Evaluation of endometrial thickness, follicular growth, and serum estradiol levels in spontaneous (fertile) vs induced (infertile) cycles via clomiphene or gonadotropin

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Abstract

Objectives: The current evaluating study was launched to assess endometrial thickness (ET), follicular growth (FG), and serum estradiol (SE) levels in spontaneous (fertile) vs induced (infertile) cycles via clomiphene or gonadotropin.

Patients and methods: The work included two groups; a study group (SG) and a control group (CG). The SG contained 196 patients who suffered infertility and was divided into two subgroups according to the treatment that the patients received, clomiphene (SGC) or gonadotrophin (SGG). The CG included 130 healthy, fertile, individuals who received no treatment. Transvaginal ultrasonography (TVU) was used to evaluate the treatment effects on the ET and FG plus ovulation. The SE levels of the group members were measured using a competitive radioimmunoassay (CRIA).

Results:A trilaminar endometrium was ultrasonically recognized in the SGC and the CGshowing three hyper-echogenic lines with inner hypo-echogenic regions. ET was significantly (p<0.05)reduced in the SGCwhen compared with that in the CG.The follicular diameter (FD) was significantly (p<0.05) larger in the SGs than that in the CG. However, the FD significantly (p<0.05) increased in the SGG in comparison to that in the CG. The SE levels were significantly (p<0.05) higher during the mid of the cycle in the SGs than those in the CG.

Conclusion: The assessed effects of the clomiphene or gonadotropin on the endometrial features, ovulation, and serum estradiol levels provide significant prognostic information regarding the use of those treatments in infertile women.

Keywords: Clomiphene, endometrial thickness, follicular growth, gonadotrophin, serum estradiol.

Introduction

Some structural alterations in the endometrium are occurred during the menstrual cycle, and this is considered as implantation preparation. These changes in the endometrium is partially controlled by increasing levels of estrogen produced by the growing follicles in the ovaries. After the ovulation is occurred, progesterone subsides estrogen to be released by the corpus luteum (CL)initiating secretory-based changes. The CL can be regressed if the implantation fails to occur (Kovacs et al., 2003).

The TVU enhances monitoring endometrial changes during the menstrual cycle and providing vital information about the FG. The TVU gives clear pictures about the endometrium with ET in the mid cycle that ensure correct prediction regarding the implantation successfulness in which if ET is less than 6mm on the day after the administration of HCG, no implantation may occur (Haritha and Rajagopalan, 2003). Interestingly, transvaginal color Doppler sonography provides additional details about the pathophysiological characteristics regarding infertility which allows for the use of suitable treatment. Moreover, development in the methodology of hormonal surveillance and endocrinal pharmacology enhances the management of infertility and restoring reproduction (Haritha and Rajagopalan, 2003).

Infertility at (30%) is related to disorders affecting ovulatory cycle (Glazener et al., 1990) such as empty follicle syndrome, follicular atresia, polycystic ovarian disease, luteinizedunruptured follicles, hypergonadotropism and hypogonadotropism(Glazener et al., 1990Finding the exact etiological factor that causes infertility may increase the successful rates of applying the correct treatment enhancing ovulation induction and with constant monitoring of the case using TVU and hormonal parameters, well-status of reproduction can be restored. The therapeutic agents commonly used for induction of superovulation are clomiphene, gonadotropin (HCG), gonadotropin releasing hormone agonists (GnRH), human menopausal gonadotropin (hMG), and human chorionic gonadotropin (HCG). The superovulation with preventing of multiple follicular and pregnancy development is maintained using the best hormonal agent with frequent monitoring of the overall status using TVU and hormonal parameters (Haritha and Rajagopalan, 2003).

The current evaluating study was launched to assess endometrial thickness (ET), follicular growth (FG), and serum estradiol (SE) levels in spontaneous (fertile) vs induced (infertile) cycles via clomiphene or gonadotropin.

Patients and methods

The work included two groups; a study group (SG) and a control group (CG). The SG contained 196 patients who suffered infertility and was divided into two subgroups according to the treatment that the patients received, clomiphene (SGC) in which 99 patients that received 150mg/day for 5 days starting on the third day of the menstrual cycleand gonadotrophin (SGG) in which 97 patients given FSH (gonal F 75 IU serono) 75 IU/day for 5 days starting on day 7 of the cycle. The CG included 130 healthy, fertile, individuals who received no treatment.

The study was conducted on patients (>two years of primary or secondary infertility but had normal menstrual cycles, 3-5 days) who attended Basrah Maternity and Child Hospital, BasrahCity, Iraq, during the period between September, 2008 to September, 2009. The SGs and CG members were controlled for the age (20-40 yr. old) and weight. Individuals with pelvic infection, previous ovarian surgery, polycystic ovarian syndrome, endocrine or medical disorders, and within-the-previous-three-month use of ovulation induction drugs were excluded from the study. Monitoring of the patients was conducted starting at day 9/every other day until a follicle reached (18-25mm). SE levels were assessed at this stage.

