Changes in expression of renal Oat1, Oat3 and Mrp2 in ANIT-induced cholestatic hepatitis in rat after treatment of JBP485

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Background: To investigate the protective effects of JBP485 (cyclo-trans-4-l-hydroxyprolyl-l-serine, a dipeptide with anti-inflammatory action) on alpha-naphthylisothiocyanate (ANIT)-induced cholestatic hepatitis and whether these are mediated by the organic anion transporters Oat1 and Oat3 and the multidrug resistance-associated protein Mrp2.

Methods: The effects of JBP485 on ANIT-induced liver histologic changes, bilirubin (BIL), alanine amiotransferase (ALT), and aspartate transaminase (AST), malondialdehyde (MDA), superoxide dismutase (SOD) and myeloperoxidase (MPO) levels were examined. Plasma concentration and cumulative urinary excretion of JBP485 by intravenous administration in vivo, the uptake of JBP485 in kidney slices in vitro were determined by LC-MS-MS. RT-PCR were used for determine Oat1, Oat3 and Mrp2 mRNA.

Result: (1) JBP485 decreased BIL, ALT, AST, MDA, and MPO levels significantly, alleviated inflammation and necrosis in liver histochimistry in ANIT-treated rats. (2) The plasma concentration of JBP485 was significantly increased, cumulative urinary excretion of JBP485 and the uptake of JBP485 in kidney slices were decreased remarkably. (3) RT-PCR showed the decrease in mRNA of Oat1 and Oat3 in ANIT-treated rats, whereas, the mRNA levels of Oat1, Oat3 and Mrp2 were up-regulated with a concomitant increase in urinary BIL after treatment with JBP485 in ANIT-treated rats.

Conclusion: JBP485 improved liver inflammation condition induced by ANIT. The mechanism is related to decrease the inflammatory mediators release and improvement of the expression and function for Oat1, Oat3 and Mrp2 as well as facilitation of urinary excretion for hepatotoxic substance. JBP485 might be a good candidate for a new therapeutic agent for cholestatic hepatitis.

Study on the protective effects of mesenchymal stem cells on ischemic reperfusion injury of intestine in rats

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Background: To study the effects of bone marrow mesenchymal stem cells (BM MSCs) allograft on the recovery of ischemic reperfusion injury and tight junction of intestine in rats.

Methods: (1) BM MSCs were isolated from femur of male Wistar rats by the density gradient centrifugation, the third generation cultured cells were prepared as suspension. (2) Intestinal ischemic reperfusion injury models were established in male Wistar rats, which were divided into the experimental group (1 ml BM MSCs suspension was injected into the intestinal submucosa) and the control group (1 ml saline was inject into the intestinal submucosa). Then, serum and intestinal tissue samples were collected at different time after injection, which were analyzed by luciferase tracing, immunohistochemistry, ELISA, transmission electron microscope and Western Blot.

Results: BM MSCs were isolated and cultured successfully with high purity and homogeneity, and intestinal ischemic reperfusion injury models were established successfully. Submucosal injected BM MSCs were colonized in the intestine and survived long-term. BM MSCs relived the damage of intestinal villi structure under light microscope and restored the destruction of intestinal villi and tight junction under transmission electron microscope. Diamine oxidase (DAO) and D-lactate were tested by ELISA. The DAO and D-lactate in the experimental group at 6 h and 24 h are lower than those of the control group (P <0.05), which showed that BM MSCs could decrease the DAO and D-lactate. BM MSCs could decreased the expression of tumor necrosis factor (TNF-α) at 6 h, 24 h and 72 h after injection. BM MSCs could also promote the synthesis of ZO-1 protein tested by Western Blot, which was time-dependant.

Conclusion: Intestinal injected BM MSCs could promote both the expression of tight junction protein and the recovery of intestinal ischemic reperfusion injury in rats, in which TNF-α may play some role.

Effects of Cornel iridoid glycoside on apoptosis-related factors in hippocampus of global ischemic gerbils

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Objective: To investigate the effects of Cornel iridoid glycoside (CIG) on apoptotic neurons and the expression of B cell lymphoma/leukemia-2 (Bcl-2) and Cystein-Asparate Protease-3 (Caspase-3) in hippocampus CA1 area after global ischemia in gerbils.

Methods: The global brain ischemic model was made by occluding common carotid arteries for 5 min in gerbils. One week after ischemia, the apoptotic neurons were detected in hippocampal CA1 area by TUNEL method. The expression of Bcl-2 and Caspase-3 was detected by immunocytochemical method.

Results: Intragastrical administration of CIG significantly decreased the number of apoptotic neurons in hippocampal CA1 area, inhibited the expression of caspase-3 and increased Bcl-2 expression.

Conclusions: CIG can protect neurons against apoptosis induced by cerebral ischemia. The paper is funded by National Basic Research 973 Program (No. 2003CB517104), National Natural Science Foundation of China (No. 90709011, 30472184), Beijing Natural Science Foundation of China (No. 7050001, 7062051)