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Genetic analysis in relation to vascular endothelial growth factor level in Saudi women with previous ovarian hyperstimulation syndrome

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The ovarian hyperstimulation syndrome (OHSS) is a serious and potentially life-threatening physiologic complication, classically encountered in patients who undergo controlled ovarian hyperstimulation (COH) cycles. OHSS is a rare iatrogenic complication of ovarian stimulation occurring during the luteal phase or during early pregnancy. It is characterized by enlargement of the ovaries, fluid retention, and weight gain. Ovarian hyperstimulation syndrome is self-limiting and will undergo gradual resolution with time. The pathophysiology of OHSS is characterized by increased capillary permeability, leading to leakage of fluid from the vascular compartment, with third-space fluid accumulation and intravascular dehydration. Young age, an explosive response to gonadotropin stimulation evident with rapid increase of serum estradiol (E2) levels, development of multiple follicles (<20) during stimulation and the presence of polycystic ovary syndrome have been described as risk factors for the development of the syndrome in IVF patients. There is evidence that several other factors such as vascular endothelial growth factor may play a modulatory role on ovarian physiology and in the pathogenesis of ovarian hyperstimulation syndrome. Two possible mechanisms for the cause of spontaneous OHSS are described in the literature. The first one relates to the similarities in the hormone specific beta subunits of the glycoprotein hormones: follicle stimulating hormone (FSH), luteinizing hormone (LH) and chorionic gonadotropin (hCG) and the other described is through different molecular mechanisms. During the last decade, several cases of spontaneous and familial OHSS have been reported, suggesting a possible genetic cause for OHSS. The first aim of this study was to describe the molecular level of OHSS. Genomic RNA was extracted from granulosa cells during the aspiration for 23 samples, group one (H-OHSS) were patients with polycystic ovarian syndrome (PCOS) visiting in vitro fertilization (IVF) clinic and having a positive history of OHSS (n=6) and group two (PCOS) were the control group. These patients had PCOS and visiting IVF clinic and had no history of OHSS (n=17). Whole genome mRNA expression profiling was analyzed for all patients referring to PCOS group using Affymetrix Gene Chip® human genome U133 plus 2.0. The result was confirmed by using quantitative reverse transcriptase polymerase chain reaction (qRT-PCR). The results of this study showed a group of genes whose expression was significantly dysregulated in H-OHSS group compared to PCOS group (P-value <0.05). Among these genes, there were 65 most significantly altered genes with more than 1.5 fold change and there was a strong correlation found between the results of gene expression and qRT-PCR in this study (r=0.9). The second aim was to measure the Vascular Endothelial Growth Factor (VEGF) which is a homodimeric 34-42 kDa, heparin binding glycoprotein with potent angiogenic, mitogenic and vascular permeability-enhancing activities specific for endothelial cells. The serum was obtained from 38 patients, control group, healthy patients (n=8) visiting Dr. Sameer Abbas IVF clinic, H-OHSS group (n=10) and PCOs group (n=20) visiting the IVF clinic in King Faisal Specialist hospital. The level of VEGF was measured by using enzyme-linked immunosorbent assay (ELISA) technique. The observed differences in the VEGF between the different groups were statistically significant (P<0.05). It was found that VEGF level in H-OHSS and PCOs groups were statistically higher when they were matched to control group. The VEGF levels were markedly the highest among H-OHSS group compared to the control group. The levels were almost seven times higher among H-OHSS patients (718.186±421.241 pg/ml) compared to normal control (86.149±73.825 pg/ml). The observed differences in the VEGF between the different groups were statistically significant (P<0.05). The VEGF levels were higher among the PCOs group compared to the control group. The levels were almost three times higher among PCOs patients (350.806±252.478 pg/ml) compared to normal control (86.149±73.825 pg/ml). The observed differences in the VEGF between the different groups were statistically significant (P<0.05). The levels of VEGF were almost two times higher among H-OHSS group (718.186±421.241 pg/ml) compared to PCOs group (350.806±252.478 pg/ml). The observed differences in the VEGF between the different groups were not statistically significant (P=0.0577). The correlations between VEGF, anthropometric measurement, metabolic and hormone variables were performed in the three groups. In H-OHSS group, only a negative correlation was significant between the testosterone level and the weight of patients. In PCOS group, the level of VEGF was correlated significantly and negatively with estradiol (E_2) level. A negative significant correlation was found between the level of E_2 and the age, and between E2 and the weight of patients. Also the testosterone level was correlated significantly and positively with the level of FSH.

Biography

Alqahtani Huda A has completed her MD from King Saud University, College Sciences, Major Animal Physiology & Development. She has been a Lecturer in King Saud University, Zoology Department since 2011 in different specializations include Physiology, Molecular Biology, Parasitology, Insects and Ecology. She has applied her research in King Faisal Specialist Hospital & Research Center, and she has an intensive experience in different areas of Molecular Techniques. She was a Member of a national project that analyzed the genetic level of Saudi women who had polycystic ovarian syndrome and developed to ovarian hyperstimulation syndrome. Recently, she has been moving to USA to complete her PhD in Molecular Endocrinology major.

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