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NBD多肽预处理改善大鼠肝移植缺血再灌注损伤的

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Title: NBD peptides pretreatment protects rats against ischemia reperfusion injury after orthotopic liver transplantation

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关键词: NBD多肽; NF- κ B; 缺血再灌注损伤; 肝移植

Keywords: NF- κ B essential modulator binding domain peptides; NF- κ B; ischemia reperfusion injury; liver transplantation

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摘要: 目的 采用SD-SD大鼠原位肝移植模型, 观察NBD多肽预处理供肝对术后肝脏缺血再灌注损伤(ischemia reperfusion injury, IRI)的影响, 并探讨其可能的保护机制。
方法 105只SD大鼠采用抽签法随机分为3组, NBD预处理组(24对动物, 供体术前2 h经腹腔注射8 mg/kg的NBD多肽并建立原位肝移植模型)、移植组(24对动物, 注射同体积的生理盐水作为对照)和假手术组(9只动物)。术后3、6、24 h分别处死动物

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物, 检测3组中ALT水平, ELISA检测血清中TNF- α 含量。取NBD预处理组和移植组肝脏组织, HE染色观察肝脏病理学改变。采用TUNEL检测肝细胞凋亡, EMSA检量NF- κ B转录活性, Western blot检测p-IKK-2和I κ B α 在肝组织的表达。结果 NBD预处理组和移植组术后各时间点的ALT水平、TNF- α 含量均明显高于假手术组。NBD预处理组中ALT水平、NF- κ B活性、p-IKK-2表达、TNF- α 含量较移植组均明显降低($P<0.05$); I κ B α 表达则较移植组明显增强($P<0.05$); 术后6 h, NBD预处理组中病理损伤、凋亡细胞较移植组明显减轻。结论 NBD多肽预处理供体可通过抑制供肝中NF- κ B活性, 有效改善肝移植IRI。

Abstract: Objective NF- κ B essential modulator binding domain peptides (NBD peptides) interfere the formation of I κ B kinase complex (IKK) and down-regulate the classical NF- κ B signaling pathway. The aim of this study was to determine the effects of NBD peptides pretreatment on ischemia reperfusion injury (IRI) after orthotopic liver transplantation in rats. Methods A total of 105 Sprague Dawley (SD) rats were randomly divided into 3 groups, NBD group (donors were given 8 mg/kg NBD peptides intra-peritoneally in 2 h before surgery and performed orthotopic liver transplantation according to the Kamada technique, totally 24 pairs), control group (treated with the same volume of physiological saline, totally 24 pairs) and sham-operation group ($n=9$). Animals were sacrificed at 3, 6, and 24 h after surgery. The serum levels of alanine aminotransferase (ALT) and tumor necrosis factor (TNF- α) were measured in the 3 groups. The levels of IKK phosphorylation and I κ B α degradation, NF- κ B transcriptional activity and cell apoptosis were detected by Western blotting, EMSA and TUNEL respectively. Morphological changes of liver tissues were observed after HE staining. Results The levels of ALT and TNF- α in the both NBD group and control group were significantly higher than that of sham-operation group ($P<0.05$). Compared with the control group, pretreatment with NBD peptides had significantly lower ALT level, NF- κ B transcriptional activity, IKK complex phosphorylation, and TNF- α levels ($P<0.05$), while enhanced I κ B α expression ($P<0.05$). NBD peptides pretreatment also ameliorated the pathological damages and cell apoptosis in 6 h after operation. Conclusion NBD peptides pretreatment attenuates hepatic IRI by preventing NF- κ B activation.

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