Original article

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MOLECULAR MECHANISMS OF POTENTIAL SYNERGISTIC EFFECT OF KETOPROFEN AND MELOXICAM WITH CONVENTIONAL CYTOSTATICS IN HUMAN CERVIX CANCER CELL LINE

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Cyclooxygenases clearly appear to be implicated in carcinogenesis. It has been reported that COX-2 is active throughout the entire process of cancer development and progression. Various molecular mechanisms may be responsible for this. Epidemiological and experimental studies have revealed that nonselective non-steroidal anti-inflammatory drugs (NSAIDs) and selective COX-2 inhibitors can reduce the risk of cancer. Inhibition of COX provides a plausible explanation of the data on NSAIDs and cancer. However, the molecular pathways of this effect are still unclear, more complex and likely involve multiple COX-2-dependent and independent mechanisms, where pro- and anti-apoptotic Bcl-2 family members may take part.

We examined the effects of ketoprofen (KT), as nonselective COX-1/2, and meloxicam (MK), as selective COX-2 inhibitor, alone and combined with 5-fluorouarcil (FU) and cisplatin (CP), on the proliferation by MTT test and Bcl-2/Bax expression in HeLa cells (human cervical carcinoma cells).

MC alone or combined with conventional anticancer drugs, FU and CP, showed better cytotoxic and antiproliferative effect than KT. The levels of Bcl-2 were decreased while the levels of Bax were increased dose-dependently by KT and MC. A significant increase in the expression of Bax protein in HeLa cells was more pronounced for MC.

The synergy observed in the effects of ketoprofen and meloxicam with cisplatin and 5-fluorouracil on the cervical cancer cell line was generated by an enhancement of apoptosis. Therefore, ketoprofen and meloxicam may represent therapeutic candidates to improve access of cervical cancer chemoprevention and chemotherapy.

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