Rosiglitazone diminishes the high-glucose-induced modulation of 5-fluorouracil cytotoxicity in colorectal cancer cells.

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Abstract

Colorectal cancer (CRC) is the third most leading cause of morbidity and mortality throughout the world. 5-fluorouracil (5-FU), which is often administrated to disrupt carcinogenesis, was found to elevate blood glucose level among CRC patients. Thus, this study was conducted to evaluate the influence of rosiglitazone on antiproliferative effect of 5-FU using cellular model. Two human colonic carcinoma cell lines (HCT 116 and HT 29) were cultured in the presence of 5-FU, rosiglitazone or in combination under normal and high glucose concentration. The drug cytotoxicity was evaluated using the MTT assay whereas the assessment of cell cycle was carried out using the flow cytometry technique. Combination index (CI) method was used to determine the drug interaction between rosiglitazone and 5-FU. High glucose diminished the cytotoxic effect of 5-FU but at a high drug dosage, this effect could be overcome. Cell cycle analysis demonstrated that 5-FU and rosiglitazone caused G1-phase arrest and S-phase arrest, respectively. CI values indicated that rosiglitazone exerted synergistic effect on 5-FU regardless of glucose levels. This study is the first to demonstrate the influence of rosiglitazone on cytotoxicity of 5-FU under normal or high glucose level. Rosiglitazone may be a promising drug for enhancing the efficacy of 5-FU in the treatment of CRC associated with hyperglycemia.

KEYWORDS:

5-fluorouracil; MTT; cell cycle; colorectal cancer cell; high glucose; rosiglitazone

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