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Oxidative Stress and Antioxidant Therapy: Their Impact in Diabetes-Associated Erectile Dysfunction

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Oxidative stress is believed to affect the development of diabetic-associated vasculopathy, endothelial dysfunction, and neuropathy within erectile tissue. Our hypothesis is that, given adequate concentrations of the oxygen free radical scavenger vitamin E, enhanced levels of circulating nitric oxide (NO) should improve erectile function with the potential for a synergistic effect with a phosphodiesterase type 5 (PDE5) inhibitor. Twenty adult male Sprague-Dawley streptozotocin-induced (60 mg/kg intraperitoneally) diabetic rats were placed in 4 therapeutic groups (n = 5 per group) as follows: 1) peanut oil only (diabetic control), 2) 20 IU of vitamin E per day, 3) 5 mg/kg of sildenafil per day, and 4) vitamin E plus sildenafil using oral gavage for 3 weeks. In addition, 5 age-matched rats served as normal nondiabetic controls (normal). Erectile function was assessed by measuring the rise in intracavernous pressure (ICP) following cavernous nerve electrostimulation. Penile tissue was evaluated for neuronal NO synthase (nNOS), smooth muscle α -actin, nitrotyrosine, and endothelial cell integrity. Urine nitrite and nitrate (NO_x) concentration was quantified, and electrolytes were tested by a serum biochemistry panel. A significant decrease in ICP was recorded in the diabetic animals, with improvement measured in the animals receiving PDE5 inhibitors either with or without vitamin E; the controls had a pressure of 54.8 ± 5.3 cm H₂O, the vitamin E group had a pressure of 73.5 ± 6.6 cm H₂O, the sildenafil group had a pressure of 78.4 ± 10.77 cm H₂O, and the vitamin E plus sildenafil group had a pressure of 87.9 ± 5.5 cm H₂O (P < .05), compared with the normal cohorts at 103.0 ± 4.8 cm H₂O. Histoexaminations showed improved nNOS, endothelial cell, and smooth muscle cell staining in the vitamin E plus sildenafil group compared to the control animals. Urine NO_x increased significantly in all the diabetic groups but was blunted in the vitamin E and vitamin E plus sildenafil groups. A significant increase in positive staining for nitrotyrosine was observed in the vitamin E plus sildenafil group. Vitamin E enhanced the therapeutic effect of the PDE5 inhibitor in this study, supporting the potential use of oxygen free radical scavengers in salvaging erectile function in diabetic patients.

Key words: Impotence, vitamin E, sildenafil, nitric oxide, phosphodiesterase type 5

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