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Effects of chronic Hydrogen Peroxide Exposure on mitochondrial Oxidative Stress genes and mitochondrial dynamics in HL60 Cells

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Abstract

Hydrogen peroxide (H_2O_2) is a reactive species also involved in the redox regulation of cells because of it is relative stability. In numerous pathological situations, a chronic increase in the production of reactive species is observed, which is related to oxidative stress and cellular damage. The aim of this study was to evaluate the effects of long-term exposure to different H_2O_2 concentrations on oxidative stress biomarkers and mitochondrial dynamics in HL60 cells. HL60 cells were treated with a sustained production (0.1, 1.0 and 10.0 nM/s) of H_2O_2 for one hour. H_2O_2 production and malondialdehyde (MDA) levels, as a lipid peroxidation marker, increased progressively in HL60 cells in accordance with higher H_2O_2 exposure, with significant differences between the 10nM/s H_2O_2 group to the control and 0.1 nM/s groups. Similarly, progressive increase in genes related with the mitochondrial antioxidant defences and mitochondrial dynamics were also observed. Significant increases in the 10 nM/s H_2O_2 with respect to the control group was observed for manganese superoxide dismutase (MnSOD), peroxisome proliferator-activated receptor gamma coactivator 1- transcription alpha (PCG1α), nuclear respiratory factor 2 (Nrf2), transcription of the transcription factor mitochondrial A (Tfam), mitofusins 1 and 2 (Mfn-1 and Mfn-2) and uncoupling protein 3 (UCP3), whereas no significant changes were observed in the COXIV gene expression. In conclusion, exposure to different sustained production of H_2O_2 is related to a progressive increase in mitochondrial dynamics gene expression and redox processes in HL60 cells but also to oxidative damage at the higher H_2O_2 production.

Key Words: *reactive species, antioxidants, mitochondria, gene expression*