Molecular mechanism of nitric oxide-induced osteoblast apoptosis.

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摘要

Abstract

Nitric oxide (NO) can regulate osteoblast activities. Our previous study showed that NO induced osteoblast apoptosis. This study was further aimed to evaluate the mechanism of NO-induced osteoblast apoptosis from the viewpoints of mitochondrial functions, intracellular oxidative stress, and the anti-apoptotic Bcl-2 protein using neonatal rat calvarial osteoblasts as the experimental model. Exposure of osteoblasts to sodium nitroprusside (SNP), an NO donor, significantly increased amounts of lactate dehydrogenase in the culture medium, and decreased cell viability in concentration- and time-dependent manners. Administration of SNP in osteoblasts time-dependently led to DNA fragmentation. The mitochondrial membrane potential was significantly reduced following SNP administration. SNP decreased complex I NADH dehydrogenase activity in a time-dependent manner. Levels of cellular adenosine triphosphate (ATP) were suppressed by SNP. In parallel with the mitochondrial dysfunction, SNP time-dependently increased levels of intracellular reactive oxygen species. Immunoblotting analysis revealed that SNP reduced Bcl-2 protein levels. Exposure to lipopolysaccharide (LPS) and IFN-gamma significant increased endogenous nitrite production. In parallel with the increase in endogenous NO, administration of LPS and IFN-gamma suppressed cell viability, mitochondrial membrane potential, and ATP synthesis. Results of this study show that NO released from SNP can induce osteoblast insults and apoptosis, and the mechanism may involve the modulation of mitochondrial functions, intracellular reactive oxygen species, and Bcl-2 protein.