Abstract

Introduction: Mitochondrial dynamics help to the maintenance of cellular homeostasis, and its dysfunction involves pathological situations such cardiotoxicity. Collectively, multiple lines of evidence strongly suggest that the cardiotoxicity of methamphetamine involves direct mitochondria-related toxicity. Here, we investigated this hypothesis that methamphetamine could directly cause mitochondrial dysfunction through oxidative stress-related pathways and calcitriol as main regulator of mitochondrial functions and antioxidant agent could reduce the adverse effects in isolated cardiac mitochondria obtained from rat heart.

Materials and Method: The isolated cardiac mitochondria obtained from rat heart and got prepared with mechanical lysis and differential centrifugation. The mitochondria were cotreated with 3 calcitriol (1, 2.5 and 5 μM) and methamphetamine (250 μM) for 60 minutes at 37 °C. Then the mitochondrial toxicity parameters such as mitochondrial membrane potential (MMP) collapse, mitochondrial swelling, succinate dehydrogenase (SDH) activity, reactive oxygen species (ROS) production and lipid peroxidation was measured.

Here, we investigated this hypothesis that methamphetamine could directly cause mitochondrial dysfunction through oxidative stress-related pathways and calcitriol as main regulator of mitochondrial functions and antioxidant agent could reduce the adverse effects in isolated cardiac mitochondria obtained from rat heart.

Results: The data indicated that 250 μM methamphetamine caused a deleterious alteration in mitochondrial functions, ROS production, MMP collapse, mitochondrial swelling, oxidative stress and lipid peroxidation. While our study results clearly indicate that calcitriol (5 μM) can reduce methamphetamine-induced changes in isolated cardiac mitochondria. Altogether, the results of the current study showed that methamphetamine directly induce mitochondrial dysfunction through oxidative stress in isolated cardiac mitochondria, which were ameliorated by calcitriol with its antioxidant potential.

Discussion: Altogether, the results of the current study showed that methamphetamine is a potent cardiotoxic substance and it can cause serious damages to the mitochondria and the calcitriol can ameliorate these damages by it's antioxidant activity.

Key Words: Vitamin D, Oxidative Stress, Cardiotoxicity, Cardiomyopathy, Illicit Drugs