RESEARCH ARTICLE

STUDY OF FOLLICULAR DYNAMICS AFTER SPONTANEOUS AND INDUCED OVULATION BY ULTRASONOGRAPHY IN INFERTILE WOMEN

*Dr. Sushma Singh

Assistant Professor, Vardhman Institute of Medical Science, Pawapuri, India

ARTICLE INFO	ABSTRACT
	Introduction: Infertility affects 10-15 % of couple in reproduction age group (novak, 13th edition, 2002). Ovulation dysfunction is a common cause of infertility. Approximately, 40% of female infertility is due to anovulation (Speroff *et al.,* 1999). However, with the advent of USG, a simple and non invasive, more accurate method to study ovulation has been established. **AIMS and objective:** 1. To study the follicular dynamics after spontaneous and induced ovulation by non invasive method in infertile women. 2. To study the effect of various ovulation inducing agent on pregnancy rate. The above study by predicting the timing of ovulation can help in 3. Women undergoing intrauterine insemination 4. Timing of intercourse in infertile women 5. It wil also help to minimize the risk of ovarian hyper stimulation syndrome. **Material and Methods:** The present work was undertaken in dept of obstetrics and Gynecology and Department of Radiology of VIMS, Pawapuri from Nov 2015 to 2016. Patients of infertility both primary and secondary were selected and tests were carried out to know the causes of infertility. Group I – constituted 25 infertile women with ovulatory cycle; Group II – constituted 25 infertile women with anovulatory cycle. **Method of Induction:** In all cases treatment was started from D2 of cycle for ovulation. For ovulation induction oral clomiphene citrate (50mg) D2 to D6 of menstrual cycle. (Regimen I) Those pts who failed to respond to Regimen I were put on a combination of (CC+FSH). Single dose of HCG (10000 IU) given IM when dominant follicle attained a diameter of 18 – 20 cm USG monitoring done from D10 on was of cycle to see the no of follicle, diameter of follicle, rate of growth and endometrial thickness. Couples were advised to live together from D10 -15 on alternate day. Result: The leading follicular diameter was significantly larger (22- 26) in CC stimulated cycle as compared to spontaneous cycle (16- 21). The ovulate rate and pregnant rate was higher with regimen II. **Conclusion:** It helps in prediction of timing of ovulation and correct prediction of timing of ovulation is critical for infertility therapies such as intrauterine insemination and timing of intercourse, and helps to increase the pregnancy rate.

INTRODUCTION

The problem of infertility is faced by mankind since time immemorial and will remain forever. Infertility affects 10 – 15% couples in the reproductive age group (novak, 13th edition, 2002). Ovulatory dysfunction is a common cause of infertility. Approximately, 40% of female infertility is due to anovulation (speroff at, 1999). WHO classification of anovulation is based on defects either organic or functional of 3 principle endocrine glands.

Group I anovulation – Hypothalamicpituitary failure
Group II anovulation – Hypothalmic pituitary dysfunction
Group III anovulation – ovarian failure

Ovulation has been conventionally studied by a rise in basal body temp, endometrial histopathology, serum estradiol and LH surge. However with the advent of ultrasonography, a simple and non invasive, more accurate method to study ovulation has been established. It isa easy and quick method to directly view ovarian follicle development, requires a short time and has no known harmful effects to oocyte or reproductive tract. Serial ultrasonography can be used to monitor follicular growth and determine when ovulation occurs. selection of dominant follicle is thought to occur by cycle day 5 to 7 but is not sonographically apparent until cycles day 8 to 12mm. Follicle destined to ovulate will increase linearly in size at rate of I to 2 day reaching a diameters of 18 to 24 cm before ovulation.

The ultrasonography signs of ovulation are

- Complete disappearance of follicles
- Decrease in size of follicles
- Irregularity of follicular contour
- Fluid in pouch of douglas
- Hyper echogenic secretary endometrium.
- Ovulation inducting agents are used for anovulatory or oligo ovulatory patients desirous of fertility.
- Ovulation induction is done for improved timing for intrauterine insemination.

MATERIAL AND METHODS

The present work was undertaken in the department of obstetrics and gynecology and the Department of Radiology at VIMS, Pawapuri from Nov 2015 – Dec 2016. A total of 50 patients of infertility were screened and specialized investigations were carried out to know the cause of infertility. Among the specialized investigation husbands seminal fluid exam, tubal patency test by Hysterosalpingography/ laparoscopy and Chromotubtiontest and test for ovulation by Ultrasonography done from D10 onwards of cycle. Hormonal assay done in those cases presented with Oligomenorrhoea or amenorrhoea. After analyzing the laboratory report in patients found suitable for therapy the treatment was initiated after councelling.

