HUMAN FOLLICULAR FLUID IN NORMAL AND POLYCYSTIC OVARIIES

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ABSTRACT
Polycystic ovarian syndrome is a heterogeneous condition with a broad clinical and pathological spectrum that may reflect the effects of diverse etiologic factors. Polycystic ovarian syndrome is an abnormality in the maturation of the follicles which can result in abnormal composition of follicular fluid. By analysis and comparison of the biochemical composition of human follicular fluid in normal and polycystic ovaries, we endeavored to find the etiology of arrested follicular development in this syndrome and to gain an insight into the role of biochemical constituents of follicular fluid on follicular development.

The results of our study indicate higher concentration of potassium, lower concentration of testosterone and higher level of pH in normal ovaries relative to polycystic ovaries. In conclusion, potassium and testosterone concentrations and pH level seem to be some of the most important factors in the oocyte maturation and the acquisition of follicular development, and changes in them may have important role in the etiology of polycystic ovarian syndrome.

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Key Words: Polycystic ovarian syndrome, follicular fluid, biochemical constituents

INTRODUCTION

Follicular fluid (FF) is a complex extracellular fluid that is serousviscous and yellow in colour. It is a derivative of blood plasma and secretions synthesized in the follicle wall (1,2,3).

Ovarian physiology is controlled by many exogenous and endogenous factors including the endocrinological alterations which occur in the follicular fluid throughout the menstrual cycle (4). These changes in follicular fluid may influence steroidogenesis, oocyte maturation, ovulation and transport of the oocyte to the oviduct as well as the preparation of the follicle for subsequent corpus luteum formation and function (5).

Polycystic ovarian syndrome (PCOS) is an abnormality in the maturation of the follicles which can result in abnormal composition of follicular fluid. Recent data suggest that follicular fluid may play an important role in the endocrine balance of PCOS, probably by acting on the theca granulosa cell relationship (6). By analysis of this fluid and comparison of it with normal follicular fluid, we hoped to gain an insight into the role of biochemical constituents of follicular fluid on follicular development and identify any component which might enhance oocyte maturation.

MATERIALS AND METHODS

Study Patients
A total of 40 women with infertility, treated in IVF Center of Mirzakoecheh Khan Hospital, participated in the present study. The age of the patients ranged between 15.40 years. Follicular fluid was collected from the patients who were negative for HIV infection, syphilis and hepatitis B antigen to prevent infection. Patients who had severe endometriosis, immunologic factors or unknown factors were excluded from the follicular fluid collection (7). The patients were divided into two groups: patients with normal ovaries and patients with polycystic ovaries. The diagnosis was made by ultrasound, clinical and hormonal findings according to the proposed diagnostic criteria of the United States National Institute of Health (NIH) (8).

Collection of Follicular Fluid
During the oocyte aspiration in the human IVF programs, follicular fluid was collected from the follicles that were > 18 mm in diameter. Whenever possible, non-blood-stained follicular fluid was collected, but the fluid mixed with a small amount of blood was also collected (7).

Preparation of Follicular Fluid
Fluid was centrifuged at 2000 rpm for 20 minutes, and the supernatant was heat-inactivated at 56 °C for 35 minutes. The heated fluid was cooled and sterilized with a filter (0.22 µm pore size filters). All follicular fluid samples were kept at 40 °C until the time of analysis.

Analysis of Follicular Fluid
Follicular fluid samples were subjected to a range of biochemical measurements. Samples were all defrosted at room temperature and analysed after daily calibration of the machines by the analysis of
appropriate controls. A total of 16 tests were carried out on follicular fluid, using Zist Chini and Pars Azmun kits.

Statistical Analysis
Results are presented as the mean ± SEM. Comparison of means was done with the unpaired t-test and ANOVA (1-way, 2-way). Significance was set at \( P < 0.05 \). Statistics were calculated using the Statistical Package for Social Sciences (SPSS) - version 9 program.

RESULTS

Values in the Table 1 represent mean ± SEM concentration of selected molecules, electrolytes, lipids, sterols, pH and osmolarity measured in human follicular fluid (FF) of normal and poly cystic ovaries. Also shown are the results of statistical analysis. The ionic composition of the fluid of normal ovaries was characterized by high concentration of K, relative to the fluid of poly cystic ovaries (P=0.05).

Testosterone concentration in follicular fluid of normal ovaries was significantly lower than follicular fluid of poly cystic ovaries (P<0.01).

pH studies showed that follicular fluid of normal ovaries is more alkaline than follicular fluid of poly cystic ovaries (P < 0.01).

There were no significant differences between the concentrations of other components such as Na, P, Cl, Ca, Mg, etc.

DISCUSSION

Poly cystic ovarian syndrome is a heterogeneous condition with a broad clinical and pathologic spectrum that may reflect the effects of diverse etiologic factors (9). Since the follicular fluid is in intimate contact with the ovocyte and granulosa cells, changes in the concentration of its different components in PCOS may lead to understand the etiology of the arrested follicular development in this syndrome and to gain an insight into the role of biochemical constituents of follicular fluid on follicular development. By the time of our study, there was not any other experiment to determine human follicular fluid composition.

The results of our study indicate much higher concentration of K in follicular fluid of normal ovaries than poly cystic ovaries. This high concentration may show the effect of K on the maturation of ovocyte. This agrees with the findings of Moody and Bosma (10), who showed that potassium level of ovocyte increase during meiotic maturation and this increase is closely associated with the migration of the germinal vesicle to the cell periphery. The results of our own study show similar trends to the former studies that reported higher concentration of K in follicular fluid than human serum (11). The mechanism of K effect on the maturation of ovocyte is not obvious, but one possibility is its effect on plasma membrane potential (12). Further studies are needed to determine the importance of the ionic composition of the follicular fluid for normal human preimplantation development.

The results obtained in this study indicate that testosterone concentration in follicular fluid of normal...
ovaries was significantly lower than follicular fluid of polycystic ovaries. Increased androgen concentrations are thought to be detrimental to oocyte maturation and reproductive potential (13). Depending on the diagnostic data available from patients with polycystic ovaries, various steroidogenic enzyme blocks have been postulated mostly implicating higher-than-normal production of circulation delta-4-androstenedione, testosterone, and in some cases, dehydroepiandrosterone. These high levels of androgens, because of their peripheral conversion to estrogens, lead to inappropriate secretion of gonadotropins in PCOS (9). A rising from these observations was the suggestion that an aromatase enzyme block existed (9). The recent studies suggest a potential role for 5 alpha - reduced androgens in the etiology of PCOS (14).

pH studies showed that follicular fluid of normal ovaries is more alkaline than polycystic ovaries which suggests that a high pH is required for preimplantation embryo development. The mean value of 7.55 in human follicular fluid that we report here is comparable with the value of 7.4 given by Dale et al (15) and is higher than the value of 7.2 given by Edwards (1).

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REFERENCES


