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## Evaluation of chronic losartan treatment effect on cardiac chronotropic dysfunction in biliary cirrhotic rats

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Cirrhosis is associated with cardiac chronotropic and inotropic dysfunction which is known as cirrhotic cardiomyopathy. Cardiac responsiveness to adrenergic stimulation is impaired in cirrhosis. Moreover, there is vagal nerve dysfunction which is related to neuromodulatory dysfunction of the angiotensin II in the cirrhosis. This study was aimed to explore the hypothesis that administration of losartan-angiotensin II receptor antagonist- increases cardiac chronotropic response to isoproterenol in cirrhotic rats; and if so, whether this is associated with altered cardiac TGF- $\beta$  receptor expression. Cirrhosis was induced by surgical ligation of the bile duct (BDL) in male Wister rats. Half of the BDL-group and control group were treated with losartan for four weeks. Four weeks after bile duct ligation or sham surgery the atria were isolated and spontaneously beating rate and chronotropic responsiveness to  $\beta$ -adrenergic stimulation was assessed using standard organ bath. Pathological assessment was done on the atria. Moreover, the expression of TGF- $\beta$  was assessed the atria using quantitative RT-PCR. Bile duct ligation could induce a significant hypo-responsiveness to adrenergic stimulation. In cirrhotic rats, the chronotropic responses increased after chronic treatment with losartan but it was not significant. Pathological study showed that losartan decreases fibrosis in atria in losartan treated cirrhotic group. TGF- $\beta$  expression is markedly increased in cirrhotic rats which are significantly decreased in atria following administration of losartan. These results might be considered as angiotensin II role in cirrhotic cardiomyopathy but further studies are required to elaborate the mechanism as well as possible advantage of losartan. We conclude that cirrhosis in rats is associated with altered expression of TGF- $\beta$  in atrium which losartan can ameliorate it.

## **Biography**

Farahnaz Jazaerijooneghani has completed his MD and PhD at Tehran University of Medical Sciences. She has been Assistant Professors at Tehran University of Medical Sciences, Pharmacology department since 2013. She has published more than 10 papers in reputed journals and presented posters in EASL Congress (Europe) and Pharma Nutrition Congress in Philadelphia. She has supervised and advised more than 10 medical students, masters and PhD students.

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