

EFFECT OF SORAFENIB IN PRIMARY CULTURES OF HUMAN PARATHYROID TUMORS

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Purpose Parathyroid carcinoma (PC) is a rare cause of primary hyperparathyroidism. The definitive cure of PC is surgery, but it may present as recurrent or metastatic disease even after iterative surgery. Unfortunately, in these cases the outcomes of chemotherapy and radiotherapy are poor. Thus, new chemotherapeutic agents are needed. This study was aimed to investigate the role of Sorafenib, a tyrosine kinase inhibitor, in primary cultures of human parathyroid tumor cells. Methods We treated human PC from 2 patients and 4 sporadic parathyroid adenomas with Sorafenib (1-0.1-0.01 μM) for evaluating potential cytotoxic effects, cell viability, cell cycle, apoptosis and PTH release after 72h of treatment. Results Proliferation assay. Treatment with Sorafenib at 72h induced a dose-dependent reduction of cell growth in both primary PCs and in all adenoma parathyroid cultures. Cell cycle analysis. Sorafenib 1 μM at 72h inhibits cell cycle and induced an increase of apoptotic Sub-G0/G1 phase with a reduction of G1, S and G2/M phases. Apoptosis analysis. FACS analysis by Annexin V-FITC and Propidium Iodide showed an increased level of apoptosis after treatment with Sorafenib 1 μM at 72h. PTH release. The levels of PTH measured in the medium of cell cultures declined after sorafenib 1 μM treatment both in PCs and in 2 adenomas. Conclusions Sorafenib seems to have good potential effects in reducing cell proliferation and PTH secretion in vitro; it inhibits cell cycle and produce an increase of early and late apoptosis with a reduction of viability cells. The results obtained are promising, but more data are needed to fully explore the role of Sorafenib as potential anticancer drug in parathyroid carcinomas usually resistant to chemo-interventions.