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A review of the protective role of melatonin during phosphine-induced cardiotoxicity: focus on mitochondrial dysfunction, oxidative stress and apoptosis.

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Abstract

OBJECTIVES: Acute poisoning with aluminium phosphide (AlP) is a major cause of mortality in developing countries. AlP mortality is due to cardiac dysfunction leading to cardiomyocyte death. The main mechanism is an inhibition of cytochrome c oxidase in the cardiomyocyte mitochondria, resulting in a decreased ATP production and oxidative stress. Unfortunately, the administration of exogenous drugs does not meet the desired requirements of an effective therapy. Melatonin is an amphiphilic molecule and can easily pass through all cellular compartments with the highest concentration recorded in mitochondria. It is known as a vigorous antioxidant, acting as a potent reactive oxygen species (ROS) scavenger. Our aim is to summarize the mechanisms by which melatonin may modulate the deteriorating effects of AlP poisoning on cardiac mitochondria.

KEY FINDINGS: Melatonin not only mitigates the inhibition of respiratory chain complexes, but also increases ATP generation. Moreover, it can directly inhibit the mitochondrial permeability transition pore (mPTP) opening, thus preventing apoptosis. In addition, melatonin inhibits the release of cytochrome c from mitochondria to hinder caspase activation leading to cell survival.

SUMMARY: Based on the promising effects of melatonin on mitochondria, melatonin may mitigate AlP-induced cardiotoxicity and might be potentially suggested as cardioprotective in AlP-intoxicated patients.

KEYWORDS: aluminium phosphide; apoptosis; cardiotoxicity; melatonin; mitochondrial dysfunction

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