The effect of cytarabine on mitochondrial activity of KG1-a and $CD34^-$, $CD34^+$

Abstract:

Background: Cancer is a malignant disease caused by the accumulation of cancer stem cells (CSCs). Although recovery is possible for people with cancer after chemotherapy, the disease returns after a while due to the presence of cancer stem cells. On the other hand, mitochondria play an important role in the development of cancer stem cells. Many vital parameters of the cell, such as energy production, redox status, ROS production, control of cytosolic calcium levels, and initiation of apoptosis by mitochondria, also occur. Metabolic flexibility and mitochondrial dependence are two basic requirements of CSCs resistance to chemotherapy. As a result, we can target mitochondria because of the unique characteristics of mitochondria in cancer stem cells.

Aim: Determining the effect of cytarabine on mitochondrial activity of $CD34^+$ and $CD34^-$ cells in KG1-a cell line.

Materials and Methods: In this study, acute myeloid leukemia cancer cells of KG1-a c were treated with different concentrations (0 to 1000 μM) of cytarabine for 48 hours. Cell viability was assessed by MTT assay. The MACS system was used to isolate $CD34^+$ and $CD34^-$ cells. Acridine orange / ethidium bromide staining was used to evaluate cell apoptosis after cytarabine treatment. Flow cytometric dyes Dcfh-da and rhodamine ۱۲۳ were used to evaluate the active oxygen species and mitochondrial membrane potential (MMP) in the cells, respectively.

Results: We obtained an IC۵۰ of 45.83 μM for cytarabine in KG1-a cells by MTT. For this reason, we continued the experiments with different concentrations of IC۵۰. The results of acridine orange ethidium bromide staining showed that with increasing cytarabine concentration, $CD34^+$ cells had less apoptosis than $CD34^-$ and KG1-a cells. Evaluation of mitochondrial membrane

potential by staining with rhodamine 123 flow cytometry staining showed that $CD34^+$ group was less altered after treatment with Ara-c than other groups. In ROS experiments performed with Dcfh-da staining, we found that the ROS of $CD34^+$ cells increased less after treatment.

Conclusion: According to the observed observations and studies, the cells isolated from patients with cytarabine-resistant AML had low ROS and high oxidative phosphorylation, and their MMP was less altered after exposure to cytarabine. In our studies, $CD34^+$ cells extracted from KG1-a had the same characteristics as cells isolated from patients with cytarabine-resistant AML.

Key words: Mitochondria, cytarabine, $CD34^+$ cells and reactive oxygen species