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A Castrated Mouse Model of Erectile Dysfunction

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To establish a mouse model for the study of venoocclusive erectile dysfunction, we investigated erectile function in wild-type (WT), castrated (CAST), and castrated mice receiving immediate testosterone replacement (TEST). Adult C57BL6 mice (≈30 g) underwent electrical stimulation of the cavernous nerve in vivo (parameters: 16 Hz frequency, 5 ms duration, 4V stimulatory voltage) with intracavernosal pressure (ICP) monitoring. A total of 55 mice (5 WT, 25 CAST, and 25 TEST) were evaluated. CAST and TEST (5.0 mg/pellet, 60-day release) mice were divided into groups of 5 and evaluated at 24 hours, 72 hours, 1 week, 2 weeks, and 4 weeks. Penile tissue was immunohistochemically stained for α-actin (marker for smooth muscle cells) and CD-31 (marker for endothelial cells). Stained slides were analyzed using Image Pro-plus software. In secondary studies, a Doppler flow meter was employed to evaluate penile blood flow. ICP measurements (mm Hg) were significantly decreased in CAST mice at 24 hour-, 72 hour-, 1 week-, 2 week-, and 4-week time points compared with WT mice (41.9 ± 14.9, 19.1 ± 4.2, 17.5 ± 8.2, 14.2 ± 4.4, and 10.0 ± 3.8, respectively, vs 50.2 ± 2.8), but TEST animals maintained or had an increase in ICP in comparison with WT mice (48.0 ± 1.4, 52.3 ± 1.3, 60.8 ± 7.6, 80.5 ± 2.1, and 81.5 ± 1.2, respectively). Mean systemic arterial pressure remained approximately 80 mm Hg irrespective of treatment. CAST mouse penis specimens revealed decreased α-actin and CD-31 immunoreactivity only at the 4-week interval, compared with WT and TEST specimens. Doppler ultrasound flow rates (centimeter per second), taken before, during, and immediately after cavernous nerve stimulation, were WT 45.4 ± 7.3, 30.6 ± 5.2, 55.3 ± 8.2 vs CAST (2 weeks) 22.2 ± 2.5, 25.0 ± 1.5, 23.1 ± 2.0 vs TEST (2 weeks) 30.5 ± 6.5, 25.7 ± 2.0, 45.2 ± 4.5. This prominently showed that intrapenile flow was not reduced normally during erectile stimulation in CAST mice. This is the first described mouse model of castration-induced veno-occlusive erectile dysfunction. Erectile response abnormalities as measured by ICP and Doppler ultrasound studies in CAST mice may be attributed to hypogonadal effects on erectile tissue function. Morphologic changes in the cavernosal tissue of CAST mice coincide with these abnormalities to some extent. This study defines an androgen-dependent mechanism of veno-occlusive erectile function in the mouse. The castrated mouse model can be applied in future studies of veno-occlusive erectile dysfunction.

Key words: Penile erection, castration, penis, androgen, testosterone, animal model

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