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PI3K 特异性抑制剂LY294002 对卵巢癌紫杉醇耐药细胞株逆转作用的研究

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Reversal Effect of Phosphatidylinositol 3'-kinase Inhibitor LY294002 during Chemotherapy on Paclitaxel Resistance of Ovarian Cancer Cell Lines

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摘要

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摘要 研究磷脂酰肌醇-3-激酶 (PI3K) 特异性抑制剂LY294002对卵巢癌紫杉醇耐药细胞株 (A2780/Taxol) 多药耐药逆转的影响。方法: 将PI3K特异性抑制剂LY294002处理卵巢癌紫杉醇耐药细胞24 h后, 用CCK-8 (Cell Counting Kit-8) 法检测细胞的增殖速度、对紫杉醇敏感性的分析; 采用流式细胞技术检测细胞周期和凋亡。应用Western blot检测细胞中P-glycoprotein (P-gp)、Akt和p-Akt蛋白的表达情况。结果: 用LY294002处理A2780/Taxol细胞后细胞增殖速度变慢、对紫杉醇的半数抑制浓度 (IC50) 降低。实验组和对照组细胞的凋亡率分别是 (2.64±0.90) %和 (10.98±1.16) % (P<0.05)。LY294002处理后的G0/G1期细胞增加, S期明显减少, 差异有统计学意义 (P<0.05)。LY294002处理后的细胞与对照组相比P-gp和p-Akt的蛋白表达降低。结论: LY294002能够有效的逆转卵巢癌紫杉醇耐药细胞A2780/Taxol产生的多药耐药。

关键词: LY294002 PI3K/Akt P-glycoprotein 卵巢癌紫杉醇

Abstract: To study the effect of the phosphatidylinositol 3'-kinase (PI3K/Akt) inhibitor LY294002 during chemotherapy on the paclitaxel-resistant ovarian cancer cell line A2780/Taxol. Methods: The effect of treatment with LY294002 on A2780/Taxol cell lines was determined based on the 50% inhibition concentration (IC50) of paclitaxel, and on cell proliferation using the cholecystokinin octapeptide (CCK-8) assay. The apoptotic rates and cell cycle stages were detected by flow cytometry. The expression of PI3K/Akt, its phosphorylated form p-Akt, and phosphorylated P-glycoprotein (P-gp) protein was analyzed using Western blot. Results: The CCK-8 results showed that the proliferation of A2780/Taxol cell lines after 24 h since being treated with LY294002 was significantly slower compared with the untreated A2780/Taxol cell lines. The IC50 of paclitaxel in A2780/Taxol cells treated with LY294002 was also significantly lower than that in the original A2780/Taxol cell line. Flow cytometry demonstrated that the apoptotic ratio of the experiment group was significantly higher than that of the control group. Both groups showed some changes in the cell cycle, and there were statistically significant differences between the two groups (P < 0.05). phosphorylated Akt and P-gp protein levels in A2780/Taxol cells were inhibited by LY294002, compared with the untreated A2780/Taxol cells. Conclusion: The PI3K/Akt inhibitor LY294002 has a reversal effect on the paclitaxel-resistance of the A2780/Taxol cell line.

Key words: LY294002 PI3K/Akt P-glycoprotein Ovarian cancer Paclitaxel

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