Abstract:

Bevacizumab, the first inhibitor of the vascular endothelial growth factor (VEGF), has become one of the best-selling drugs in the world. Heart failure has been seen in 2–4% of patients on bevacizumab. Mitochondria play an important role in myocardial tissue homeostasis and deterioration in mitochondrial function will eventually lead to cardiomyocyte cell death and consequently cardiovascular dysfunction.

Materials and Method :

The aim of our study is to search the effects of bevacizumab on isolated rat heart mitochondria and survey the effect of curcumin as a mitochondrial protective agent and cardioprotective. Rat heart mitochondria were isolated with mechanical lysis and differential centrifugation. Using by biochemical and flowcytometry evaluations, the parameters of mitochondrial toxicity including: succinate dehydrogenase (SDH) activity, mitochondrial swelling, mitochondrial membrane potential (MMP) collapse, reactive oxygen species (ROS) formation and lipid peroxidation (LP) was evaluated.

Results :

Results revealed that bevacizumab (up to 50 μg/ml) induced a concentration- and time-dependent rise in mitochondrial ROS formation, MMP collapse, mitochondrial swelling, lipid peroxidation and inhibition of succinate dehydrogenase in rat heart mitochondria. Our results showed that curcumin (10-100 μM) significantly ameliorated bevacizumab-induced mitochondrial toxicities.

Discussion :

These results indicate that the cardiotoxic effects of bevacizumab are associated with mitochondrial dysfunction and ROS formation, which finally ends in MMP collapse and mitochondrial swelling as the “point of no return” in the cascade of events leading to apoptosis. Also, results of this study suggest that the combination therapy of bevacizumab with curcumin could decrease mitochondrial effects of this drug.

Keywords: Bevacizumab, Cardiotoxicity, Isolated Mitochondria, Heart failure, Curcumin, Cardioprotective