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ROLE OF PROGESTERONE ESTIMATION IN INFERTILITY

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This study was conducted on 50 subjects (30 infertile and 20 fertile) taken from Sir Ganga Ram and Lady Aitchison Hospitals, Lahore and hormonal assays carried out at PGMI, Lahore. The infertile subjects were between 18-35 years of age and were married for more than 2 years. The results showed that 18 out of 30 infertile patients (64%) had luteal phase deficiency (LPD) and 12 out of 30 (56%) had normal progesterone levels. It was thus concluded that estimation of serum progesterone levels in infertile subjects is simple, easy but important investigation. It determines the presence of L.P.D or otherwise. This assay is closely corelated to endometrial biopsy results and therefore can be used as an alternate non-invasive procedure in the work up of infertility.

INTRODUCTION

Endocrine status is suggestive of ovulatory dysfunction which is found to be associated with many pathological processes in hypothalmic pituitary ovarian axis (HPO), leads to Luteal phase deficiency (LPD) which plays its role in infertility even including unexplained infertility[1]. The high E2/progesterone concentration observed in poor progesterone surge cycles were not associated with reduced estradiol concentration observed in poor progesterone surge (PPS). In conception cycles basically these are interlinked, the decreased levels of progesterone/E2 in infertile subjects indicate anovulation which is one of the major causes of infertility[2].

The latest advancement in biotechnology revealed that fertility depends upon neuroendocrinology of women with functional integrity of anatomical structure which evaluates potential role of progesterone/E_2 in female. It should be preferred over other difficult procedures. Most of research workers have emphasized much on luteal phase deficiency (LPD) and its role in infertility.

Histological assessment of endometrium, single and multiple biochemical assays of progesterone and basal body temperature changes, all have limitations. Luteal phase deficiency is not unusual in women with unexplained infertility[3]. It is well recognized that FSH is the stimulation to the antral follicle's proliferation of granulosa cells leading to eventual dominance of a single follicle from which most of circulating E2 is produced[4].

Although follicular growth profiles in the poor progesterone surge (PPS) did not differ markedly from normal, the E2 and FSH data suggest that the dominent follicles recruited in these cycles could have been abnormal, providing less negative feedback suppression of FSH. This combination, was in many cases, associated with luteal cyst formation.

The physiology of regulation of progesterone in menstrual cycle is normal. The high luteal phase FSH concentrations observed in PPS cycles were not associated with reduced E_2 concentration and may be a consequence of differences in the secretion of inhibin like products by the abnormal corpora lutea[5].

MATERIALS AND METHODS

The present study was carried out in fifty subjects. These included thirty infertile and twenty control subjects. These subjects were found from infertility advisory center, Sir Ganga Ram Hospital Lahore, while the control subjects were mostly their relatives.

The endocrine diseases including diabetes mellitus, hypothyroidism, Cushings syndrome, polycystic ovarian disease as well as congenital anomalies of genital tract were excluded. A detailed history and thorough physical examination were carried out in all these patients.

Patients were also screened for PID, tuberculosis and tuberculous endometritis by clinical check up and relevant investigations.

STUDY GROUP

(a) Subjects with primary infertility. In this group the subjects were included who never had any pregnancy (live, still born or definite abortion). This group consisted of patients, who were screened by consultants and gynaecologists, for tubal blockage, pelvic adhesions, endometriosis, primary ovarian tumours, which could prevent the

spermatozoa to reach the cervix.

These subjects were thirty in number, fulfilling the following criteria:

l. Age 18-3 5 years.
2. Duration of marriage > 2 years
3. Subjects were not using any contraceptives

(b) Secondary infertile females, normal healthy females who were having the only issue and wanted to conceive again. They were also full filling the following criteria:

1. Age of patient 23-25 years.
2. Age of 1st child > 2 years
3. The subjects were not using, contraceptive devices after 1st child. An examination of husbands semen was carried out and those females whose husbands semen analysis was found normal underwent investigation such as complete blood count, urine complete examination, cervical culture if needed, bar body examination, endometrial biopsy and ultrasonic evaluation of pelvic organs.

