

GLYCYRRHIZIC ACID ATTENUATES THE CYTOTOXICITY INDUCED BY HIGH GLUCOSE IN NEUROBLASTOMA CELL LINE

Laura Ciarlo¹, Francesca Marzoli¹, Paola Minosi¹, Amalia Di Giannuario¹, Paola Matarrese², Stefano Pieretti¹

¹National Centre for Drug Research and Evaluation, Istituto Superiore di Sanità, Rome - Italy, ²Center for Gender-Specific Medicine, Oncology Unit Istituto Superiore di Sanità, Rome - Italy

Introduction: Hyperglycemia, as a common diabetes symptom, plays a great important role in the development of diabetic neuropathy. Hyperglycemia induces oxidative stress in neurons, which in turn results in neuronal cell apoptosis and mitochondrial dysfunction. The objective of this study is to verify whether a natural substance such as glycyrrhizic acid, whose anti-inflammatory and anti-apoptotic activity is known, is able to inhibit/attenuate the cytotoxicity induced by treatment with high glucose concentrations.

Materials and methods: We investigated the effect of glycyrrhizic acid in neuroblastoma cells, SHSY-5Y. These cells, when treated with high glucose, showed results similar to those observed using DRG neurons and Schwann cells. Quantitative evaluation of apoptosis was performed by a double staining flow cytometry method using fluorescein isothiocyanate conjugated Annexin V/ Trypan blue apoptosis detection kit. The mitochondrial membrane potential both control and treated cells with high glucose, was studied by using 5-5',6-6'-tetrachloro-1,1',3,3'-tetraethylbenzimidazol-carbocyanine iodide (JC1) probe. We also evaluated the mitochondrial organization by immunofluorescence analysis after staining with anti-mitochondria specific proteins.

Results: We demonstrated that the glycyrrhizic acid reduced the cytotoxic effect induced by high glucose (300 mM) in the SHSY-5Y cell line, using cytofluorimetric assay. The analysis of mitochondrial membrane potential performed by flow cytometry, after cell staining with JC1, revealed that glycyrrhizic acid significantly reduced the percentage of cells with high mitochondrial membrane potential detectable in high glucose treated cells. The morphological analysis revealed that in the cells treated with high glucose the mitochondria network became more organized and characterized by fused elongated structures. Instead, the simultaneous treatment with glycyrrhizic acid and high glucose restored a normal condition.

Discussion and conclusion: In the present study we evaluated the potential effect of glycyrrhizic acid on neuroblastoma cells treated with high glucose. Our results showed that the treatment with glycyrrhizic acid improved mitochondrial network.