

POSTERS

injection, the atria were isolated and spontaneously beating rate and chronotropic responsiveness to cholinergic stimulation was assessed using standard organ bath. The expression of Toll-like receptor 4 (TLR4) was assessed in isolated atria using quantitative RT-PCR.

Results: The expression of atrial TLR4 mRNA increased 24.3 folds in cirrhotic rats compared with controls. Immunohistochemical study showed that TLR4 is mainly expressed in the endocardial layer in cirrhotic atria. LPS injection could induce a significant hypo-responsiveness to cholinergic stimulation in control rats. However, LPS injection was unable to make a difference in cardiac chronotropic responsiveness to a cholinergic agonist in cirrhotic rats.

Conclusions: Our data shows that although TLR4 is over expressed in cirrhotic atria, cirrhosis is associated with development of tolerance to cardiac chronotropic effect of endotoxin in rats.

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MYOCARDIAL INFARCT-SPARING EFFECT OF ISCHEMIC PRECONDITIONING ABROGATED IN CIRRHOTIC RAT THROUGH INVOLVEMENT OF MITOCHONDRIAL PERMEABILITY TRANSITION PORE

V. Khori¹, A.R. Dehpour², N. Mohsen², H.R. Mohimani², F. Jafrazedeh². ¹Golestan Cardiovascular Research Center, Golestan University of Medical Sciences, Gorgan, ²Dept. of Pharmacology, School of Medicine, Tehran University of Medical Sciences, Tehran, Iran
E-mail: vaph99@yahoo.com

Despite all studies undertaken mechanism of cirrhotic cardiomyopathy the role of cirrhosis on ischemia-reperfusion (I/R) injury and ischemic preconditioning (IPC) phenomenon hasn't been explored yet. The aim of present study is to assess the relation between cirrhosis and IPC and the mitochondrial permeability transition pore (mPTP) role in IPC cardioprotective effects in cirrhotic rats.

Material and Method: Rat's heart were isolated and perfused with Krebs buffer by Langendorff method. Animals were equally divided into six groups (n=6): (I) I/R; hearts were subjected to 30 min ischemia and 45 min reperfusion, (II) IPC; IPC was induced via four cycle of 5 min regional ischemia followed by 5 min of reperfusion (III) common bile duct ligated (CBDL); hearts were subjected ischemia and reperfusion in cirrhotic rats, (IV) IPC-CBDL; four cycle of 5 min regional ischemia followed by 5 min of reperfusion in cirrhotic rats (V) CSA; Cyclosporine A was added 40 min prior to main ischemia (VI) CBDL+CSA.

Results: Infarct size was increased significantly in IPC-CBDL group in comparison with IPC group (p<0.05). Addition of CSA in CBDL+CSA group significantly decreased infarct size in comparison with IPC-CBDL group (p<0.05). Ventricular arrhythmia severity was decreased significantly in IPC group compared to IR group, whereas it was increased significantly in IPC-CBDL group compared to IPC group (p<0.05). CSA did not decrease arrhythmia score in CBDL group.

Conclusion: The results showed that the cardioprotective effects of IPC are eliminated in cirrhosis. MPTP signaling in partly involve in cirrhotic cardiomyopathy.

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T-CELL IMMUNODEFICIENCY IN CIRRHOSIS: DEFECTIVE PERIPHERAL REPLENISHMENT OF DEPLETED CIRCULATING T-HELPER CELLS

M. Lario^{1,2}, L. Muñoz^{1,2}, M. Úbeda^{1,2}, M.J. Borrero^{1,2}, L.E. Chara^{1,3}, M.A. Sánchez¹, J. Monserrat^{1,2}, D. Díaz^{1,2}, M. Álvarez-Mon^{1,2,4}, A. Albillos^{1,2,5}. ¹Department of Medicine, University of Alcalá, Alcalá de Henares, ²CIBERehd, Institute of Health Carlos III, Madrid, ³University Hospital of Guadalajara, Guadalajara, ⁴University Hospital Príncipe de Asturias, Alcalá de Henares, ⁵University Hospital Ramón y Cajal, IRYCIS, Madrid, Spain
E-mail: mlario2005@yahoo.es

Background: Depletion of circulating CD4⁺ T helper (Th) cells, especially naïve-Th, is a common finding in cirrhosis. Although consequent effects on the TCR repertoire could increase susceptibility to bacterial infection, the pathogenesis of Th-cell depletion in cirrhosis is still poorly understood.

Aim: To investigate the pathogenic mechanisms involved in naïve and memory Th depletion in cirrhosis.

Methods: Circulating naïve-Th and memory-Th lymphocytes were examined by flow cytometry in 60 patients with cirrhosis (90% Child B/C) and 37 healthy controls. Thymopoiesis, cell survival and apoptosis, and cell activation and proliferation were assessed through CD31, Annexin-V, HLA-DR, and Ki-67 expression, respectively. Serum LPS binding protein (LBP) levels and spleen size (by ultrasound) were measured as indicators of bacterial translocation and splenic pooling, respectively.

Results: Compared to controls, patients showed reduced absolute numbers of Th-cells (median, 801 vs 382/μl, p<0.01) involving a greater depletion of the naïve-Th than memory-Th compartment (2.7 vs 1.5-fold, respectively). Numbers of recent thymic emigrants (CD31⁺ naïve-Th) were drastically diminished in patients (242 vs 67/μl, p<0.01). Patients with cirrhosis also showed higher levels of spontaneous and PHA-induced naïve-Th cell apoptosis (Annexin-V⁺) (p<0.01) along with increased activated HLA-DR⁺ memory Th-cells (7.3 vs 10.6%, p<0.01), which were directly correlated with LBP levels (r=0.54, p<0.05). Increased proliferating Ki-67⁺ memory-Th cells in patients (3.3 vs 4.6%, p<0.01) were negatively correlated with naïve-Th numbers (r=-0.38, p<0.01). Naïve-Th cell numbers were negatively correlated with the percentage of apoptotic naïve-Th cells (r=-0.32), percentage of activated memory-Th cells (r=-0.62), serum LBP (r=-0.34) and spleen size (r=-0.55). Multivariate analysis revealed the independent correlation of defective thymopoiesis, increased memory Th-cell activation and splenomegaly with naïve Th-cell depletion.

Conclusions: The pathogenesis of Th-cell depletion, especially of naïve Th-cells, in cirrhosis is complex, and mainly attributable to defective thymopoiesis, elevated LPS-driven activation and splenic pooling. Our findings indicate that despite efforts to increase the peripheral homeostatic proliferation of memory Th-cells, this strategy is unable to restore the reduced pool of circulating Th-cells.

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GUT DECONTAMINATION USING NANOPOROUS CARBONS REDUCES PORTAL PRESSURE AND PREVENTS LIVER FAILURE IN BILE-DUCT LIGATED CIRRHOTIC ANIMALS BY REDUCING KUPFFER CELL ACTIVATION

J. Macnaughtan¹, J. Soeda¹, A. Mouralidarane¹, S. Sandeman², C. Howell³, S. Mikhailovsky³, S. Kozynchenko⁴, S. Tennison⁴, N. Davies¹, J. Oben¹, R. Mookerjee¹, R. Jalan¹. ¹UCL, London, ²University of Brighton, ³Brighton University, Brighton, ⁴Mastcarbon, Guildford, UK
E-mail: j.macnaughtan@ucl.ac.uk

Background and Aims: Gut-derived bacterial products and the associated dysregulated inflammatory response play a central role