Nitric oxide induced osteoblast apoptosis through a mitochondrial-dependent pathway.

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Abstract

Osteoblasts contribute to bone remodeling. Nitric oxide can regulate osteoblast activities. In this study, we attempted to evaluate the pathophysiological effects of nitric oxide on osteoblasts and its possible mechanism using neonatal rat calvarial osteoblasts as the experimental model. Exposure of osteoblasts to sodium nitroprusside, a nitric oxide donor, decreased alkaline phosphatase activities and cell viability in a concentration- and time-dependent manner. Apoptotic analysis revealed that sodium nitroprusside time-dependently increased the percentages of osteoblasts undergoing apoptosis. Administration of sodium nitroprusside reduced the mitochondrial membrane potential of osteoblasts. In parallel with the mitochondrial dysfunction, levels of intracellular reactive oxygen species and cytochrome c were significantly elevated following sodium nitroprusside administration. Exposure of osteoblasts to sodium nitroprusside significantly increased caspase-3 activity. Results of this study show that nitric oxide, decomposed from sodium nitroprusside, can induce osteoblast apoptosis through a mitochondrion-dependent cascade that causes mitochondrial dysfunction, release of intracellular reactive oxygen species and cytochrome c from mitochondria to cytoplasm, and activation of caspase-3.