CONTROL GROUP

Twenty females who were age-matched fertile with one or more children, apparently healthy and not suffering from endocrine disorders were chosen as controls. Mostly they were attendants or relatives of patients. These were subjected to following tests: Estimation of hormone levels. Estradiol, prolactin, progesterone, FSH, LH,. semen analysis of male partner, urine complete examination and blood complete examination.

COLLECTION OF BLOOD SAMPLE

Ten ml of blood were drawn from vein under sterile conditions with disposable syringes

Blood samples were collected randomly between 8 and 10 a.m. Two ml. of blood was immediately delivered into dry vial containing EDTA as an anticoagulant for routine blood examination. The remaining 8.0 ml. of blood was delivered into centrifuge test tube and was allowed to clot at room temperature for 30-45 min. till the clot was well retracted and was centrifuged at 3000 rpm for 10 to 15 min. The serum was separated and stored in aliquotes at - 20°C[6]. The routine blood tests were performed on the same day.

SPECIAL INVESTIGATIONS

The subjects were advised to visit PGMI twice during the menstrual cycle. The blood sample was collected in the morning to avoid diurnal variations. The following precautions were taken for prolactin estimation. Samples were collected during day time just to avoid effect of sleep on prolactin level.

The sample was preferred in fasting, or 45 min. following meals because of rise of prolactin level immediately following meals. The sample was, however, drawn on any day of menstrual cycle as its levels are not related to cycle changes of other hormones. For example oestrogen. FSH and LH samples were taken on 14th day of mentstmal cycle and Estradiol and progesterone were assayed at 21st day of menstrual cycle by RIA technique.

RESULTS

Mean serum progesterone levels were found to be 3.6±4.2 ng/ml in the study group while in controls it was 3.2±3.0 ng/ml. The difference was statistically non- significant. The range in infertile subjects was 0.3 -15.1 ng/ml.

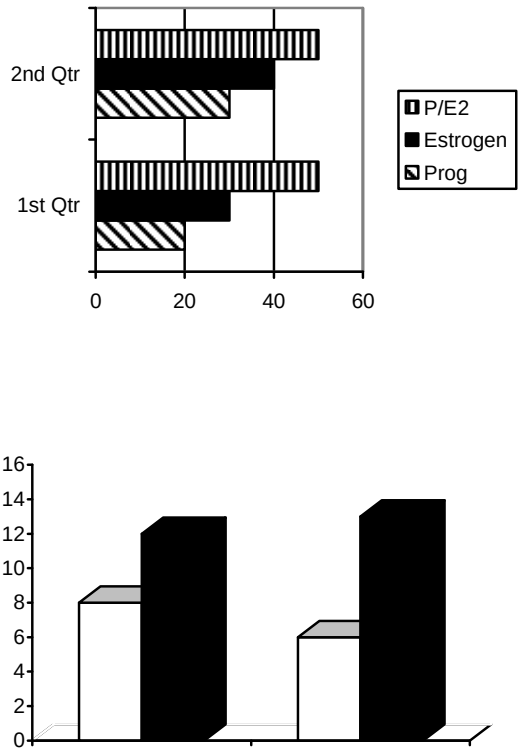

Fig. Comparison of serum progesterone in infertile subjects and controls.

The infertile subjects showed the clinical presentation of oligomenorrhoea, galactorrhea, dysparunia, dysmenorrhea, ammenorrhea and menorrahagia. Oligomenorhea was the most

Comparison of Serum Hormone Levels of infertile with control subjects Values representating mean ± SD. The figures in parenthesis refer the reference range.

