ATORVASTATIN PLUS TEMOZOLOMIDE INCREASES APOPTOSIS AND REDUCES CELLS MIGRATION IN HUMAN GLIOMA CELLS

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Introduction and Objectives: Malignant gliomas are a tumor group that comprises 70% of Central Nervous System (CNS) tumors, with origin in astrocytic precursors. Despite all the knowledge, the patient survival remains poor. Researches have demonstrated the potentiality of statins and chemotherapics in combination therapy in cancer treatment, decreasing proliferation, inhibiting cell migration and inducing cell death. The aim of this study was to evaluate the temozolomide TMZ and ATOR effect in cell viability, migration, apoptosis and autophagy in A172 human glioma cells, as well as in primary culture of cortical astrocytes viability. Materials and Methods: A172 glioma cells and primary cortical astrocytes were cultured. After confluence, the cells were treated with TMZ and/or ATOR, for 48 hours. Viability analysis was performed through reduction MTT assay, migration was analyzed through wound healing assay. Apoptosis occurrence was evaluated through flow cytometry and autophagy (acidic vesicular organelles AVOs) by acridine orange staining. Results and Conclusions: ATOR (50 nM to 20 µM) treatment did not change astrocytic viability. In A172 cells, ATOR showed cytotoxic effect at 10 µM and 20 µM. TMZ 500 µM reduced cell viability. TMZ and ATOR association did not show additive effect in cell viability. ATOR, TMZ and both association decreased cell migration. ATOR increased apoptosis, TMZ did not change this parameter, but the drugs association showed somatory effect, enhancing apoptosis occurrence. ATOR and TMZ treatment elevated AVOs presence in A172 cells. In this way, our results show the ATOR cytotoxic effect in glioma cells, suggesting that these cells are more susceptible to ATOR toxicity then astrocytes. Even, the ATOR plus TMZ effect in cell death may indicate these drugs association as a new potential therapeutic option in glioma treatments. Acknowledgements: This study was supported by grants from the Brazilian funding agencies CNPq, FAPESC and CAPES. Key words: Glioma, atorvastatin, viability.