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论著

转染PDGF-B反义核酸和tPA基因预防狗冠脉搭桥术吻合口再狭窄

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摘要 目的： 探讨联合应用组织型纤溶酶原激活物（tPA）基因质粒和血小板源性生长因子（PDGF-B）反义核酸预防冠状动脉搭桥术后吻合口再狭窄。方法： 建立狗冠状动脉搭桥术吻合口再狭窄模型，构建tPA基因质粒并设计合成（PDGF-B）反义寡核苷酸，在冠状动脉搭桥术同时以超声波辅助转染心肌细胞和吻合口血管平滑肌细胞，采用常规病理、免疫组织化学、原位杂交以及形态测量方法观察对吻合口局部血栓形成、血管内膜细胞增殖细胞核抗原（PCNA）和PDGF-B mRNA表达以及内膜增生的影响。结果： 成功转染tPA基因和（PDGF-B）反义核酸；2种基因联合应用显著抑制血管内膜细胞表达PCNA和PDGF-B mRNA，抑制率分别为65.01%和81.75%；显著减少局部血管内膜厚度、内膜面积和吻合口血栓形成，使吻合口狭窄率显著减少62.63%。结论： 联合转染tPA表达质粒和PDGF-B的反义寡核苷酸在一定程度上抑制猪实验性冠状动脉搭桥术后吻合口再狭窄。

关键词 冠状动脉再狭窄 组织型纤溶酶原激活物 血小板源性生长因子

分类号 R363

Co-transfection of PDGF-B antisense oligonucleotide and tissue-type plasminogen activator gene prevents vascular anastomotic restenosis after coronary bypass

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Abstract

<FONT face=Verdana>AIM: To elucidate the co-transfection of platelet derived growth factor B(PDGF-B) antisense oligonucleotide and tissue-type plasminogen activator gene to prevent vascular anastomotic restenosis after coronary bypass.
METHODS: A dog model of vascular anastomotic restenosis after coronary bypass was constructed.A constructed tissue-type plasminogen activator (tPA) gene plasmid and a designed PDGF-B oligonucleotide were used to transfect into the dog cardiomyocytes and anastomotic vascular smooth muscle cells(VSMCs) at the same time of coronary bypass,using a therapeutic ultrasound for the gene delivery.Effects of these two genes on thrombosis in local anastomotic vessels,the expressions of proliferating cell nuclear antigen(PCNA) and PDGF-B mRNA by VSMCs and the proliferation of vascular intima were observed with the methods of routine pathological,immuno-histochemical staining,in situ hybridization and morphometry.
RESULTS: PDGF-B antisense oligonucleotide and tissue-type plasminogen activator gene were succesfully transfected.These two genes significantly inhibited the expressions of PCNA and PDGF-B mRNA in intimal VSMCs with the inhibitory rates of 65.01% and 81.75%,respectively.The local intimal thickness and area also reduce markablely and the thrombosis of the anastomosis was prevented followed by the reduction of the anastomotic restenotic rate of 62.63%.
CONCLUSION: Co-transfection of PDGF-B antisense oligonucleotide and tissue-type plasminogen activator gene inhibits the dog experimental anastomotic restenosis after coronary bypass.</FONT>

Key words Coronary restenosis Tissue plasminogen activator Platelet-derived growth factor

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