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论文

一氧化氮合酶抑制剂(*L*-NAME)的药理作用与慢性血管效应

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摘要：

目的：探讨N^{ω}-硝基*L*-精氨酸甲酯(*L*-NAME)对不同动脉的慢性血管效应及其与抑制内皮依赖性一氧化氮(EDNO)合成的关系。方法：采用大鼠离体动脉环的张力测定，一氧化氮合酶活性测定及组织学、生化学等方法。结果：给药8周后大鼠尾动脉压明显升高、体重及胸主动脉的内皮依赖性舒张功能明显下降并释放内皮依赖性收缩因子，肠系膜微动脉的内皮依赖性舒张功能无改变。给药8周后出现了动脉中膜肥厚及其周围纤维化。N^{ω}-硝基*D*-精氨酸甲酯(*D*-NAME)的慢性给药亦可引起与*L*-NAME同样的动脉周围纤维化。结论：*L*-NAME对大鼠胸主动脉及肠系膜微动脉的作用不同，其慢性血管效应与抑制EDNO合成以外的其它机制相关。

关键词： 一氧化氮合酶抑制剂(*L*-NAME) 一氧化氮 内皮依赖性收缩因子 慢性血管效应

PHARMACOLOGICAL ACTIONS AND CHRONIC VASCULAR EFFECTS OF N^{ω}-NITRO-L-ARGININE METHYL ESTER, AN INHIBITOR OF NITRIC OXIDE SYNTHASE

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Abstract:

AIM: This study was designed to better understand the effect of chronic treatment with N^{ω}-nitro-*L*-arginine methyl ester(*L*-NAME) with special reference to endothelium-derived nitric oxide (EDNO) synthesis in different arteries. METHODS: The change of the tension of rat artery ring in vitro was determined. The NOS activity was measured by citrulline assay and the histological staining was performed using the methods of hematoxylin-eosin and masson trichrome staining. RESULTS: The blood pressure of rats treated with *L*-NAME for 3 days and 1 and 8 weeks showed significant increase. Endothelium-dependent relaxation of the aorta induced by acetylcholine (Ach) was reduced after the 3 day treatment, recovered at 1 week and again reduced at 8 weeks. However, the relaxation of small mesenteric arteries was unaltered throughout the experimental period. At 8 weeks, the indomethacin-sensitive endothelium-dependent contraction induced by Ach was noted. Citrulline assay demonstrated that substantial levels of constitutive NO synthase activity remained unchanged in the aorta during the experiments. Chronic treatment with N^{ω}-nitro-*D*-arginine methyl ester (*D*-NAME) also caused perivascular fibrosis as did *L*-NAME. CONCLUSION: These results suggest that mechanism(s) other than simple inhibition of EDNO synthesis are involved in the chronic cardiovascular effects of *L*-NAME in the rat mesenteric artery.

Keywords: *L*-arginine analogues nitric oxide endothelium-derived contracting factor chronic vascular effects inhibitor of nitric oxide synthase(*L*-NAME)

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