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JOURNAL ARTICLE

Nitric oxide induces oxidative stress and mediates cytotoxicity to human cavernosal cells in culture

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Nitric oxide (NO) is a product of nitric oxide synthase (NOS) activity and is recognized as the main mediator of penile erection by induction of cavernosal smooth muscle relaxation. Although excessive NO can be generated via inducible NOS activation under certain inflammatory and noninflammatory conditions, for example, in response to TGF-beta and gamma-IFN (the proinflammatory cytokines), the effect of excessive NO produced as reactive nitrogen radical (NO.-) in the corpora cavernosa is not known. The present study was designed to evaluate whether the effect of NO.- on human cavernosal cells in primary culture is via oxidative stress. Cell growth was monitored by DNA synthesis, and mitochondrial function was evaluated by adenosine triphosphate (ATP) production. Primary culture was initiated with explants from human corpora cavernosa, and the monolayer cavernosal cells (passage 2-3) were plated on 12-well tissue culture plates. At 70%-80% confluency, the cells were incubated with varying concentrations of sodium nitroprusside (SNP) for 16 hours. The cell growth (DNA synthesis) was monitored by measuring [3H] thymidine incorporation, ATP levels (nanomoles per 10(4) cells) were measured by chemiluminescence assay using a luminometer, the total oxidative stress was monitored by measuring the levels of 8-iso PGF2alpha (picograms per milliliter) by using an enzyme-linked immunosorbent assay kit, and NO production was monitored by accumulation of nitrite levels (micrometer per 10(4) cells). Human cavernosal smooth muscle cells (HCSMC) exposed to SNP (0 to 0.8 mM) exhibited a dose-dependent (two- to fivefold) decrease in DNA and ATP synthesis, accompanied by a two- to threefold increase in the levels of 8-iso PGF2alpha and about an eightfold increase in nitrite accumulation. These findings suggest that the NO released by SNP (>0.8 mM) exhibited a significant cytotoxicity to HCSMC, mediated by increased oxidative stress to these cells.

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