of purines resulting from cell death
Lactate dehydrogenase (LDH)	In the cytosol of metabolizing cells.	Ubiquitous

with a reduction or disappearance of the cardiac damage.⁶ It has not been possible to identify clinical predictors of recovery and it is still controversial whether recovery does or does not depend on the extent of the histological myocardial lesions that have already developed.

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