Effect of Genistein in Comparison with Trichostatin A on Reactivation of DNMTs Genes in Hepatocellular Carcinoma.

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Abstract

Background and Aims: DNA methylation and histone modification are epigenetic modifications essential for normal function of mammalian cells. The processes are mediated by biochemical interactions between DNA methyltransferases (DNMTs) and histone deacetylases. Promoter hypermethylation and deacetylation of tumor suppressor genes play major roles in cancer induction, through transcriptional silencing of these genes. DNA hypermethylation is carried out by a family of DNMTs including DNMT1, DNMT3a and DNMT3b. In hepatocellular carcinoma, a significant positive correlation between over-expression of these genes and cancer induction has been reported. The DNA demethylating agent genistein (GE) has been demonstrated to reduce different cancers. Previously, we reported that GE can induce apoptosis and inhibit proliferation in hepatocellular carcinoma PLC/PRF5 and HepG2 cell lines. Besides, histone deacetylase inhibitors, such as trichostatin A (TSA), were successfully used to inhibit cancer cell growth. The present study was designed to assess the effect of GE in comparison with TSA on DNMT1, DNMT3a and DNMT3b gene expression, cell growth inhibition and apoptosis induction in the HepG2 cell line. ***Methods:*** Cells were seeded and treated with various doses of GE and TSA. The MTT assay, flow cytometry assay, and real-time RT-PCR were used to determine viability, apoptosis, and DNMT1, DNMT3a and DNMT3b gene expression respectively. ***Results:*** Both agents inhibited cell growth, induced apoptosis and reactivated DNMT1, DNMT3a and DNMT3b gene expression. Furthermore, TSA demonstrated a significantly greater apoptotic effect than the other agent, whereas GE improved gene expression more significantly than TSA. ***Conclusions:*** Our findings suggest that GE and TSA can significantly inhibit cell growth, induce apoptosis and restore DNMT1, DNMT3a and DNMT3b gene reactivation.

KEYWORDS:

Apoptosis; DNA methyltransferases; Genistein; Hepatocellular carcinoma; Trichostatin A