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Abstract

Therapeutic potential of antidepressants in malignant glioma: clinical experience with clomipramine

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1535

Background: Despite conventional therapeutic approaches available for the management of malignant glioma the outlook remains dismal. Current therapy consists of surgery and radiotherapy along with cytotoxic chemotherapy given concomittantly, sequentially or at time of relapse. This approach is rarely curative. Our laboratory-based research has shown that a number of heterocyclic drugs (including clomipramine, desmethyl clomipramine, doxepin and amitriptyline) and selective serotonin re-uptake inhibitors (including citalopram, fluoxetine and fluvoxamine maleate) elicit mitochondrially-mediated apoptosis in malignant glioma cells by targeting complex III of the respiratory chain and altering membrane potential which results in liberation of cytochrome C and activation of a caspase pathway to cell death. **Methods:** Over a 4.5 year period a series of 27 patients with malignant glioma were prescribed clomipramine as an adjuvant to their conventional treatment at an escalating dose from 25mg daily up to a maintenance dose of 150mg daily. Outcome in this small series, based on survival time and MRI imaging was recorded. The results were favourable when compared with the average survival times of historical controls. **Results:** 5 patients (19.2%) showed disease progression whilst on medication. 21 patients (80.8%) showed a good partial response (clinically and radiologically). Survival rates were calculated using the Kaplan-Meier method; the median survival being 27 months. **Conclusions:** These early results from a rather selected group of patients has led to a larger trial. The side-effect profile is good with only 5% of patients withdrawing due to gastro-intestinal or neurological side-effects. This well tolerated drug, designed to cross the blood-brain barrier is worthy of further study.

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