The Proliferative Potential of Human Adrenocortical Tumor Cell Lines Exposed to Chemotherapy Drugs in 2D and 3D Cell Culture Systems.

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Introduction: Adrenocortical carcinoma (ACC) is a rare malignancy and represents 0.2% of all deaths from cancer. The incidence of pediatric ACC is 10 times higher in southern Brazil than the rest of the world, due to a germline TP53 mutation. The primary treatment is surgery, and Mitotane (o,p’-DDD) has been used as a single agent or in combination with other cytotoxic chemotherapies. Here, we examined the proliferative potential of Zoledronic Acid alone and Sunitinib in combination with Mitotane. Material and Methods: NC1-H295R and SW13 adrenocortical tumor cell lines in monolayer (2D) and spheroid (3D) cell culture were treated with different drugs concentrations, analyzed by MTS assay. Results and Discussion: Combination of Mitotane (100µM) and Sunitinib (5.0µM) reduced cell viability in relation to control by 29±0.02% (p≤0.05), in H295R, monolayer, after 72hs of treatment. Mitotane (300µM) in combination with three different concentrations of Sunitinib (1.25µM-2.5µM and 5.0µM) resulted in a significant inhibition of proliferation in relation to control, after 48hs and 72h of treatment, respectively, [19±0.1% (p≤0.05), 21±0.1% (p≤0.05) and 22±0.08% (p≤0.05)] and [29±0.1% (p≤0.01), 44±0.1% (p≤0.001) and 95±0.01% (p≤0.001)]. Zoledronic Acid treatment promoted cell viability decreased only at higher concentration (500µM) and after 72hs of treatment [19±0.1% (p≤0.05)]. In spheroids cell culture, all treatments showed a lower response than those observed in monolayer. Furthermore, there was a significant variation in response to treatments between H295R and SW-13 adrenocortical cell lines; in fact, SW13 was more resistant to different treatments. Conclusion: The combination of Mitotane and Sunitinib treatment was more efficient in decrease the proliferative potential of cell cultures than the drugs alone. Moreover, this effect depends on the ACC cell type analyzed and the model system utilized, monolayer or spheroid cell culture.

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