Quercetin alters uterine fluid volume and aquaporin (AQP) subunits (AQP-1, 2, 5 & 7) expression in the uterus in the presence of sex-steroids in rats

Huma Shahzad, Nelli Giribabu, Kamarulzaman Karim, Sekaran Muniandy, Normadiah M. Kassim, Naguib Salleh

ABSTRACT

Effects of quercetin on uterine fluid volume and aquaporin (AQP) expression in the uterus were investigated. Estradiol (E) or estradiol followed by progesterone (E + P) were given to ovariectomised rats with or without quercetin (10, 50 or 100 mg/kg/day) treatment. Uteri were harvested and its inner/outer circumference ratio was determined. AQP-1, 2, 5 and 7 mRNA and protein levels in uterine were quantified by Real-time PCR and Western blotting respectively. Protein distribution was observed by immunohistochemistry. Administration of quercetin in E-treated rats decreased the uterine fluid volume and uterine AQP-2 expression. In E + P-treated rats, administration of 100 mg/kg/day quercetin increased uterine fluid volume, AQP-1 and 2 expression but decreased AQP-7 expression in uterus. AQP-1 was distributed in stromal blood vessels while AQP-2, 5 and 7 were distributed in uterine epithelium.

Conclusions: Quercetin-induced changes in uterine fluid volume and AQP subunits expression in uterus could affect the uterine reproductive functions under different sex-steroid influence.

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1. Introduction

Precise regulation of the uterine fluid volume is essential for successful reproduction [1]. In rodents, uterine fluid volume increases following estrogen treatment [2] but decreases following progesterone treatment [3]. In humans, decreased in uterine fluid volume has been reported in the luteal phase of the menstrual cycle [4]. Further evidence which indicate sex-steroids influence the uterine fluid volume was the difference in the volume of fluid retrieved from the uterus at different days of the menstrual cycle in fertile patients [5]. These findings suggest the influence of female sex hormones on uterine fluid volume regulation. Changes in uterine fluid volume are related to the amount of H₂O that moves between different uterine compartments. H₂O moves secondary to NaCl movement [6]. The movement of H₂O occurs via paracellular pathway or specific protein channel, known as the aquaporin (AQP), which are abundantly expressed in secretory epithelia [7]. The up-regulation of AQP channels will enhance H₂O transport while the down-regulation of this channel will cause vice versa [8].

AQP is a small, hydrophilic, integral membrane protein that mediates passive movement of H₂O [9]. Specific AQP channel subunits have been identified in the uterus which are AQP-1, 2, 5 and 7 [10]. AQP-1 is abundantly expressed in the endometrial stroma blood vessels as documented in rats [11], humans and pigs [12,13]. In rats, expression of AQP-1 in uteri was found to be up-regulated by estrogen and progesterone [14]. AQP-2 was also reported to be expressed in the uterus. In humans, uterine AQP-2 expression was highest at the mid-secretory phase of the menstrual cycle [15]. AQP-2 was reported to be expressed in endometrial luminal and glandular epithelia as reported in bitches [16].

In rats, AQP-5 was reported to be expressed at high levels at the apical membrane of uterine luminal and glandular epithelia at the time of implantation [11,17]. This subunit was found to be up-regulated by progesterone [14]. Similarly, in mice, AQP-5 expression was also reported to be high in uterine glandular epithelia at the time of implantation [18]. Recently, AQP-5 expression in the uterus was found to be up-regulated by testosterone [19].