

Toxicity of popular NSAIDs on heart mitochondria

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Abstract

Introduction: Several chemical compounds and drugs have been known to directly or indirectly modulate cardiac mitochondrial function, which can account for their cardiotoxic and arrhythmic properties. Non-steroidal anti-inflammatory drugs (NSAIDs) are most prescribed drugs in human and veterinary medicine that provide anti-inflammatory, antipyretic, analgesic, antispasmodic and anticoagulant effects.

Methods and Results: Rat heart mitochondria were obtained by differential ultracentrifugation and incubated with different concentrations of highly prescribed NSAIDs (diclofenac, naproxen, celecoxib). Our results showed that NSAIDs (diclofenac, naproxen, celecoxib) induced a rise in cardiac mitochondrial reactive oxygen species (ROS) formation, lipid peroxidation, and mitochondrial membrane potential (MMP) collapse before mitochondrial swelling ensued on isolated rat heart mitochondria. Disturbance in oxidative phosphorylation was also confirmed by the decrease in ATP concentration in the NSAIDs (diclofenac, naproxen, celecoxib)-treated heart mitochondria. In addition, the collapse of MMP and mitochondrial swelling produced the release of cytochrome c via outer membrane rupture or mitochondrial permeability transition (MPT) pore opening.

Conclusions: Our results suggested that NSAIDs (diclofenac, naproxen, celecoxib)-induced toxicity in heart tissue is the result of disruptive effect on mitochondrial respiratory chain that leads to ROS formation, lipid peroxidation, MMP decline, and cytochrome c expulsion which results in apoptosis signaling and cell loss in heart myocardial tissue.

Key words: Isolated mitochondria; Mitochondrial dysfunction; Cytochrome c release