Effect of Simvastatin as an Adjuvant Therapy to Temozolomide in Glioma Model

Pino Gomes, R; Cruz, O,M; Ribeiro, C,S,P; Bark, J,M; Castro, B,C,L; Winniscofer, S,M,B

1 Federal University of Parana - UFPR
e-mail: rafaelapinogomes@yahoo.com.br

Gliomas have heterogeneous characteristics that hinder the understanding of their tumor biology, as well as the control of invasive procedures, proliferative and cell survival. The most aggressive type, called glioblastoma multiforme (GBM), is characterized by rapid progression, high resistance to radiation, chemotherapy, and poor prognosis. Today for the treatment of gliomas is commonly used Temozolomide, associated with radiotherapy. However, the actual treatment is not effective leaving a range of questions related to cellular defense mechanisms and the constant search for new and more effective treatment alternatives. In previous studies it was found that simvastatin, a lipophilic statin, display antitumor activity and has wide effects on the glioma cells. This study was conducted to evaluate the effect of simvastatin as an adjuvant therapy to Temozolomide. Viability of human glioblastoma cells was accessed by the MTT, Neutral Red and Crystal Violet assays. U87MG cells were treated with Temozolomide at concentrations of 50μM and 100μM associated with Simvastatin at concentrations of 0.25μM and 1.0μM for 3, 5 and 7 days. After 3 days of treatment, we observed a decrease in cell viability of 19.72% and 20.2% after single-agent Temozolomide at 50μM and 100μM respectively; 14.05% and 28.34% after single-agent Simvastatin at 0.25μM and 1.0μM respectively. 62.95% of viability reduction after treatment of Temozolomide (100μM) plus Simvastatin (1,0μM). Combined treatment of Temozolomide and Simvastatin inhibited cell viability in a time- and concentration-dependent manner, reaching 78.37% of viability reduction after 7 days. In addition, similar results were observed using other cell viability assays, such as Neutral Red incorporation and Crystal Violet staining. All together, these data showed that combined therapy of Temozolomide and Simvastatin is more effective than a single therapy alone and supports the efficacy of Simvastatin as an add-on therapy to Temozolomide in glioblastoma model.

Keywords: Glioma, Temozolomide, Simvastatin