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GRP78和CHOP蛋白表达增加与脓毒性休克大鼠肺血管通透性改变的关系(PDF)

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Title: Relationship of GRP78 and CHOP expression with pulmonary vascular permeability in rat model of endoplasmic reticulum stress during septic shock

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关键词: 内质网应激; GRP78; CHOP; 脓毒性休克; 血管通透性

Keywords: endoplasmic reticulum stress; glucose-regulated protein78; C/EBP homologous protein; septic shock; vascular permeability

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摘要: 目的 研究脓毒性休克大鼠内质网应激模型中葡萄糖调节蛋白78（glucose-regulated protein78，GRP78）和C/EBP环磷酸腺苷反应元件结合转录因子同源蛋白（C/EBP homologous protein，CHOP）蛋白表达的变化及其与血管通透性改变的关系。 方法 42只成年SD大鼠，雌雄各半，体质量200～220 g，随机分为3组：①假手术组；②盲肠造瘘组，按照术后时间长短盲肠造瘘组又分为术后1、2、4、6、8 h等5个亚组；③盲肠造瘘+牛磺酸组（n=6）。用异硫氰酸荧光素标记的牛血清白蛋白注入肺组织，在术后1、2、4、6、8 h时分别取各组相应大鼠肺脏，牛磺酸干预组于术后6 h取出，生理盐水进行肺灌洗，观察其荧光物质渗透率的变化测量肺毛细血管通透性；Western blot方法测量肺血管内皮细胞GRP78和CHOP蛋白的表达并对各组进行比较。 结果 ①大鼠盲肠造瘘术后1、2、4、6、8 h后GRP78和CHOP蛋白表达均呈递增趋势[（P（GRP78）<0.05; P（CHOP）<0.05]，肺血管荧光物质渗透率也随着时间的延长呈直线递增的趋势（P=0.006<0.05），盲肠造瘘组各组GRP78和CHOP蛋白的表达与肺血管荧光物质渗透率的改变呈正相关（R^2=0.785，P<0.05；

R^2=0.881，P<0.05）；②牛磺酸处理后，6 h点肺血管荧光物质渗透率显著低于单纯盲肠造瘘术后（P=0.007<0.05），GRP78和CHOP蛋白的表达也较盲肠造瘘组低（P=0.004<0.05）。 结论 脓毒性休克内质网应激参与了血管通透性增高的发生，GRP78和CHOP蛋白为重要的参与分子。

Abstract: Objective To explore the changes of glucose-regulated protein78 (GRP78) and C/EBP homologous protein (CHOP) in rat model of endoplasmic reticulum stress during septic shock and its relationship with pulmonary vascular permeability. Methods A total of 42 adult SD rats, with half females and half males weighing 200 to 220 g, were randomly divided into 3 groups, sham-operation group (n=6), cecal ligation and puncture (CLP) group, CLP plus taurine group (5 mL/kg taurine through intravenous injection immediately before CLP establishment, n=6). CLP group was further divided into 5 subgroups, in 1, 2, 4, 6 and 8 h respectively after CLP, each subgroup having 6 rats. After fluorescein isothiocyanate-labeled albumin bovine serum was injected intravenously, lung tissues of rats were taken at above time points after CLP in CLP group, and at 6 h after CLP in CLP plus taurine group. The pulmonary vascular permeability was determined by observing the permeability of fluorescein. The expression of GRP78 and CHOP in pulmonary vascular endothelial cells were determined by Western blotting. Results The expression of GRP78 and CHOP at protein level were also increased in a time-dependent manner after CLP (P<0.05).The permeability of fluorescein was in a straight line up in a time-dependent fashion after CLP as compared to sham-operation group （P<0.05）. The expression of GRP78 and CHOP was positively correlated with the changes of vascular permeability（R^2=0.785, P<0.05; R^2=0.881, P<0.05）. Taurine intervention resulted in significantly decreased permeability of fluorescein compared with CLP group （P<0.05）, and significantly decreased expression of GRP78 and CHOP （P<0.05）. Conclusion Endoplasmic reticulum stress during septic shock participates in the increase of vascular permeability, and GRP78 and CHOP are important participating molecules.

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