GW23-e0847

**DEFICIENCY OF INSULIN-LIKE GROWTH FACTOR 1
REDUCES VULNERABILITY TO CHRONIC ALCOHOL
INTAKE-INDUCED CARDIOMYOCYTE MECHANICAL
DYSFUNCTION: ROLE OF AMPK**

doi:10.1136/heartjnl-2012-302920a.217

¹Wei Ge, ²Qun Li, ²Subat Turdi, ¹Xiao-Ming Wang, ²Jun Ren, ¹Wei Ge. ¹Department of Geriatrics, Xijing Hospital, Fourth Military Medical University, Xi'an, China; ²Center for Cardiovascular Research and Alternative Medicine, University of Wyoming College of Health Sciences, Laramie, WY, USA

Objectives Circulating insulin-like growth factor I (IGF-1) levels are closely associated with cardiac performance although the role of IGF-1 in alcoholic cardiac dysfunction is unknown. This study was designed to evaluate the impact of severe liver IGF-1 deficiency (LID) on chronic alcohol-induced cardiomyocyte contractile and intracellular Ca^{2+} dysfunction.

Methods Adult male C57 and LID mice were placed on a 4% alcohol diet for 15 weeks. Cardiomyocyte contractile and intracellular Ca^{2+} properties were evaluated including peak shortening (PS), maximal velocity of shortening/relengthening ($\pm \text{dL/dt}$), time-to-relengthening (TR90), change in fura-fluorescence intensity (ΔFFI) and intracellular Ca^{2+} decay. Levels of apoptotic regulators caspase-3, Bcl-2 and c-Jun NH2-terminal kinase (JNK), the ethanol metabolising enzyme mitochondrial aldehyde dehydrogenase (ALDH2), as well as the cellular fuel gauge AMP-activated protein kinase (AMPK) were evaluated.

Results Chronic alcohol intake enlarged myocyte cross-sectional area, reduced PS, $\pm \text{dL/dt}$ and ΔFFI as well as prolonged TR90 and intracellular Ca^{2+} decay, the effect of which was greatly attenuated by IGF-1 deficiency. The beneficial effect of LID against alcoholic cardiac mechanical defect was ablated by IGF-1 replenishment. Alcohol intake increased caspase-3 activity/expression although it downregulated Bcl-2, ALDH2 and pAMPK without affecting JNK and AMPK. IGF-1 deficiency attenuated alcoholism-induced responses in all these proteins with the exception of Bcl-2. In addition, the AMPK agonist 5-aminoimidazole-4-carboxamide-1- β -D-ribofuranoside abrogated short-term ethanol incubation-elicited cardiac mechanical dysfunction.

Conclusions Taken together, these data suggested that IGF-1 deficiency may reduce the sensitivity to ethanol-induced myocardial mechanical dysfunction. Our data further depicted a likely role of Caspase-3, ALDH2 and AMPK activation in IGF-1 deficiency induced 'desensitisation' of alcoholic cardiomyopathy.