Transvaginal ultrasonography (TVU) with a 6.5-MHz sector transducer was used to evaluate the treatment effects on the ET and FG plus ovulation. The SE levels (pg/ml) of the group members were measured using a competitive radioimmunoassay (CRIA).

As recommended, central endometrium measurement was ensured via the visualization of the cervical canals in the same plane. The day of the ovulation was used to compare between the groups.

Statistical analysis

The datawere analyzed using a Chi-square method. Significant result was concluded if$p<0.05$.

Results

Women were distributed according to certain demographic factors showing comparable age and body mass parameters, table 1.

Table 1: Distribution of women according to certain demographic factors.

Factors	Study groups				Control group (CG)	
	SGC		SGG			
Age (years)	No.	%	No.	%	No.	%
20-24	20	20.2	18	18	25	19.2
25-29	23	23.2	20	21	30	23.1
30-34	32	32.3	30	31	37	28.5
35-40	24	24.3	29	30	38	29.2
Total	99	100	97	100	130	100
Parity						
Nullipara	62	26.6	72	74.2	0	
Multipara	37	37.4	25	25.8	130	100
Total	99	100	97	100	130	100
Fertility						
Primary	62	26.6	72	74.2		
Secondary	37	37.4	25	25.8		
Total	99	100	97	100		
BMI						
<18	10	10.1	15	15.5	12	9.2
18-24	30	30.3	27	27.8	55	42.3
24-25	39	39.4	25	25.8	43	33.1
>25	20	20.2	30	30.9	20	15.4

A trilaminar endometrium was ultrasonically recognized in the SGC and the CG showing three hyper-echogenic lines with inner hypo-echogenic regions. ET was significantly (p<0.05) reduced in the SGC when compared with that in the CG.The ET in 79% of the SGG women was >7mm which is greater (p<0.005) than that, 55%, in the CG, table 2.

Table 2: Endometrial thickness (ET)in the SGG vs the CG

ET (mm)	Cases		Control	
	No.	%	No.	%
6	3	3.09	7	5.38
6.1-6.4	7	7.22	11	8.47
6.5-6.9	10	10.33	28	21.54
7-7.4	23	23.71	39	30.0
7.5-7.9	20	20.61	18	3.84
8-8.4	18	18.55	24	18.46
8.5-8.9	6	6.18	3	2.31
>9	10	10.31		
Total	97	100	130	100

The follicular diameter (FD) was significantly (p<0.05) larger in the SGs than that in the CG. However, the FD was significantly (p<0.001) increased in the SGG in comparison to that in the CG, table 3.

Table 3: The follicular diameter (FD) in the SGG vs CG

FD	SGG		CG	
	No.	%	No.	%
1-1.5	5	5.15	63	48.47
1.6-2	20	20.62	52	40.0
2.1-2.5	59	60.83	14	10.77
>2.5	13	13.40	1	0.76
Total	97	100	130	100

The SE levels were significantly (p<0.001) higher during the mid of the cycle in the SGG than those in the CG, table 4.

Table 4: The serum estrogen (SE) in the SGG vs CG

SE (pg/ml)	SGG		CG	
	No.	%	No.	%
100-200	16	16.5	61	47
200-300	20	20.5	33	25.3
300-400	34	35	23	17.7
400-1000 & more	27	28	13	10
Total	97	100	130	100

Discussion

Therapeutic-induced ovarian response can be monitored using biophysical parameters related to this induction such as follicular diameter and hormonal changes especially serum estrogen levels. The clomphene citrate showed development of the follicles at different rates with that Fossum et al demonstrated that the largest diameter was ranged between 22 to 31mm (Fossum et al., 1990);however, the current work revealed higher rate (61%) than that from other studies(50%) (Haritha and Rajagopalan, 2003; Randall and Templeton, 1991). For better results, follicle size can be developed if HCG is givenwhena follicle reaches 15 to 18mm (Marss*et al*.,1983). Forthe SGG,the FD was higher (94%) in the SGG than that (52%) in the CG. This was shown by various studies that also revealed the presence of multiple large follicleswith the subsequentoccurrence ofhyperstimulationsyndrome (Macfaul*et al*., 1989; Forrest *et al*., 1988).

In the case ofETsurveillance, at the late proliferative stage or periovulatory phase of the endometrial development, a distinguishable multilayered endometrium

can be seen especially in women with frequent pregnancy achievement (Forrest *et al*., 1988). In the SGC, the ET was thinner than that in the control group, (65%) and (31%), respectively,and this was also recorded by many studies (Haritha and Rajagopalan, 2003;Forrest *et al*., 1988;Huneeus*et al*., 1994). For the SGG, the ET was greater than that in the CG, and this agrees with (Nakamura et al., 1997) who documented the same results.

The SE was higher in both SGC and SGG women than that in the CG women. These results were also proved by some studies (Haritha and Rajagopalan, 2003; lenz and Lindenberg, 1990). No positive correlation between the follicular size and the SE was notice in the present study (Mio et al., 1992; Wolman *et al*.,1994).

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Conclusion

The assessed effects of the clomiphene or gonadotropin on the endometrial features, ovulation, and serum estradiol levels provide significant prognostic information regarding the use of those treatments in infertile women

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