Comparative Analysis of the Effects of Valproic Acid and Tamoxifen on Proliferation, and Apoptosis ofHuman Hepatocellular Carcinoma WCH 17 CellLine

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Abstract

Background: Histone deacetylation of tumor suppressor genes such as estrogen receptor alpha (ER alpha) can induce cancer, which is reversible by epi-drugs such as valproic acid (VPA). The previous result indicated that tamoxifen (TAM) induced apoptosis in hepatocellular carcinoma (HCC). This study was designed to assess the apoptotic and antiproliferative effects of VPA and TAM and also the effect of VPA on ER alpha gene expression in HCC.

Material and Methods: The cells were treated with various doses of VPA and TAM and the MTT assay, Real-Time RT-PCR, and flow cytometry assay were done to determine viability, ER alpha gene expression, and apoptosis.

Results: Both agents inhibited viability and induced apoptosis. ER alpha gene expression was increased by VPA, which in turn increased the apoptotic effect of TAM. The half-maximum inhibitory concentration (IC50) value for VPA and TAM was 5 and 20 mu M respectively. VPA inhibited cell growth by 88 % to 38 % at 24 h ($P < 0.001$) and 76 % to 28 % at 48 h ($P < 0.002$) and also TAM inhibited by 92 % to 40 % at 24 h ($P < 0.006$) and 84 % to 32 % at 48 h ($P < 0.001$). Thepercentage of VPA-treated apoptotic cells were reduced by about 35 and 43 % (P. 0.001) and that of TAM-treated 32 and 38 % (P. 0.001) after 24 and 48 h, respectively.

Conclusion: VPA and TAM can significantly inhibit viability and induce apoptosis and also VPA play a significant role in ER alpha reactivation.

Keywords: Hepatocellular Carcinoma; Tamoxifen; Valproic acid