- The couples were informed about success and failure rate of therapy, multiple Preg and ectopic Preg.
- Couple was taught about the importance of properly timed intercourse.

Procedure for USG follicular monitoring by transvaginal probe.

In case of TVS 6.5 MHZ vaginal transducer was used in case of transvaginal Ultrasonography. A new condom was slipped over the prove before each examination and a small amount of coupling gel was applied to inner surface of the topof condom to assure better contact and transducer (6.5MHG) was introduced gently into the vagina.

METHODS

Group I – Constituted 25 infertile women with ovulatory cycle.

Group II – Constituted 25 infertile women with an ovulatory cycle in whom study of follicular dynamics were done after induction of ovulation.

In all case treatment was started from day 2 of cycle for ovulation.

Regimen I: Clomiphene citrates (50mg) from D2 to D6 if ovulation failed then doses were increase in next cycle to 100 mg daily. This regimen was used for 3 consecutive cycles. single dose of HCG(10,000 IU) was given IM when dominate follicle attained a diameter of 18-20mm. Follicles were monitored by Ultrasonography from D10 onwards.

Regimen II: Those patients who did not ovulate with CC+HCG were put on a combination of (CC + rFSH +HCG) for inducing ovulation. Recombinant FSH was added on D3, D5 and D7 and injection HCG to trigger ovulation.

Timing of HCG Injection:

Single dose of HCG (10,000 IU) was given intramuscularly when a dominant follicle attained a diameter of 18-20 mm. HCG was not administered when more than one parameters were present.

1. Presence of polycystic ovary
2. Occurrence of ovarian hyper stimulation syndrome in previous cycle.
3. Presence of 20 or more follicles particularly small and intermediate size.

Conformation of ovulation by USG done by following signs-

1. Complete disappearance of the follicles.
2. Decrease in size of follicle
3. Appearance of multiple echoes in a previously echofee follicle
4. Appearance of fluid in POD
5. Hyperechogenic secretory endometrium.
- Couples were advised to live together from D10 –D18 alternate day.

The patients were followed up and were asked to report after they missed their period and pregnancy was confirmed by pregnancy test of Urine.

RESULTS

Table I. Out of 50 cases of infertility

Type of infertility	No. of patients	% of patients
Primary	36	72%
secondary	14	28%
	n = 50	

Table II. Showing distribution of cases according to Age

Age in years	No. of patients	% of patients
<20	2	4%
21- 25	10	20%
26 – 30	20	40%

Table III. Distribution of patients according to menstrual irregularities

Menstrual irregularity	No. of patients	% of patents
Oligomenorrhoea	18	36%
Normal cycle	20	40%

Table IV. Classification of the causes of anovulation

Causes	No. of patients	% of patients
PCOD	12	24%
POF	1	2%
Unknown	5	10%

Table V. Study of follicular dynamics by USG in ovulatory cycles

Investigations	No. of patients	% if patients
Appearance of multiple echoes in a previously echo free follicle	2	8%
Change in shape	1	4%
Disappearance of follicle	10	40%
Appearance of fluid in POD	12	48%

Table VI. Comparison of leading follicular diameter

Mean Follicular Diameter (in mm)			
Day	Spontaneous	Clomiphene Induced	Gonodotrophins
Day – 3	16	22	15.5
Day – 2	19	24	16
Day – 1	21	26	18

Average Growth rate.

Spontaneous	Ind
2.1mm	2.2mm/day

Table VIII. Inducing ovulation

Different protocols	No. of patient (n=25)	Ovulation in	% of patients in which ovulation occurred
Regimen I	25	17	68%
Regimen II	8	6	75%

Table IX. Pregnancy achieved and cumulative pregnancy rate after ovulation induction by different regime

	No. of patient	Pregnancy achieved in	Cumulative pregnancy rate
Regime I	25	8	32.0%
Regime II	8	4	50.0%

Table X. Multiple pregnancy rate

	No. of patient	No.of pregnancy achieved	No.of multiple pregnancy	Multiple Pregnancy rate
Regimen I CC + HCG	25	8(32%)	1	12.5%
Regimen II	8	4(50)%	1	25.0%

