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Erythropoietin Augments Survival of Glioma Cells After Radiation and Temozolomide

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Purpose

Despite beneficial effects of irradiation/chemotherapy on survival of glioblastoma (GBM) patients, collateral damage to intact neural tissue leads to “radiochemobrain” and reduced quality of life in survivors. For prophylactic neuroprotection, erythropoietin (EPO) is a promising candidate, provided that concerns regarding potential tumor promoting effects are alleviated.

Methods and Materials

Human GBM-derived cell lines U87, G44, G112, and the gliosarcoma-derived line G28 were treated with EPO, with and without combinations of irradiation or temozolomide (TMZ). Responsiveness of glioma cells to EPO was measured by cell migration from spheroids, cell proliferation, and clonogenic survival. Implantation of U87 cells into brains of nude mice, followed 5 days later by EPO treatment (5,000 U/kg intraperitoneal every other day for 2 weeks) should reveal effects of EPO on tumor growth *in vivo*. Reverse transcriptase-polymerase chain reaction was performed for EPOR, HIF-1 α , and epidermal growth factor receptor (EGFR)vIII in cell lines and 22 human GBM specimens.

Results

EPO did not modulate basal glioma cell migration and stimulated proliferation in only one of four cell lines. Importantly, EPO did not enhance tumor growth in mouse brains. Preincubation of glioma cells with EPO for 3 h, followed by irradiation and TMZ for another 24 h, resulted in protection against chemoradiation-induced cytotoxicity in three cell lines. Conversely, EPO induced a dose-dependent decrease in survival of G28 gliosarcoma cells. In GBM specimens, expression of HIF-1 α correlated positively with expression of EPOR and EGFRvIII. EPOR and EGFRvIII expression did not correlate.

Conclusions

EPO is unlikely to appreciably influence basal glioma growth. However, concomitant use of EPO with irradiation/chemotherapy in GBM patients is not advisable.

[Recombinant human EPO](#), [Proliferation](#), [Migration](#), [Clonogenic survival](#), [Xenograft model](#)

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