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Changes in Myocardial *SERCA2a* Expression in Mouse Model of Chronic Alcohol Abuse

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Abstract

Chronic alcohol consumption remains a global health problem and has been implicated in many chronic and acute diseases. Alcohol consumption is a major risk factor for sudden cardiac death; chronic alcohol consumption contributes to collagen accumulation, myocardial fibrosis, and arrhythmias. However, the mechanism remains poorly understood. We hypothesized that chronic alcohol consumption causes an imbalance in the expression of MMPs and TIMPs, and also alters the regulation of proteins, including SERCA2a and CTGF, resulting in myocardial remodeling and cardiac dysfunction. After 6 weeks on diet, cardiac tissue isolated from ethanol-exposed mice and non-exposed mice were assayed for *Serca2a*, *Ctgf*, *Timp-1*, and *Mmp-3* expression by western blotting and QqRT-PCR. Ethanol exposure yielded a significant accumulation of the transcripts of *Ctgf* and *Mmp3*, without significantly affecting the levels of the corresponding proteins. *TIMP-1* mRNA and protein expression were not changed. Expression of the SERCA2a protein was significantly reduced in the ethanol group compared with the control group, despite the lack of significant changes in the accumulation of corresponding mRNA. Our findings on mRNA expression of the CTGF, MMP3, and TIMP1 encoding genes are consistent with previous reports on protein expression of these signal transducers, given that the data for the western blots did not reveal significant changes in the accumulation of these proteins. MMP/TIMP imbalance induced by extended alcohol exposure may significantly contribute to myocardial

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remodeling and cardiac dysfunction, which are responsible for sudden cardiac death in ethanol abusers.

Key words: Chronic alcoholism, Sudden death, Cardiac remodeling, MMPs, TIMPs