Abstract

Cytotoxic effects of dacarbazine and all-trans retinoic acid on CD117$^+$ cells derived from malignant melanoma

Background & objective: *Melanoma is a common form of skin cancer that contain different cell types recognized by various cell surface markers. CD117$^+$ receptors located on the melanocyte that stem cell growth factors attach to it and CD117$^+$ receptor signaling leading to metastasis and proliferation. Dacarbazine is the only chemotherapeutic agent* approved *by the FDA for* treatment *of* melanoma. Studies showed that *RARβ expressed in the melanoma cells. RARβ-mediated signaling is important to inhibit glycolysis. Here, we evaluated cytotoxic effects of ATRA and dacarbazine on CD117$^+$ melanoma cells.*

Methods: *The A375 melanoma cell line were cultured in DMEM medium and CD117$^+$ cells were isolated using magnetic activated cell sorting (MACS). Cytotoxic effects of ATRA (8, 10, 16, 24, 32 and 64 µM), dacarbazine (800, 1000, 1200, 1400 and 1800 mg/ml) and ATRA/dacarbazine were studied using cell proliferation assay (MTT), acridine orange/ ethidium bromide staining. We performed flow cytometry to evaluate cell cycle arrest (using DAPI staining).*

Results: *We determined IC_{50} value after treatment with various concentration of ATRA and dacarbazine in CD117$^+$ cells. We found that 20 µM ATRA with dacarbazine caused significantly decrease in IC_{50} value when compared to dacarbazine alone ($p<0.05$). Our results showed that increasing ATRA concentration in combination group (ATRA/dacarbazine) caused more apoptosis and necrosis. In addition, ATRA/dacarbazine mediated cell cycle arrest at G0/G1 phase and dacarbazine alone inhibited the cells in S phase.*

Conclusion: *Our results showed that ATRA combination with dacarbazine cause more cytotoxic effects on CD117$^+$ cells and it may be used in future to treat melanoma.*

Key words: *cancer stem cells, A375 melanoma cell line, CD117$^+$, all-trans retinoic acid, dacarbazine*