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Overexpression of Endothelial Nitric Oxide Synthase in Transgenic Mice Accelerates Testicular Germ Cell Apoptosis Induced by Experimental Cryptorchidism

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Surgical induction of cryptorchidism in experimental animals causes testicular germ cell apoptosis and infertility. The mechanisms of germ cell apoptosis have been associated with oxidative stress or testicular exposure to elevated temperature. Nitric oxide (NO) has been associated with apoptosis in a number of cell types. The objective of this study was to investigate whether overexpression of endothelial NO synthase (eNOS) could accelerate apoptosis of germ cells in the testes of transgenic mice. There are 3 NOS isoforms, and we restricted the analysis to eNOS at this time. For the colocalization of eNOS, staining in degenerating germ cells that were apoptotic cells suggested that eNOS may be related to germ cell apoptosis. eNOS overexpression in the testes of eNOS transgenic (eNOS-Tg) mice was examined using Western blot analysis. Unilateral cryptorchidism was surgically induced in both eNOS-Tg and wild-type (WT) adult mice. The testes were evaluated 1, 3, 5, 7, and 14 days after the operation by weighing the testes and examining histopathologic features and cell apoptosis using in situ microscopic analysis of DNA fragmentation. Immunoblotting for eNOS protein demonstrated increases in eNOS protein expression in testes, as well as the lung and aorta. In eNOS-Tg mice, weight reduction of cryptorchid testis was significantly increased on days 3, 5, and 7 (P = .02, .02, and .04, respectively). The numbers of spermatocytes and spermatids of eNOS-Tg cryptorchid testis significantly decreased compared with those of WT cryptorchid testis from day 3 (spermatocytes: P = .04; spermatids: P = .02). Moreover, terminal deoxynucleotidyl transferase-mediated dUTP-biotin nick end labeling demonstrated that eNOS-Tg mice significantly accelerate germ cell apoptotic changes induced by experimental cryptorchidism compared with WT mice from day 3 (P = .03). We have provided evidence that eNOS plays a functional role in mouse spermatogenesis in cryptorchidism-induced apoptosis.

Key words: Immunoblotting, TUNEL, spermatocytes, spermatids, spermatogonia

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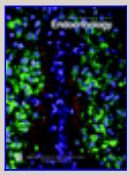

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