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Changes of visceral vascualr endothelia cells in early stage after burn injury in rabbits

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Abstract In order to investigate the patterns of the damages of vascular endothelial cells (VECs), bood colloid osmotic pressure (BCOP), circulating endothelial cells (CECs), angiotensin converting enzyme (ACE) and myeloperoxidase (MPO) were measured in 25 rabbits after they were randomized into control, 6 h, 12 h, 24 h and 48 h groups and inflicted with 30% TBSA full thickness burns. Meanwhile, the pathological changes of the VECs of the heart, kidneys, intestines, liver and lungs were observed with optical and electron microscopy and the distribution of ACE and MPO in the organs determined. It was found that BCOP was markedly decreased from 6 h to increase afterwards. The activity of ACE was enhanced in 6 h and then decreased tradually in the serum but it was significantly decreased in 6 h and then elevated after that time in the organs except the lungs. The activity of MPO was higher in the burned than in the controll in plasma and was increased to the peak in 6 h; it was increased in 6 h in the lungs; and it was increased in 24 h in the kidneys and intestines. Pathologically, it was found that the VECs in many organs underwent cytoplasmic projection, as villous process and organelle enrichment in the early stage and then they became constricted and rounded. The degree of VEC damages was different among the organs. The separation of pullmonary VECs from the basement membrane occurred in the 6th hour and the damage of VECs was the most severe in the lungs among all the organs studied in the early stage postburn.

All these findings suggest that VECs are damaged extensivelly in the early stage after burn injury and contineus to be damaged extensively in the early play an important role in the damages of many organs in the early stage after burns.

Key words burns; vascular endothelial cell; angiotensin converting enzyme; myeloperoxidase

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mdr1基因表达与肺癌多重抗药性关系的研究

论文摘要

Expression of mdr 1 gene and multidrug resistance of lung cancer

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多重抗药性(MDR)是肺癌化疗失败的主要原因之一。通过逐渐增加药物浓度的方法,以顺铂(CDDP)选择培养人肺腺癌细胞系LC-3 8个月,建立了MDR细胞系LC-3/CDDP。该细胞系对CDDP抗药性为亲代细胞的7.96倍,对ADM、VCR、5-FU、VP-16具有交叉抗药性。LC-3/CDDP细胞一般形态、倍增时间与亲代细胞无显著差异,但超微结构显示细胞具有异质性。对细胞内药物浓度测定发现,LC-3/CDDP细胞内ADM聚集量较亲代细胞明显减少。细胞周期测定发现S期、G_2+M比例升高,DNA指数增加,DNA合成速率明显上升,提示细胞对DNA损伤的修复功能增强。LC-3/CDDP细胞的另一特征是染色体延长、双微体增多。二性霉素B、芳香维甲酸乙酯使LC-3/CDDP细胞内ADM聚集量显著增加,相对抗药度(RR)下降,两者协同应用基本上可使LC-3/CDDP细胞的抗药性逆转。

斑点杂交结果显示,LC-3/CDDP细胞mdr1 mRNA含量明显高于LC-3细胞。原位杂交结果表明,LC-3细胞内未出现阳性杂交信号,而LC-3/CDDP细胞内显示紫蓝色颗粒状阳性杂交信号,主要分布于细胞浆内,部分阳性颗粒位于胞核内。抗P-gp McAb免疫细胞化学染色结果表明,LC-3细胞染色阴性,而经CDDP选择培养后P-gp表达由阴性转为阳性,致完全抗药表型产生时表达最强。这些结果表明,mdr1基因表达与LC-3/CDDP细胞抗药性产生密切相关。

对正常组织进行免疫细胞化学染色显示,正常肾高度表达P-gp,脑、肺、肝、结肠、脾中度表达,胰腺弱表达,P-gp在正常组织中可能具有分泌与防御功能。斑点杂交结果表明,肺腺癌组mdr1 mRNA含量明显高于磷癌组,腺癌组P-gp表达阳性率亦明显高于磷癌组。这些结果表明,mdr1基因表达可能为肺癌产生内在抗药性的重要原因。

关键词 肺肿瘤;多重抗药性;多重抗药基因;P-糖蛋白;顺铂;逆转;化学治疗

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