The effect of newly synthesized derivative of dehydroepiandrosterone on glioma cell proliferation and reactive oxygen species generation

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Gliomas are one of the most common types of malignant tumors worldwide, however, an effective therapeutic strategy have not yet been fully determined [1]. In gliomas and glioblastomas, an increased basal level of reactive oxygen species (ROS) play an important role as chemical mediators in the regulation of signal transduction [2]. H_2O_2, which can oxidize signaling proteins, inducing the formation of a disulfide bond in phosphatase and kinase domains, regulates glioma cell apoptosis, proliferation, and survival. Novel therapeutic alternatives are now focused on immune recognition and immune response enhancing, blocking of survival metabolism pathways, and modulating cellular redox status. Drug resistance in cancer cells is closely related to their redox status [3]. To modify the net physiologic balance between interconvertible oxidized and reduced equivalents within subcellular compartments that remain in dynamic equilibrium, the change of concentration of either ROS or antioxidants can be induced.

Steroid hormones may influence the glioma progression through interaction with their receptors and metabolism and transcription of target genes regulation [4]. We synthesized a new derivative of dehydroepiandrosterone (DHEA) namely N-(3-indolylethyl)-3β-hydroxyandrost-5-en-17β-amine (IS-1). The aim of this work was to investigate the effects of DHEA, IS-1 and abiraterone acetate (known anticancer agent) on proliferative activity and ROS generation of C6 glioma cells. It is worth saying, that no oxidation of IS-1 into 3-ketosteroid, a requisite for hormonal activity in biogenic steroids, were detected in C6 glioma cells exposed to IS-1 for 24 h using mass spectrometry. Therefore, it can be implied that the mode of action of indole steroids does not involve signaling via steroid receptors or interference with CYP17A1 activity.

DHEA-derived decrease in cell proliferation was revealed. At 10·μM, abiraterone acetate decrease cell proliferation by 36±12 %, whereas IS-1 do so by 52±13 %. And at 1 μM, abiraterone acetate leads to the decrease in cell proliferation by 28±13 %, whereas IS-1 do so by 22±11 %. Treatment of cells with IS-1, abiraterone acetate for 30-60 min did not cause cell viability.

As shown in [5], the intracellular ROS levels gradually increased with the rising of concentration of DHEA in cancer cells. At the addition of IS-1 and abiraterone acetate at 1-10 μM concentration, the ROS level was the same as in control samples. These results indicate, that steroid derivatives could not induce ROS generation in glioma cells, as DHEA. Such data may be due to the high level of antioxidants in the cells. So, the antioxidant status of C6 glioma cells needs further investigation.

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