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Regulation and function of the human Fallopian tube

AKADEMISK AVHANDLING

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ABSTRACT

The Fallopian tube is essential for human reproduction. Transport of the spermatozoa, the egg, and later the pre-embryo is believed to be aided by muscular contractions in the wall of the Fallopian tube and cilia in the mucosa. An optimal environment in the Fallopian tube is of importance for fertilization of the egg and development of the pre-embryo. Progesterone (P) and prostaglandins (PG) are important regulators of reproductive processes. Leukemia Inhibitory Factor (LIF) is an important cytokine involved in embryo development and endometrial receptivity. The function of the Fallopian tube and its correlation to fertility is still not fully investigated.

The aims of the studies were to investigate (i) the uptake of intra-abdominal particles into the Fallopian tube, (ii) the transport of particles from the pouch of Douglas to the cervical mucus, (iii) the effect of hormones on the muscular contractions in the Fallopian tube, (iv) the presence of receptors for PGE₂ and PGF₂α in the human Fallopian tube and how they are regulated by hormones, and (v) the presence of receptors for LIF and gp130, and their regulation by P in the human Fallopian tube and the endometrium, as well as their localization in the pre-implantation embryo.

Healthy volunteers and patients undergoing surgery for benign causes or legal sterilization were included in the studies. All subjects were of fertile age and had regular menstrual cycles. Using gamma camera imaging and autoradiography we found evidence for uptake of radio labelled particles in the Fallopian tube after intra abdominal deposition. In-vitro contractility studies of longitudinal strips of the Fallopian tube showed different effects of hormones and drugs on muscular contractions. P, mifepristone, PGE₁, levonorgestrel, human chorionic gonadotrophin (hCG), and oxytocin decreased, whereas PGF₂α and PGE₂ increased the contractions.

Immunohistochemistry (IHC), confocal microscopy, reverse transcriptase PCR, and real time PCR were used to detect and confirm the expression of PGE and PGF₂α receptors, and c-kit in the Fallopian tube. The PG receptors were mainly expressed in the apical part of the luminal epithelial cells, in the muscular wall, and in the vessels. Treatment with mifepristone reduced the staining. IHC showed staining of LIF receptor (LIFR) and gp130 protein in the Fallopian tube, the endometrium, and pre-implantation embryos. LIFR was mainly seen in the apical and basolateral parts of the luminal epithelial cells, in the muscular wall, and vessels. The staining for gp130 was weak. Real time PCR showed expression of mRNA for LIFR and gp130 in the Fallopian tube and the endometrium. In the pre-implantation embryo, LIFR staining was seen in all cells, at all stages. Gp130 was present in all cells up to the morula stage, but only in the inner cell mass of the blastocyst.

In conclusion: Uptake of particles in the Fallopian tube suggests a retrograde transport mechanism. Muscular contractions in the Fallopian tube are regulated by PG and P. PG receptors are expressed in the human Fallopian tube and regulated by P. LIFR and gp130 are expressed in the human Fallopian tube, the endometrium, and the pre-implantation embryo. The pattern of LIFR expression indicates that LIFR is likely to be of importance for communication between the embryo and the Fallopian tube.

Keywords: Fallopian tube, endometrium, embryo, transport, prostaglandin, receptors, progesterone, mifepristone, LIF, LIFR, gp130

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