Câncer de mama. O 3-bromopiruvato inibe o ciclo celular e aumenta a apoptose no câncer

Inhibitive effect of 3-bromopyruvic acid on human breast cancer MCF-7 cells involves cell cycle arrest and apoptotic induction.

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Abstract

BACKGROUND: Breast cancer is one of the most common malignancies in women and is highly resistant to chemotherapy. Due to its high tumour selectivity, 3-bromopyruvic acid (3-BrPA), a well-known inhibitor of energy metabolism has been proposed as a specific anticancer agent. The present study determined the effect of 3-BrPA on proliferation, cell cycle and apoptosis in the human breast cancer MCF-7 cell line and other antitumour mechanisms.

METHODS: MCF-7 cells were treated with various concentrations of 3-BrPA for 1 - 4 days, and cell growth was measured by 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyl tetrazolium bromide assay. Marked morphological changes in MCF-7 cells after treatment with 3-BrPA were observed using transmission electron microscopy. The distributions of the cell cycle and apoptosis were analyzed by flow cytometry. Immunohistochemistry was used to indicate the changes in the expression of Bcl-2, c-Myc, and mutant p53.

RESULTS: 3-BrPA (25 microg/ml) significantly inhibited the proliferation of MCF-7 cells in a time-dependent manner. The MCF-7 cells exposed to 3-BrPA showed the typical morphological characteristics of apoptosis, including karyopycnosis, nuclear condensation and oversize cytoplasmic particles. In addition, flow cytometric assay also showed more apoptotic cells after 3-BrPA stimulation. The cells at the G0 and G1 phases were dramatically decreased while cells at the S and G2/M phases were increased in response to 3-BrPA treatment after 48 hours. Furthermore, 3-BrPA stimulation decreased the expressions of Bcl-2, c-Myc and mutant p53, which were strongly associated with the programmed cell death signal transduction pathway.

CONCLUSION: 3-BrPA inhibits proliferation, induces S phase and G2/M phase arrest, and promotes apoptosis in MCF-7 cells, which processes might be mediated by the downregulation of the expressions of Bcl-2, c-Myc and mutant p53.

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