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Myocardial Effects of Ethanol Consumption in the Rat With Streptozotocin-Induced Diabetes

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Background: Rats with streptozotocin (STZ)-induced diabetes exhibit alterations in cardiac function, ventricular remodeling, and changes in cell signaling, which includes protein kinase C (PKC) isoforms. Moderate consumption of ethanol has a beneficial effect on cardiovascular outcomes in the general population, an effect that has recently been found to extend to patients with diabetes mellitus. We studied the effect of low-dose ethanol consumption on cardiac function, geometry, and PKC isoforms in the rat with STZ-induced diabetes.

Methods: Four groups of rats were studied over 8 to 10 weeks: control, STZ-induced diabetes, 12% (v/v) ethanol consumption, and STZ-induced diabetes plus 4% (v/v) ethanol consumption. Invasive hemodynamic measurements were performed; myocardial tissue was obtained for analysis for total PKC and cytosolic and membrane protein content of PKC-α, PKC-δ, and PKC-ε, and two-dimensional and M-mode echocardiograms were obtained.

Results: Compared with rats with diabetes alone, consumption of 4% ethanol prevented the decrease in left ventricular dP/dt seen with diabetes alone, as well as the increase in left ventricular internal dimension. Up-regulation of PKC-α, -δ, and -ε occurring in the diabetic animals was also prevented by ethanol consumption, whereas ethanol alone had no effect on PKC isoform pattern.

Conclusions: These data suggest that STZ-induced cardiac remodeling and dysfunction are associated with increases in PKC activity, particularly PKC-α, -δ, and -ε, and that consumption of ethanol can prevent these changes.

Key Words: Diabetes Mellitus, Protein Kinase C, Ethanol, Myocardium.

THE CARDIOVASCULAR CONSEQUENCES of diabetes mellitus are the principal causes of death and disability (Deckert et al., 1978; Garcia et al., 1974; Ruderman and Haudenschild, 1984) and include macrovascular (atherosclerosis) and microvascular sequelae and cardiomyopathy. Cardiomyopathy, and the resultant heart failure, is common among patients with diabetes mellitus, even in the absence of coronary artery disease (CAD) (Kannel et al., 1977). Cardiomyopathy also may account for the increased mortality rate of diabetic patients with acute myocardial infarction (twice that of nondiabetic patients) that is not explained by the size of the infarct. The importance of a diabetic cardiomyopathy in cardiovascular mortality is demonstrated by the findings of the Honolulu Heart Study, in which a direct effect of diabetes on the myocardium was demonstrated (Burchfiel et al., 1993).

Individuals who consume moderate to large amounts of ethanol are susceptible to an increased risk of CAD and cardiomyopathy. High consumption of ethanol is associated with the development of cardiomyopathy, hypertension, and hemorrhagic stroke. As many as 21% of subjects with excessive ethanol intake had clinical evidence of heart failure (Schenk and Cohen, 1970), and between 60 and 80% of patients with idiopathic dilated cardiomyopathy have abused ethanol (Alexander, 1966; Massumi et al., 1965). It is recognized that consumption of moderate amounts of ethanol, compared with abstinence, is associated with a lower risk of death from CAD and recurrent myocardial infarction for the population as a whole (Klatsky et al., 1992; Steinberg et al., 1991). Thus, the risk/benefit of ethanol on the cardiovascular system may be a J- or U-shaped relationship. Although the specific pathophysiological process by which ethanol affects the heart is not yet defined, the ultimate severity of injury seems to be influenced by genetic, metabolic, and environmental factors (Mousmoush and Abi-Mansour, 1991; Regan, 1984).

Because ethanol may alter glycemic regulation and potentially aggravate the cardiovascular, neurological, and immunosuppressive changes in patients with diabetes mellitus, the previous lack of data regarding the influence of ethanol in diabetes resulted in the doctrine that ethanol

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