Testosterone Induces Increase in Aquaporin (AQP)-1, 5, and 7 Expressions in the Uteri of Ovariectomized Rats

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Abstract Testosterone has been reported to cause a decrease in uterine fluid volume in which this could involve the aquaporins (AQP). This study aimed to investigate effect of testosterone on uterine AQP-1, 5, and 7 expression in order to explain the reported reduction in uterine fluid volume under testosterone influence. Ovariectomized adult female rats received peanut oil, testosterone (1 mg/kg/day), estrogen (0.2 μg/kg/day), or combined estrogen plus testosterone for three consecutive days. Other groups received 3 days estrogen followed by 2 days either peanut oil or testosterone with or without flutamide or finasteride. A day after last injection, uteri were harvested, and the levels of AQP-1, 5, and 7 messenger RNA (mRNA) in uterine tissue homogenates were analyzed by real-time PCR (qPCR). Distributions of AQP-1, 5, and 7 proteins in uterus were observed by immunofluorescence. Levels of AQP-1 mRNA were elevated in rats receiving estrogen or testosterone-only treatment; however, levels of AQP-5 and 7 mRNAs were elevated in rats receiving testosterone-only treatment. In rats pre-treated with estrogen, testosterone treatment resulted in higher AQP-1, 5, and 7 mRNA levels compared to vehicle treatment. Testosterone effects were antagonized by flutamide but not finasteride. Immunofluorescence study showed that AQP-1 was highly distributed in uterine luminal epithelium following estrogen or testosterone-only treatment. However, AQP-5 and 7 distributions were high in uterine luminal epithelium following testosterone-only treatment. Testosterone-induced up-regulation of AQP-1, 5, and 7 expressions in uterus could explain the observed reduction in uterine fluid volume as reported under this condition.

Keywords Testosterone · Uterine fluid · AQP 1, 5, 7

Introduction

Aquaporin (AQP), a small hydrophobic, intrinsic membrane protein with low molecular weight of between 26 and 34 kDa, facilitates rapid and passive movement of H₂O (Denker et al. 1988). To date, thirteen AQP isoforms have been identified. Expression of AQP isoforms has been reported in male (Wilson et al. 2013) and female (He et al. 2006) reproductive tissues in rats, mice, marmosets, and humans. In uterus, expression of several AQP isoforms including AQP-1, 5, and 7 was found to be influenced by sex hormones (Jablonski et al. 2003). AQP-1 is the most commonly expressed isoform (Denker et al. 1988) and its expression has been reported in kidneys, lungs, red blood cells, brain, and uterus. This subunit participates in H₂O reabsorption and secretion across the secretory epithelia (Sales et al. 2013). Uterine AQP-1 was found to be distributed in stromal vasculature and was up-regulated by estrogen (Li et al. 1997).

AQP-5, a classic AQP isoform was reported to be expressed in ovaries, oviducts, and uterus (Skowronska 2010). In pig uterus, AQP-5 expression has been found to be influenced by progesterone (Skowronska et al. 2009). Meanwhile in rats, redistribution of uterine AQP-5 was observed under progesterone influence (Lindsay and Murphy 2006). AQP-7, a non-selective H₂O channels which regulate the transport of H₂O, glycerol, urea, and other