

论著

选择性环氧化酶2抑制剂NS-398对胃癌细胞AGS增殖的抑制作用

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摘要 目的 观察选择性环氧化酶2(COX-2)抑制剂NS-398对胃癌细胞AGS增殖的抑制作用,并探讨其相关机制。方法 NS-398 25, 50和100 $\mu\text{mol} \cdot \text{L}^{-1}$ 作用于AGS细胞0~48 h,用CCK-8法检测细胞存活率。NS-398 50 $\mu\text{mol} \cdot \text{L}^{-1}$ 作用于AGS细胞48 h,用流式细胞仪检测细胞凋亡率,实时荧光定量PCR检测Notch信号通路相关基因的表达,Western印迹法检测Notch胞内结构域(NICD)及下游靶基因NF- κB 和毛蛋白和断裂1增强子(Hes-1)蛋白表达。结果 NS-398 25, 50和100 $\mu\text{mol} \cdot \text{L}^{-1}$ 能抑制胃癌细胞AGS增殖,并呈时间($r_{\text{时间}}=-1.00, P=0.003$, 50 $\mu\text{mol} \cdot \text{L}^{-1}$)和浓度($r_{\text{浓度}}=-0.999, P=0.027$, 48 h)依赖性。NS-398 50 $\mu\text{mol} \cdot \text{L}^{-1}$ 作用48 h,AGS细胞凋亡率为(20.1 \pm 3.5)%,比正常对照组(3.5 \pm 1.4)%明显增加($P<0.05$);Notch信号通路受体Notch1和Notch2及Notch信号通路配体 δ 样1(DLL1)和锯齿状1(JAG1)mRNA表达无明显变化,Notch下游靶基因Hes-1和NF- κB mRNA表达较正常对照组明显减少($P<0.05$);NICD, Hes-1和NF- κB 蛋白表达明显减少($P<0.05$)。结论 选择性COX-2抑制剂NS-398可能通过抑制Notch信号途径抑制胃癌细胞AGS增殖。

关键词 [环氧化酶2抑制剂](#) [NS-398](#) [细胞增殖](#) [胃肿瘤](#)

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Inhibition of cyclooxygenase-2 selective inhibitor NS-398 on proliferation of AGS gastric cancer cells

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Abstract

OBJECTIVE To investigate the inhibition of cyclooxygenase-2 selective inhibitor NS-398 on gastric cancer cell proliferation and the possible mechanism. **METHODS** After AGS cells were treated with NS-398 25, 50 and 100 $\mu\text{mol} \cdot \text{L}^{-1}$ for 48 h, AGS cell viability was determined by CCK-8 assay. Flow cytometric analysis was used to detect the apoptosis of AGS cells after 48 h treatment with NS-398 50 $\mu\text{mol} \cdot \text{L}^{-1}$. The expression of Notch signal pathway related genes was evaluated by real-time PCR. The protein expression of Notch intracellular domain (NICD), NF- κB 2 and Hes-1 (hairy and enhancer of split 1) in AGS cells was determined by Western blotting. **RESULTS** Treatment with NS-398 potently induced apoptosis of AGS cells in a time- ($r_{\text{Time}}=-1.00, P=0.003$, 50 $\mu\text{mol} \cdot \text{L}^{-1}$) and concentration- ($r_{\text{Concentration}}=-0.999, P=0.027$, 48 h) dependent manner. The apoptosis rate of AGS cells treated with NS-398 50 $\mu\text{mol} \cdot \text{L}^{-1}$ for 48 h increased to (20.1 \pm 3.5)% compared with the control group (3.5 \pm 1.4)% ($P<0.05$). In addition, the mRNA expression of Hes-1 and NF- κB 2 was reduced ($P<0.05$) 24 h after treatment of NS-398 50 $\mu\text{mol} \cdot \text{L}^{-1}$ while Notch1, Notch2, DLL1(delta like 1) and JAG1(jagged-1) mRNA expression was not changed obviously. Moreover, NICD, Hes-1 and NF- κB 2 protein expression was decreased ($P<0.05$). **CONCLUSION** The cyclooxygenase-2 selective inhibitor NS-398 reduces proliferation of AGS gastric cancer cells through the Notch signal pathway.

Key words [cyclooxygenase 2 inhibitors](#) [NS-398](#) [cell proliferation](#) [stomach neoplasms](#)

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