

Thymoquinone Enhances the Effectiveness of Gamma Knife in Glioma Cell Lines In Vitro Through Inducing Apoptosis and Genotoxicity

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Introduction

Patients with glioma are associated with poor prognosis despite aggressive treatment including surgery, radiation therapy and chemotherapy. Gamma Knife is a treatment option for recurrent glioma. Thymoquinone, which is a major bioactive constituent of the volatile oil of black seed, has been shown to be effective in various cancer types exerting anti-inflamatory, antioxidant, anti-angiogentic and apoptotic effect. We hypothesized that Thymoquinone enhances the effect of Gamma Knife on glioma cell lines in vitro.

Methods

To investigate the additive effect of Thymoquinone to Gamma Knife, U87 human glioma and C6 rat glioma cells were treated with different doses of Thymoquinone (0 to 200 μ M) for 24 hours and then radiated with Gamma Knife (5 Gy). Cell viability was assessed by ATP test, apoptosis was evaluated by Acridine Orange/Ethidium Bromide double (AO/EB) staining and flow cytometry, and genotoxicity was evaluated by alkaline single cell electrophoresis assay (Comet assay).

Results

Cell viability decreased significantly with increasing doses of Thymoquinone (0 μ M, 10 μ M, 20 μ M, 40 μ M and 60 μ M) when added to 5 Gy dose of Gamma Knife treatment in U87 and C6 glioma cells. In the same dosing scheme, with increasing doses of Thymoquinone in addition to Gamma Knife, apoptosis was shown to increase significantly with AO/EB staining, and apoptosis and necrosis were found to increase significantly in flow cytometry after Annexin V/PI staining; tail intensity significantly increased in Comet assay showing enhanced genotoxicity.

Conclusions

Our results showed that Thymoquinone significantly increased sensitivity of glioma cell lines to Gamma Knife in vitro. The efficacy of the combination of Gamma Knife and Thymoquinone is attributed to direct cytotoxicity, genotoxic effect and pro-apoptotic effect of Thymoquinone in tumor cells. Thymoquinone may be a promising agent to enhance the effect of radiosurgery.

Learning Objectives

Thymoquinone enhances the efficacy of Gamma Knife in glioma.