DISCUSSION

Disorders of ovulation accounts for about 30 – 40% of cases of female infertility (Speroff *et al.,* 6th edition). It is one of the treatable causes of infertility. The sequential events occurring in an ovary in the normal menstruating cycle was studied by USG in1979 in Hackeloer. Real time ovarian ultrasound provides a direct visualization of the developing follicle as well as the disappearance of the follicle at the time of oocyte release. It is a quick and easy method to directly view ovarian follicle development, is non-invasive, requires a short time and has no known harmful effects to the oocyte or reproductive tract. Serial ultrasound can be used to monitor follicular growth and determine when ovulation occurs. Year 1960 brought a revolution in the medical management of infertility. Clomiphene citrate was synthetized in 1956, introduced for clinical trial in 1960, as ovulation inducing agent. It was approved for clinical used in the United States in 1967. Since that time constant research are going on different molecule method to be used as ovulation inducing agent in infertile women. The present study was undertaken to study the follicular dynamics in women who has spontaneous ovulation as well as in women with anovulation after induction of ovulation. In follicular dynamic study, the following parameter were compared in both spontaneous and induced cycle.

1. Size of the follicle
2. No. of follicle
3. Growth rate of follicle
4. Endometrial thickness

After induction of ovulation by different regimens, the ovulation, the

-Ovulation rate
-Pregnancy rate
-Multiple pregnancy
-OHSS was studied

The result were as follows in Table I.

Table I: Out of 50 cases included in the present series 72% were of primary infertility and 28% were of secondary infertility. The incidence of primary infertility has been reported to be more than that of secondary infertility.

Table II: In the present series of our study, majority of the women 60% were between 21-30 yrs. Of age (mean age – 25.5yrs). Peterson and Bhrman found the median age of patients in their series to be 25.4 yrs.

The influences of age on fertility is significant because the patients below 30 yrs. Of age have better chance of conceiving.

Table III: In present study the period of infertility ranged from 1 to 10 yrs with maximum number having a duration of 3 to 6 years. Mathews Duncan (1934) however, postulated that failure of conception after attending to conceive for one year is enough ground for investigating due case of infertility.

Table IV: In our study majority of the patients were of primary infertility and therefore they presented with oligomenorrhoea which could be due to the associated condition like PCOD, Hyperprolactinaemia, Tuberculosis and hypothyroidism.

Table V: The various tests were done to know the cases of infertility. Husband's seminal fluid analysis was done in all case to detect male factor infertility. Post coital tests were done cases of male factor infertility and in unexplained infertility.

Table VI: In our present study, anovulation was found to be the commonest cause (50%). This observations in accordance with the incidence reported by Novak et al, 13th edition (30-40%)and by Lunenfeld and Incler(10-50%).

Table VII: The analysis of causes of anovulation was done after evaluating the history, clinical examination, ultrasonography and hormonal assay. The commonest cause of anovulation was found to be polycystic ovarian disease (24%).

Table VIII: Serial Ultrasonography (TVS) was done from D10 of cycle onwards for detection of ovulation. In the present study ovulation was detected in 50% of cases.

Table IX: In present series of study leading follicular diameter was significantly larger in stimulated cycles as compared to the spontaneous cycles. The present study is consistent with the studied of Randall *et al.* (1991)

Table X: All spontaneous cycles, were monofollicular and were ovulatory with collapse and formation of corpus luteum. In the clompiphene induced cycles in present study multifollicular development occurred with average number of follicles >16 mm was 2.5 and rupture of at least done pre ovulatory follicles.

Table XI: Endometrial thickness increased from 0.750 cm to 1 cm from 3 days prior to ovulation to the day of ovulation. This phase shower linear growth with average growth rate of 0.083 cm/day.

Table XII: The average length of clomiphene induced cycle in present study was 29± 1 days whereas in spontaneous cycle it was reduced (27± 2days).

Conclusion

Anovulation and ovulatory dysfunction are important factors in the aetiology of infertility. Follicular dynamics study by serial Ultrasonography is useful for monitoring patients undergoing ovulation induction. It is a quick and easy method to directly view ovarian follicle development. It is non-invasive, requires a short time and has no known harmful effects to the oocyte or reproductive tract. It helps in prediction of timing of ovulation. The correct prediction of timing of ovulation is critical for infertility therapies such as intrauterine insemination, artificial or therapeutic insemination using donor sperm and the timing of intercourse.

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