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Gonadotrophins and cytokines in ovarian epithelial cancer

John Alexander Latimer MB BS MRCOG

University of Adelaide

Department of Obstetrics and Gynaecology

The Queen Elizabeth Hospital

Woodville

South Australia 5011

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Abstract

Background: The vast majority of ovarian cancers are thought to arise from the malignant transformation of the ovarian surface epithelium. There is a diverse range of regulatory molecules which act by autocrine, paracrine and endocrine routes in the processes of ovulation. The age-specific incidence of ovarian cancer increases abruptly at the time of the menopause when FSH and LH levels are raised. A number of studies have recently suggested that there may be an increased risk of ovarian cancer in women who have undergone ovulation induction.

Aims: i: to compare the rates of mitotic activity of the ovarian surface epithelium (OSE) and the peritoneal mesothelium (PM) and the effects of ovarian hyperstimulation using a rodent model.

ii: to provide information about cytokine expression and production in benign and malignant ovarian tissue.

Methods: i: The mitotic rates of the PM and OSE were found using silver staining of nucleolar organising regions and semi-automated image analysis.

ii: The cytokine message was measured by ribonuclease protection assay (RPA) and semi-quantitative reverse transcription polymerase chain reaction. Cytokine protein was measured in ascites, cyst fluid and serum by enzyme-linked immunosorbent assay. A total of 42 women were enrolled into the study.

Results: i: The mitotic rate of the OSE was significantly higher than that of the PM. Gonadotrophin exposure insignificantly increased the mitotic rates of both the OSE and the PM.

ii: The RPA detected interferon- γ mRNA only. RT-PCR revealed cytokine mRNA expression by nearly all samples tested for CSF-1, GM-CSF, IFN- γ , IL-1 β , IL-6, IL-10 and TNF- α . Cytokine protein measurement showed detection of all cytokine proteins in all fluids (serum, cyst fluid and ascites), but only IL-6 and TNF- α were found in high concentration in more than a few of the samples.

Conclusions: The OSE has a higher rate of mitotic activity than the PM in the rat. There was an insignificant trend for ovarian stimulation to increase the mitotic rates of both the OSE and the PM.

Cytokine mRNA can be detected in ovarian tumours and benign ovarian tissue. IL-6 and TNF- α protein are relatively abundant in the serum, ascites and cyst fluids of women with ovarian cancer.