Abstract

Introduction: Ifosfamide is an anti-neoplastic prodrug that is used in various malignancies and has various side effects, including kidney side effects. On the other hand, mitochondria, as one of the most important cellular organelle, provide the necessary energy for kidney cells by providing adenosine triphosphate (ATP) needed for its activity. The kidney needs a lot of energy due to its high activity, and for this reason, it is one of the organs that contains a high number of mitochondria. The normal activity of the kidney is dependent on the mitochondria, and any factor that leads to the disruption of the mitochondrial function leads to problems in the activity of the kidney. In this study, the assumption that ifosfamide can lead to renal dysfunction by having a negative effect on kidney mitochondria was investigated.

Materials and methods: Mitochondria were isolated from fresh male rat's renal tissues using mechanical lysing and differential centrifugation techniques. Then, the isolated mitochondria were divided into the following groups: control and concentration of Ifosfamide 0/50, 100, 500 μM). The effects of Ifosfamide were assessed on a series of mitochondrial parameters including mitochondrial succinate dehydrogenases (SDH) activity, mitochondrial swelling, reactive oxygen species (ROS) formation, mitochondrial lipid peroxidation during ۱ hour incubation with Ifosfamide.

Results: Ifosfamide did not cause deleterious alterations in mitochondrial functions, mitochondrial swelling, SDH, lipid peroxidation, ROS formation and MMP in mitochondria isolated from kidney. Altogether, the data of this study showed that Ifosfamide is not directly toxic in in mitochondria isolated from kidney, and suggests that probably other pathways and metabolisms have role in the toxicity of this compound.

Conclusion: The findings of this study proved that mitochondria alone not play the main role in the toxicity of Ifosfamide, and suggests to reduce the toxicity of this drug, other pathways resulting in the production of toxic metabolites and should be considered.

Key words: Kidney toxicity, Nephropathy, Ifosfamide, Mitochondrial function