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Synergistic effect of genistein and BCNU on growth inhibition and cytotoxicity of glioblastoma cells.

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Abstract

OBJECTIVE: Recent experiments have shown that dietary soy isoflavones such as genistein can significantly suppress invasiveness and growth of a number of human malignancies. This study examined whether genistein, at a concentration typical of plasma levels following soy diet intake, in combination with 1,3-bis(2-chloroethyl)-1-nitrosourea (BCNU, carmustine) exhibited an additive or synergistic inhibitory effect on the growth of glioma cells.

METHODS: The human glioblastoma multiforme (GBM) cell line U87 and the rodent C6 glioma were treated with genistein at 4 microM, combined with BCNU (0-50 microM). Monolayer cell growth and cytotoxicity, as measured by colonogenic survival in soft agarose, were then compared in control and drug-treated cultures. Presence of apoptosis, using the DNA ladder assay and laser scanning cytometry (LSC), was investigated in all cell lines at those concentrations where an enhancement of antiproliferative effect of BCNU in presence of genistein was observed.

RESULTS: A 32-41% increase in monolayer growth inhibition and a 28-42% increase in colony cytotoxicity in the U87 cell line were observed when genistein (4 microM) was added to BCNU in the 0-10 microM dose range. In the C6 cell line, a 30-36% increase in monolayer growth inhibition and a 39-54% increase in colony cytotoxicity were observed with the BCNU dose range of 0-50 microM. All experiments showed a significant increase in growth inhibition and a decrease in colonogenic survival ($P < 0.05$). We were unable to detect apoptosis in any of the lines when genistein was combined with BCNU.

CONCLUSION: These results indicate that genistein at typical adult dietary plasma levels can significantly enhance the antiproliferative and cytotoxic action of BCNU. The implication for treatment of GBM may be a reduction in the chemotherapeutic dose recommendations of these agents and subsequently a decrease in the risk of treatment sequelae for these patients.

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