Effect of betulinic acid on anticancer drug-resistant colon cancer cells.

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Abstract

Primary or acquired resistance of tumours to established chemotherapeutic regimens is a major concern in oncology. Attempts to improve the survival of cancer patients largely depend on strategies to prevent tumour cell resistance. 5-Fluorouracil (5-FU)-based chemotherapy with a combination of other drugs such as irinotecan (IRT) and oxaliplatin (OXT) has been reported to be effective, even though an optimal regimen has yet to be defined due to the relatively high toxicity of the procedure. The aim of this study was to examine the effect of betulinic acid (BetA) as a chemosensitizer for anticancer drug treatment in chemoresistant colon cancer cell lines. A chemoresistant cell line to 5-fluorouracil (SNU-C5/5FU-R), irinotecan (SNU-C5/IRT-R) and oxaliplatin (SNU-C5/OXT-R) treatment were derived from the wild-type colon adenocarcinoma cell line (SNU-C5/WT). The effect of BetA or a combination of anticancer drugs and BetA on the multidrug resistance-related genes, caspases, Bcl-2, Bad and cell death in the SNU-C5/WT and SNU-C5/R cell lines was analysed. BetA alone was an effective chemotherapeutic drug for the SNU-C5/WT, SNU-C5/5FU-R and SNU-C5/OXT-R cells. The combination of BetA with IRT or OXT was effective against SNU-C5/5FU-R cells, and the combination of BetA with 5-fluorouracil, IRT or OXT was effective against SNU-C5/OXT-R cells. BetA induced cancer cell death by apoptosis through the mitochondrial pathway. These findings indicate that the use of BetA as a chemosensitizer may be a new strategy to enhance the efficacy of chemotherapy. However, further studies will be needed for confirmation.

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