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论著

# 氨基胍对大鼠缺血性脑损伤的保护作用及其机制

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摘要 目的 观察选择性一氧化氮合酶抑制剂氨基胍（AG）保护大鼠缺血性脑损伤的可能机制。方法 采用线栓法复制 大鼠大脑中动脉梗塞模型，缺血后2，6或12 h 开始给予AG（100 mg·kg$^{-1}$，ip，每天2次，给药3 d）治疗。测定脑梗死体积，脑线粒体肿胀度和呼吸链的完整性，脑线粒体内NO和丙二醛（MDA）含量，总ATP酶、超氧化物歧化酶（SOD）和谷胱甘肽过氧化物酶（GSH-Px）活性； 培养大鼠神经元细胞， 观察AG（10， 20和100 μmol·L$^{-1}$）对神经元细胞形态、活力及乳酸脱氢酶（LDH）释放和NO含量的影响。 结果 AG显著降低脑缺血后脑梗死体积，改善缺血后神经元超微结构变化，减轻脑线粒体肿胀度和呼吸链损伤；降低NO和MDA含量，增加总ATP酶、SOD和GSH-Px活性。AG使体外培养的缺血神经细胞损伤程度明显减轻，NO含量降低，LDH释放减少，细胞活力增加。结论 AG可能通过抑制氧自由基生成，增加线粒体抗氧化作用，改善线粒体能量代谢和保护线粒体形态与功能的完整而对大鼠脑缺血损伤产生保护作用。

关键词 脑缺血 一氧化氮 氨基胍 线粒体 细胞,培养的

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# Mechanism of protective effect of aminoguanidine on experimental cerebral ischemic

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**Abstract**

**AIM** To investigate the beneficial effects of aminoguanidine(AG), a selective inducible nitric oxide synthase (iNOS) inhibitor, on cerebral ischemic injury of rats and the possible mechanism. **METHODS** The middle cerebral artery occlusion model was prepared with thread embolism. AG 100 mg·kg$^{-1}$ was injected ip first at 2, 6 and 12 h, respectively, after ischemia, then 2 times a day for 3 consecutive days. The infarct volume of brain tissue was determined with tetrazolium chloride staining. The mitochondria in brain tissue were isolated for measuring integrity of electron transport chain (ETC), mitochondrial swelling, NO and malondialdehyde (MDA) contents, ATPase, superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) activities. In addition, the neuronal cells of newborn rats were cultured in glucose-free medium with sodium hydrosulfite for cell viability, lactate dehydrogenease (LDH) and NO analysis. **RESULTS** AG significantly reduced infarct volume, ameliorated neuronal ultramicrostructural damages induced by ischemia. And the swelling of mitochondria, the lesions of ETC, the contents of MDA and NO in mitochondria were markedly decreased, the activities of ATPase, SOD and GSH-Px in mitochondria were increased. In vitro, compared with the ischemic group, AG（10, 20 and 100 μmol·L$^{-1}$）increased the cell viability and reduced the contents of LDH and NO in culture medium. **CONCLUSION** AG has protective effects on cerebral ischemic injury through inhibiting the production of oxygen free radical, increasing antioxidation, ameliorating energy metabolism, and beneficially improving the integrity of structure and function of mitochondria in brain tissue.

**Key words** brain ischemia nitric oxide aminoguanidine mitochondria cells cultured

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