Subjects	Progesterone (ng/ml)	Estradiol Pg/ml	
		Follicular phase	Lutal Phase
Infertile Subjects N=30	3.6 ±4.2 (0.3-15.1)	114.6± 48.7 58.4-194.4)	232.2 +70.8 135.8-376
Control subjects N-20	1.2 ±3.6 0.4 -10.6	87.6 28.0 39.9-138.5	186.1 ± 63.7 (990.3006) Pg/nl
Level of significance (infertile subjects vs. control)	Non significant	* P0.01	*P<0.9

N.S Non significant * P0.01- highly significant

Clinical Presentation of the Infertile Subjects

Clinical disorder	Number of subjects	Percentage %
Unexplained infertility	3	10
Endometriosis	2	6.7
Polycystic ovarian disease (PCOD)	1	3.3
Luteal phase deficiency (LPD)	18	60
Hyper prolactinaemia	4	13.3
Asymptomatic	2	6.7

prevalent clinical presentation seen in 33.3%, whereas least subjects presented with menorrhagia.

The clinical disorders were correlated with abnormalities in serum hormone levels. The LPD was the most common disorder seen in 62%. The incidence of hyperprolactinaemia, unexplained infertility, endometriosis and PCOD was 13.2%, 10%, 6.6% & 3.3% respectively, whereas 2 subjects (6.6%) were asymptomatic. The endometrial, ovarian and tubal factors already evaluated for infertile subjects were tabulated.

DISCUSSION

It was an attempt to correlate the serum progesterone values with endomaterial biopsy reports and concluded that 18 of infertile subjects 62% showed LPD & twelve subjects 40% showed normal levels of progesterone, 17- patients (56.1%) normal secretory endometrium while 3 pt, (10%) had proliferative endometrium. In the present study it was observed that five out of seventeen subjects (29.4%) showed a correlation between hormonal levels and endometrial biopsy reports.

Mid luteal progesterone levels translate the endometrium but it is not a measure of LPD. Two patients showed ovarian cyst formation on USG which were probably luteal as these were painless.

PPS may be related with these cysts and may cause cyst entrapments. A high incidence of cyst of cycles demonstrating lutelinized unruptured follicles was reported in population of women with unexplained infertility. Further work can reveal exact relationship of serum progesterone with endometrial biopsy.

Two subjects who presented with recurrent miscarriages showed LPD. A revolution in science is not simply an accumulation of data, a harvest of results or a change in landscape. It is a change in way people think, in the way they look at things and change in vision itself.[6-8]

The emotional aspects of a childless state is often overlooked which causes deterioration of marital relationship. Hormone assays by these advanced techniques is very important to minimize the obstructiveness and sternousness of medical procedures.[8,9] Further work on these lines revealed exact relationship of serum progesterone with endo-metrial biopsy. Two subjects who presented with recurrent miscarriages showed LPD. Their pro-gesterone levels were 1.04 ng/ml and 0.60 ng/ml respectively.

Patient suffer from hyperprolactinaemia with galactorrhea due to prolonged intake of clomiphene citrate. These patients with endometriosis showed decrease in serum progesterone, LPD inadequacy.

The effect of vaginal progesterone administration on uterine contractility at the time of embyo transfer (ET) during IUI was also studied.

The achievement of rapid myometrial relaxation requires more intense uterine exposure to progesterone than in menstrual cycle.

Effect of vaginal progesterone in embryo transfer was noticed .Those women whose uteri were morphologically normal as confirmed by hysteroscopy and ultrasound scan were included. Clinical indications for IVF-ET were sperm abnormality 52%; tubal abnormality 33%; unexplained infertility 13%; endometriosis 2% subjects underwent FSH&E2 measurement on day 3 in their menstrual cycle. Uterine contractility and hormonal assessment P&E2 were done on the day of HCG administration and just before ET[10,11].

Environmental conditions were also standardized throughout ultrasound examination. It was concluded that vaginal progesterone administration starting 2 days before ET induces reduction in uterine contraction frequency at the time of ET.[12,13]

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