عنوان مقاله:

Co-treatment by docetaxel and vinblastine breaks down P-glycoprotein mediated chemo-resistance

محل انتشار:

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خلاصه مقاله:

Objective(s): Chemoresistance remains the main causes of treatment failure and mortality in cancer patients. There is an urgent need to investigate novel approaches to improve current therapeutic modalities and increase cancer patients' survival. Induction of drug efflux due to overexpression of P-glycoproteins is considered as an important leading cause of multidrug resistance. In this study, we investigated the role of combination treatments of docetaxel and vinblastine in overcoming P-glycoprotein mediated inhibition of apoptosis and induction of cell proliferation in human non-small cell lung carcinoma cells. Materials and Methods:Cell proliferation and apoptosis were assessed using MTT assay and DAPI staining, respectively. P-glycoprotein expression was evaluated in gene and protein levels by Real-time RT-PCR and Western blot analysis, respectively. Results: Combination treatment of the cells with docetaxel and vinblastine decreased the IC۵۰ values for docetaxel from (۳۰±۳.۱) to (۱۵±۲.۶) nM and for vinblastine from (۳۰±۵.۹) to (۵±۵.۶) nM (P≤۰.۰۵). P-glycoprotein mRNA expression level showed a significant up-regulation in the cells incubated with each drug alone (P≤۰.۰۰۱). Incubation of the cells with combined concentrations of both agents neutralized P-glycoprotein overexpression (P≤۰.۰۵). Adding verapamil, a P-glycoprotein inhibitor caused a further increase in the percentage of apoptotic cells when the cells were

treated with both agents. Conclusion:Our results suggest that combination therapy along with P-glycoprotein inhibition can be considered as a novel approach to improve the efficacy of chemotherapeutics in cancer patients with high P-glycoprotein expression.

کلمات کلیدی:

Chemoresistance Chemotherapy, H۱۲۹۹ cells, Lung cancer, Verapamil