Effects of 5-aza-2'-deoxycytidine and Valproic Acid on Epigenetic-modifying DNMT1 Gene Expression, Apoptosis Induction and Cell Viability in Hepatocellular Carcinoma WCH-17 cell line

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Abstract:

Background: DNA molecule of the eukaryotic cells is found in the form of a nucleoprotein complex named chromatin. Two epigenetic modifications are critical for transcriptional control of genes, including acetylation and DNA methylation. Hypermethylation of tumor suppressor genes is catalyzed by various DNA methyltransferase enzymes (DNMTs), including DNMT1, DNMT2, and DNMT3. The most well characterized DNA demetilating and histone deacetylase inhibitor drugs are 5-aza-2'-deoxycytidine (5-Aza-CdR) and valproic acid (VPA), respectively. The purpose of the current study was to analyze the effects of 5-Aza-CdR and VPA on cell growth, apoptosis, and DNMT1 gene expression in the WCH-17 hepatocellular carcinoma (HCC) cell line.

Materials and Methods: In this descriptive analytical study, MTT assay, flow cytometry assay, and Quantitative Real-Time RT-PCRwere done to evaluate proliferative and apoptotic effects and also gene expression.

Results: Both compounds inhibited the cell growth and induced apoptosis significantly in a dose and time depended fashion. Additionally, 5-Aza-CdR down-regulated DNMT1 gene expression. The relative expression of DNMT1 was 0.40 and 0.20 ($P < 0.001$) at different times, respectively. The percentage of VPA- treated apoptotic cells were reduced by about 28 and 34 % ($P<0.001$) and that of 5-Aza-CdR-treated were reduced by about 34 and 44 % ($P<0.001$) after treatment time periods.

Conclusion: In the current study, it was observed that 5-Aza-CdR and VPA could significantly inhibit the growth of WCH-17 cell and played a significant role in apoptosis. It was also found that 5-Aza-CdR could decrease DNMT1 gene expression.

Keywords: Apoptosis, 5-aza-2'-deoxycytidine, DNA methyltransferase 1, Hepatocellular carcinoma, Valproic Acid