

基础研究

新型多胺缀合物NMMB逆转K562/ADM细胞多药耐药及其机制

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摘要:

目的: 研究新型多胺缀合物NMMB对白血病细胞株K562/ADM的多药耐药(MDR)逆转作用,并进一步探讨其耐药逆转机制。方法: 分别以不同浓度的NMMB(10~1 000 mg/L)作用于体外培养的K562和K562/ADM细胞24 h,采用MTT法检测细胞增殖抑制率,确定NMMB的非毒性剂量;采用非毒性剂量,NMMB 0、2.5、5.0和10.0 mg/L组,分别与不同浓度ADM(0.25~100.00 mg/L)联合作用,检测各组细胞生长抑制50%的ADM浓度,即IC50,计算逆转倍数;利用流式细胞术检测NMMB联合ADM作用后K562/ADM细胞内ADM蓄积程度和细胞周期变化。结果: 随着NMMB浓度的增加,细胞增殖抑制率也相应增加,呈剂量-效应关系;NMMB的最大无毒剂量为12.5 mg/L,逆转倍数为4倍;NMMB可明显提高ADM在K562/ADM细胞内的蓄积,与未加NMMB对照组比较差异有显著性(P<0.05);K562/ADM细胞被阻滞在G0/G1期,与未加NMMB对照组比较差异有显著性(P<0.01)。结论: NMMB对白血病耐药细胞株K562/ADM有增殖抑制和多药耐药逆转作用,其部分逆转机制可能是通过增加细胞内化疗药物蓄积和将K562/ADM细胞阻滞在G0/G1期而实现的。

关键词: 多胺缀合物;多药耐药;耐药逆转;K562/ADM细胞

Effect of a novel polyamine conjugate on MDR reversal of K562/ADM cells and its mechanism

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Abstract:

Abstract: Objective To investigate the reversal effect of a novel polyamine conjugate, NMMB, on multidrug resistance (MDR) of myelogenous leukemia K562/ADM cells and discuss the possible correlative mechanism. Methods K562 and K562/ADM cells in culture medium were treated with NMMB (10-1 000 mg/L) respectively. The inhibitory rates of these cells were measured by MTT assay. Non-cytotoxic dose of NMMB was determined. K562/ADM cells at logarithmic growth phase were randomly divided into ADM control, NMMB 2.5, 5.0, 10.0 mg/L groups. The inhibitory rate 50% (IC50) and the reversal index in all groups were determined. The effects of NMMB on ADM accumulation in K562/ADM cells and cell cycle were examined by flow cytometry (FCM). Results The inhibitory rates were significantly increased when the cells were treated with different doses of NMMB (10-1 000 mg/L) in a dose-dependent manner. The available reversal concentration of NMMB was 12.5 mg/L and the reversal index was 4 folds on K562/ADM cells. ADM accumulation in K562/ADM cells was significantly increased (P<0.05). The cells were blocked at the period of G0/G1 (P<0.01). Conclusion NMMB has an effect on proliferation inhibition and MDR reversal of K562/ADM cell line. The reversal mechanisms of NMMB may be due to increasing the accumulation of chemo-drugs in cells and arresting the cells at G0/G1 phase.

Keywords: polyamines conjugate; multi-drug resistance; reversal of drug resistance; K562/ADM cell

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