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Effect of Chronic Ischemia on Constitutive and Inducible Nitric Oxide Synthase Expression in Erectile Tissue

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Arterial occlusive disease is one of the leading causes of organic erectile dysfunction (ED). Recent studies have shown that the incidence of cardiovascular disease closely correlates with the prevalence of ED. Also, ED is thought to be an early signal of impending cardiovascular problems. We previously found that the atherosclerosis of iliohypogastric arteries in the rabbit causes ED, down-regulates cavernosal neuronal nitric oxide synthase (nNOS) gene expression, and impairs NO synthesis. The goal of this study was to determine the effect of atherosclerosis-induced ischemia on cavernosal nNOS, endothelial NOS (eNOS), and inducible NOS (iNOS) expression and NO-mediated smooth muscle relaxation in the rabbit. Our study showed that iliac artery blood flow, intracavernosal blood flow, and intracavernosal oxygen tension were unchanged 4 weeks after the induction of arterial atherosclerosis, whereas they were significantly diminished at weeks 8 and 16. Erectile responses to nerve stimulation and cavernosal smooth muscle relaxation were unchanged at week 4 and were significantly diminished at weeks 8 and 16 after the induction of atherosclerosis. Western blotting showed that cavernosal nNOS and eNOS protein levels were unaffected at week 4 but were significantly decreased at weeks 8 and 16 after the induction of atherosclerosis. iNOS protein, however, markedly increased during the course of the induced arterial disease. Immunohistochemical staining showed no change in cavernosal eNOS or nNOS expression at week 4. A dramatic decrease in both was evident at 8 and 16 weeks. iNOS expression progressively increased between 4 and 16 weeks of atherosclerosis. Down-regulation of nNOS and eNOS, along with up-regulation of iNOS, may explain ischemic cavernosal smooth muscle relaxation impairment in the rabbit. Ischemically altered NOS expression may be of great pathophysiologic importance in atherosclerosis-induced ED. These data may provide further insight into the mechanism of arteriogenic ED.

Key words: Erectile dysfunction, atherosclerosis, blood flow, oxygen tension

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