Enhanced Antitumor Activity of DHMEQ, a NF-κB Inhibitor, on Cholangiocarcinoma Cell Lines by Decreasing the Expression of ABC Transporters

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Background and Objective: Cholangiocarcinoma (CCA) is markedly resistant to chemotherapy and has a dismal prognosis, but its mechanism of drug resistance is unknown. Several reports have indicated that nuclear factor-kappa B (NF-κB) is constitutively activated in a variety of cancer cells and play a key role in their growth, metastasis and chemoresistance. In the present study, we examined whether NF-κB inolved in resistance to anticancer drugs of CCA and whether dehydroxymethylepoxyquinomicin (DHMEQ), a NF-κB inhibitor, can overcome this resistance.

Methods: CCA cell lines were treated with DHMEQ and/or chemotherapeutic drugs and examined for cell viability by MTT assay, apoptosis by IN Cell Analyzer and ABC transporters expression by real time PCR.

Results: NF-κB inhibition by DHMEQ significantly enhanced anti-tumor activity of 5-fluorouracil, cisplatin and doxorubicin. A combination of chemotherapeutic drugs and DHMEQ exerted a significantly enhanced cell death. Furthermore, ABCB1 mRNA level was significantly decreased in DHMEQ treated group.

Conclusions: These findings suggest that the supplementation of DHMEQ in combination with chemotherapeutic drugs enhances the chemoresponsiveness of CCA cells and serves as a potential sensitizer, especially in chemoresistant cell lines.

Keyword: DHMEQ, NF-κB, Cholangiocarcinoma

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