CELL DIFFERENTIATION AND THE SUSCEPTIBILITY TO THE SODIUM DICLOFENAC IN HUMAN NEUROBLASTOMA

França, N.J.; Noronha, L.; Elifio-Esposito, S.

Programa de Pós-Graduação em Ciências da Saúde, Pontifícia Universidade Católica do Paraná, Curitiba, Paraná, Brasil.

Introduction: Neuroblastoma is an embryonal tumor of the sympathetic nervous system. Neuroblastoma cells contain high levels of arachidonic acid, the major substrate for cyclooxygenase (COX) and lipoxygenase (LOX). Some nonsteroidal anti-inflammatory drugs (NSAIDs), such as sodium diclofenac, have antitumor activity, but little is known about their effects on neuroblastoma cells in different degrees of differentiation.

Objective: To analyze the correlation between cell differentiation and susceptibility to sodium diclofenac in a human neuroblastoma cell line in vitro.

Methods: Viability and proliferation analysis were performed by the MTT and clonogenic assays, as well as morphological analysis by light microscopy. NB cells (CHLA20) were treated with sodium diclofenac (150 µM) after differentiation induction or not with retinoic acid for 5d. Flow cytometry was used to assess the necrotic/apoptotic state of cells by Annexin-V/7AAD staining, and intracellular hydrogen peroxide production using the probe DCFH-DA. Statistical analysis was performed using SPSS 21.0 for Windows.

Results: Diclofenac induced a decrease of 28% and 20% in cell viability for both undifferentiated and differentiated cells, respectively, comparing with untreated cells. Treatment also induced morphology alterations typical of apoptosis. Flow cytometry analysis revealed increased numbers of cells in late apoptosis stage and also increased production of hydrogen peroxide with a peak at 12 hours, 3 times higher than control. The degree of cell differentiation did not alter the cell susceptibility to diclofenac.

Conclusions: Sodium diclofenac induces apoptosis with increased levels of hydrogen peroxide production in neuroblastoma cell line independent on the degree of cell differentiation.

Keywords: Neuroblastoma, Diclofenac, Apoptosis.

Footnotes:
Funding: This work was supported by CAPES and Fundação Araucária/PR.
Conflict of interests: We declare no potential conflict of interest.