Role of fibroblast growth factor-21 in alcoholic cardiomyopathy

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Introduction – Alcoholic cardiomyopathy (ACM) resulting from chronic alcohol consumption is one of the main contributors leading to heart failure. ACM is associated with histological, cellular and structural changes within the myocardium. We previously showed that Fibroblast growth factor 21 (FGF21) is a cardioprotective factor acting in an endocrine/autocrine manner.

Purpose - We aimed to study the role of FGF21 in the cardiac damage induced by chronic alcohol consumption.

Methods – FGF21 gene expression levels and circulating levels were analyzed in human heart samples and blood samples from healthy donors or chronic alcoholic patients. Two month-old wild type (WT) and FGF21 knockout (FGF21-KO) mice were fed a 4% alcohol liquid diet or a calorie-adjusted control liquid diet for 12 weeks.

Results – We found that FGF21 gene expression levels in human heart biopsies and FGF21 circulating levels were increased in chronic alcohol patients. Our mice model of chronic alcohol consumption recapitulates what we have found in humans: higher FGF21 expression levels in heart and a tendency to increase the FGF21 circulating levels after chronic alcohol intake. Furthermore, we found that the heart weight/tibia length (HW/TL) ratio was increased by alcohol consumption indicating cardiac hypertrophy development after chronic alcohol consumption in this model but we did not observed genotype differences. However, echocardiographic measurements showed that alcohol consumption significantly increased both aortic peak and E peak only in FGF21-KO mice indicating enhanced cardiac dysfunction (systolic and diastolic) when mice lacked FGF21. Moreover, we observed a marked induction of the cardiac hypertrophy marker gene atrial natriuretic factor (ANF) and the fibrosis-related genes Collagen-3 (Col3) in FGF21-KO mice after alcohol consumption compared to WT mice. Finally, Trichrome Masson staining confirmed that chronic alcohol consumption leads to cardiac fibrosis and lack of FGF21 aggravates this process.

Conclusions- Our results show that FGF21 expression is induced by chronic alcohol consumption. In addition, the lack of FGF21 aggravates cardiac damage produced by ACM, thus pointing to FGF21 as a protective agent against alcohol-induced cardiomyopathy.