

论文

洛美利嗪逆转K562/ADM细胞多药耐药性

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摘要:

目的研究洛美利嗪(lomerizine,Lom)逆转K562/ADM细胞多药耐药性的作用及机制。方法MTT法检测细胞毒作用,流式细胞仪研究Lom对ADM和长春新碱(vincristine,VCR)的K562/ADM细胞凋亡诱导作用的影响及对罗丹明123(rhodamine 123,Rh123)外排和P-糖蛋白(P-glycoprotein,P-gp)表达的作用。结果Lom明显提高ADM对K562/ADM多药耐药细胞的细胞毒作用及ADM和VCR的凋亡诱导作用,3,10和30 μmol·L⁻¹ Lom使K562/ADM对ADM的IC₅₀值由79.03 μmol·L⁻¹分别降至28.14,8.16和3.16 μmol·L⁻¹。Lom增加胞内ADM的蓄积浓度并抑制Rh123外排;但作用72 h后对K562/ADM细胞P-gp表达无影响。结论Lom通过抑制P-gp的活性逆转K562/ADM细胞的多药耐药性。

关键词: 洛美利嗪 阿霉素 P-糖蛋白 多药耐药性

Reversal of multidrug resistance by lomerizine in K562/ADM cells

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Abstract:

AimTo study the effect of lomerizine (Lom) on the reversal of multidrug resistance (MDR) in K562/ADM cells and its mechanism. MethodsMTT assay was used to determine the influence of Lom on the cytotoxicity of adriamycin (ADM). The effect of Lom on the apoptosis induced by ADM and vincristine (VCR) in K562/ADM cells was detected using flow cytometry. Intracellular accumulation of ADM was measured by fluorescence spectrophotometry. Flow cytometry was used to investigate the efflux of rhodamine 123 (Rh123) and the expression of P-glycoprotein (P-gp) in K562/ADM cells. ResultsLom increased the cytotoxicity of ADM and the apoptosis induced by ADM or VCR in K562/ADM cells. At the concentration of 3, 10 and 30 μmol·L⁻¹, Lom reduced the IC₅₀ value of ADM from 79.03 μmol·L⁻¹ to 28.14, 8.16 and 3.16 μmol·L⁻¹, respectively. Lom increased the intracellular accumulation of ADM and inhibited the efflux of Rh123 in K562/ADM cells. No change in P-gp expression was observed after the treatment of Lom for 72 h. ConclusionLom had strong reversal effect on MDR in K562/ADM cells by inhibiting P-gp function.

Keywords: adriamycin P-glycoprotein multidrug resistance lomerizine

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