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论著

氨基胍对大鼠局灶性脑缺血损伤后TNF-α、IL-1β及细胞凋亡的作用

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摘要 目的： 观察氨基胍（AG）对局灶性脑缺血损伤后炎症因子和神经细胞凋亡的作用，探讨AG保护脑缺血损伤组织的作用机制。方法： 健康雄性SD大鼠30只，体重250-280 g，随机分为3组：假手术组（SH组）、缺血组（IS组）、AG治疗组（AG组），每组10只。IS、AG组采用线栓法制备大鼠局灶性脑缺血损伤模型。AG组每次腹腔注射AG 100 mg/kg,每日2次，连续3 d。IS组给予等量的生理盐水。将大鼠断头取脑，采用免疫组化法检测脑组织中TNF-α表达变化，放免法检测IL-1β水平变化，流式细胞仪测定脑组织神经元凋亡率、Bcl-2蛋白、Bax蛋白表达及Bcl-2蛋白与Bax蛋白比值（Bcl-2/Bax）。结果： IS组脑缺血灶范围内TNF-α表达明显强于SH组，IL-1β水平显著高于SH组，神经凋亡率及Bax蛋白表达高于SH组，Bcl-2/Bax低于SH组；AG组脑缺血灶范围内TNF-α表达明显低于IS组，IL-1β水平显著低于IS组，神经凋亡率低于IS组，Bcl-2蛋白表达及Bcl-2/Bax高于IS组，Bax蛋白表达低于IS组 。结论： AG通过抑制TNF-α和IL-1β的升高，增加Bcl-2蛋白表达，降低Bax蛋白表达，调节Bcl-2/Bax平衡，对脑缺血大鼠脑神经元产生一定程度的保护作用。

关键词 氨基胍 脑缺血 肿瘤坏死因子 白细胞介素1 细胞凋亡

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Effect of aminoguanidine on TNF-α, IL-1β and neuronal apoptosis after focal cerebral ischemic injury in rats

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Abstract

<FONT face=Verdana>AIM: To evaluate the effect of aminoguanidine (AG) on inflammatory factors and neuronal apoptosis after focal cerebral ischemic injury in rats and the possible mechanism of protective effect of AG against cerebral ischemic injury.
METHODS: Thirty male SD rats (weighing 250 g-280 g) were randomly divided into three groups: (1) sham operated group (SH group,n=10),(2) ischemic groups (IS group,n=10),(3) AG group (n=10).In AG group,AG at dose of 100 mg·kg-1 was given intraperitoneally twice a day for 3 consecutive days.In IS group,normal saline was given instead of AG.Focal cerebral ischemia was produced by middle cerebral artery occlusion (MCAO) for 12 h.A nylon thread with rounded tip was inserted into left internal carotid artery cranially until resistance was felt.The distance from bifurcation of common carotid artery to the tip of the thread was about 18-19 mm.Focal cerebral ischemia was confirmed by left Horner s syndrome and right side hemiplegia.In SH group,the carotid artery was exposed but no thread was inserted.The expression of tumor necrosis factor-α(TNF-α) was determined by immunochemistry and the content of interleulin-1β(IL-1β) was measured by radioimmunoassay.The expressions of Bcl-2 and Bax protein were detected by flow cytometry.
RESULTS: The expression of TNF-α and the content of IL-1β were markedly increased after MCAO.Significantly increased DNA fragmentation,the indication of apoptosis,was detected after MCAO.The expression of TNF-α and the content of IL-1β were significantly lower in AG group than those in IS group.The percentage of apoptosis cells and expression of Bax protein were markedly lower in AG group than those in IS group but still significantly higher than those in SH group.The expression of Bcl-2 protein was markedly higher in AG group than that in IS group.No significant difference in the expression of Bcl-2 protein between IS and SH group was observed.
CONCLUSION: AG inhibits the increase in the expression of TNF-α and the content of IL-1β,and protects neurons from apoptosis induced by focal cerebral ischemia through increasing the Bcl-2 protein expression and inhibiting the Bax protein expression.</FONT>

Key words Aminoguanidine Brain ischemia Tumor necrosis factor Interleukin-1 Apoptosis

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