中国病理生理杂志 2009 25 (5): 844-847 ISSN: 1000-4718 CN: 44-1187/R

论著

内皮衍生微粒诱导内皮细胞氧自由基产生损伤内皮功能

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收稿日期 2008-5-14 修回日期 2008-11-12 网络版发布日期 2009-8-5 接受日期 2008-11-12

摘要 目的： 探讨内皮衍生微粒（EMP)诱导内皮功能失调的机制和氧自由基(O-·2)在EMP诱导内皮功能失调中所起的作用。方法: 从人血纤维蛋白溶酶原激活抑制剂-1刺激的人脐静脉内皮细胞中提取EMP，(1)采用牛主动脉内皮细胞（BAEC）做细胞培养，分成3组。第1组不做预处理，第2组EMP (1×108/L)，第3组EMP (1×108/L) + L-nitroarginiemethylester(L-NAME, 1 mmol/L)，预处理BAEC 30 min后，用超氧化物歧化酶(SOD)可抑制的铁细胞色素C还原法，测量O-·2的产生情况。(2) 从小鼠中分离面动脉，分成4组。第1组不做预处理，第2组EMP (1×108/L)，第3组EMP(1×108/L) + SOD (2×105 U/L)，第4组EMP (1×108/L)+聚乙烯羟乙酸盐超氧化物歧化酶(PEG-SOD, 2×105 U/L) 预处理血管10 min后做乙酰胆碱（ACH）诱导下的内皮依赖血管舒张功能试验。结果:（1）EMP明显增加BAEC O-·2产生，L-NAME可以抑制50% EMP导致的O-·2产生增加。 (2) EMP明显损伤ACH诱导的血管舒张功能，SOD处理未能清除EMP对血管舒张功能的损伤，PEG-SOD可部分恢复EMP处理后的血管舒张功能。结论: EMP诱导血管内皮功能失调至少部分是通过诱导细胞内产生的O-·2所致，为将来寻找包括清除O-·2在内的综合治疗方法提供理论依据。

关键词 内皮衍生微粒； 血管舒张； 内皮； 自由基
分类号 R331.3

Endothelium-derived microparticles induce endothelial cell superoxide generation and impair endothelial function

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Abstract

<FONT face=Verdana>AIM: To investigate the mechanism of endothelium-derived microparticles (EMP)-induced endothelial dysfunction and the role of superoxide anion (O-·2) in EMP-induced endothelial dysfunction. METHODS: EMP were isolated from human umbilical vein endothelial cells stimulated with plasminogen activated inhibitor-1. (1) Cultured bovine aortic endothelial cells (BAEC) were divided into 3 groups and pretreated with nothing in group 1, EMP (1×108/L) in group 2, EMP (1×108/L) + L-nitroarginiemethylester (L-NAME, 1 mmol/L) in group 3 for 30 min and A23187 (5 μmol/L) stimulated O-·2 generation was determined by superoxide dismutase (SOD)-inhibitable ferricytochrome C reduction. (2) Facialis arteries (60-150 microns) were isolated from C57BL/6 mice and divided into 4 groups. The vessels were pretreated with nothing in group 1, EMP (1×108/L) in group 2, EMP (1×108/L) + SOD (2×105 U/L) in group 3, EMP (1×108/L) + polyethylene glycolated-SOD (PEG-SOD, 2×105 U/L) in group 4 for 10 min and acetylcholine (ACH)-induced vasodilation was measured. RESULTS: (1) EMP significantly increased O-·2 generation in BAEC culture, which was prevented about 50% by pretreating the BAEC with L-NAME. (2) EMP significantly impaired ACH-induced vasodilation. SOD could not restore EMP-impaired ACH-induced vasodilation and PEG-SOD showed partial restoration of vasodilation. CONCLUSION: These data indicate that at least some EMP-induced endothelial dysfunction occurs by inducing intracellular O-·2 generation. It may provide a theoretical evidences in finding a multiple treatment including removal of O-·2 in the future.</FONT>

Key words Endothelium-derived microparticles Vasodilation Endothelium Free radicals

DOI: 1000-4718

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