**Involvement of endothelin system in polycystic ovarian syndrome**

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**Introduction:** Polycystic ovary syndrome (PCOS) is one of the most common endocrine-metabolic disorders in women of reproductive age. PCOS is characterized by a combination of oligo/amenorrhoea, clinical or endocrine signs of hyperandrogenaemia and polycystic ovaries. Women with PCOS has higher levels of plasma endothelin (ET)-1. Endothelins are produced by endothelial cells and also by the granulosa cells of the preovulatory follicle. There is ample evidence demonstrating the presence of ET-1 in human ovary during reproductive life, this peptide has been suggested to be a negative regulator of progesterone synthesis. ET-2 on the hand was shown to initiate follicle rupture and ovum expulsion thereby promoting ovulation.

**Aim**: To examine the levels of EDN system in granulose lutein cells of PCOS patients in comparison to normally ovulating women undergoing IVF.

**Methods**: Patients with PCO and normal ovulatory women (control group) reaching IVF underwent the long suppression protocol, utilizing gonadotropin-releasing hormone agonist. Follicular aspirates containing granulosa lutein cells (GLC) were obtains from PCOS and control during oocyte retrieval. RNA and proteins were extracted and EDN system components were quantified using real time PCR and western blot analysis.

**Results**: EDN2mRNA levels were higher in human GC lutein than those of ET-1, EDN1 mRNA expression was elevated in granulosa cells of PCOS patients compared with normal ovulatory women undergoing IVF (1.6 ± 0.5 vs. 0.48 ± 0.1). EDN2 mRNA expression is reduced in granulosa cells of PCOS patients compared with normal ovulatory women undergoing IVF (2 ± 0.4 vs. 5 ± 0.7). ETA receptors mRNA expression was higher than that of ETB receptors in GC of normal ovulatory and PCOS patients and finally, ECE-1 was similarly elevated in granulosa cells of PCOS patients as well as in normal ovulatory women.

**Summary and conclusions**: EDN1 and 2 were inversely expressed in granulosa cells of PCOS patients, while EDN1 was elevated as compared with normal ovulatory women, EDN2 mRNA expression was lower in granulosa cells of these patients. The presence of ETA, and ETB to a lesser extent, in granulose cells of both groups of patients, supports autocrine/paracrine regulation of their function by EDNs. Abundant ECE-1 presence in granulosa cells of normal ovulatory and PCOS patients, enable unlimited production of EDN peptide. Enhanced expression of ECE-1 and EDN1 coupled with reduced EDN2 expression in the granulosa cells of women with PCOS may be a diagnostic and pathological marker of this condition associated with low fertility.