In-Vivo Functional Study on the Involvement of CFTR, SLC26A6, NHE-1 and CA Isoenzymes II and XII in Uterine Fluid pH, Volume and Electrolyte Regulation in Rats under Different Sex-Steroid Influence

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Abstract

Precise control of uterine fluid pH, volume and electrolytes is important for the reproductive processes. In this study, we examined the functional involvement of multiple proteins including Cystic Fibrosis Transmembrane Regulator (CFTR), Cl−/HCO₃⁻ exchange (SLC26A6), sodium-hydrogen exchanger-1 (NHE-1) and carbonic anhydrase (CA) in the regulation of these uterine fluid parameters. **Methods:** Adult female WKY rats were divided into intact, non-ovariectomised at different oestrous cycle phases and ovariectomised treated with sex-steroids. Following oestrous phase identification or sex-steroid treatment, in-vivo uterine perfusion was performed with and without the presence of these inhibitors: glibenclamide, DIDS, ACTZ and EIPA. The pH, volume, Cl−, HCO₃⁻ and Na⁺ concentrations of the perfusate from different groups were then analyzed. Meanwhile, the expression of CFTR, SLC26A6, NHE-1, CAII and CAXII was visualized by immunohistochemistry (IHC). **Results:** Parallel increase in the pH, volume, Cl−, HCO₃⁻ and Na⁺ concentrations was observed at estrus (Es), proestrus (Ps) and following 17β-oestradiol (E) treatment, which was inhibited by glibenclamide, DIDS and ACTZ while parallel reduction in these parameters was observed at diestrus (Ds) and following progesterone (P) treatment which was inhibited by ACTZ and EIPA. CFTR and SLC26A6 expression were up-regulated under E dominance, while NHE-1 expression was up-regulated under P dominance. Meanwhile, CA isoenzymes were expressed under both E and P influence. **Conclusion:** CFTR, SLC26A6 and CA were involved in mediating parallel increase in the uterine fluid volume, pH and electrolyte concentration under E while NHE and CA were involved in mediating the reduction of these parameters under P.

Key words: uterus, CFTR, SLC26A6, CAII & XII, NHE-1, sex-steroid, oestrous cycle.

Introduction

Precise control of the uterine fluid volume, pH and electrolytes is important for a number of key reproductive events including sperm transport and capacitation and embryo transport and implantation [1]. To date, several membrane transporters and enzymes have been proposed to participate in uterine fluid regulation which includes Cystic Fibrosis Transmembrane Regulator (CFTR) [2], Cl−/HCO₃− exchanger (SLC26A6) [3], sodium-hydrogen exchanger (NHE) [4] and carbonic anhydrase (CA) [3]. The expression of CFTR, a cAMP activated Cl− channel has been reported in the uterus in mice [5], rats [6] and humans [7]. Additionally, CFTR activity has also been documented in the endometrial epithelia in-vitro [3].