IMPORTANCE OF PERIFOLLICULAR VASCULARITY IN PREDICTING OUTCOME IN INTRA UTERINE INSEMINATION CYCLES

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ABSTRACT

BACKGROUND

Intrauterine insemination (IUI) is usually used in the infertility treatment to get a better pregnancy rate. The common conditions where it is used are unexplained infertility, endometriosis, polycystic ovarian syndrome & male factor infertility. Various approaches have been suggested to increase the pregnancy rate in IUI cycles, e.g. double insemination, identification of conception cycles with use of colour Doppler sonography and prevention of premature LH surge. The capillary network of preovulatory follicles have been found to be more extensive in comparison to other follicles. The use of power Doppler in assessing perifollicular blood flow can be used to determine the quality of the oocyte. This information helps to predict the success of ART cycles.

Aims and Objectives- The aim of this study was to assess if we can use perifollicular vascularity in a follicle in IUI cycles to predict treatment outcome.

Settings & Design- Prospective Observational study.

MATERIALS AND METHODS

The study included 178 consecutive IUI cycles. The perifollicular blood flow on the day of HCG was measured. According to the power Doppler signal, the patients were divided into 3 groups. Group A consisted of patients with a perifollicular blood flow of 76% to 100%. Group B with a perifollicular blood flow of 51% to 75% & Group C with a perifollicular blood flow of 0% to 50%. Clinical pregnancy rates were compared.

Statistical Analysis- Statistical analysis was done using MEDCALC software. Data was statistically analysed by using Student's 't' test. Proportions were analysed using the chi-square test. Results were expressed as mean and standard error of the mean. $p < 0.05$ was considered a statistically significant difference.

RESULTS

In our study, clinical pregnancy occurred in 17 patients in Group A with a clinical pregnancy rate of 21% whereas 4 cases had a clinical pregnancy in Group B with a clinical pregnancy rate of 6.6%. No clinical pregnancy was reported in Group C. There was significant statistical difference between the 3 groups as per the pregnancy rate.

CONCLUSION

Perifollicular vascularity assessment by transvaginal power Doppler ultrasonography plays a great role in predicting the outcome of stimulated IUI cycles.

KEY WORDS

Power Doppler, Perifollicular Vascularity, Pregnancy Rate

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BACKGROUND

Intrauterine insemination (IUI) is usually used in infertility treatment to get a better pregnancy rate. The common conditions where it is used are unexplained infertility, endometriosis, polycystic ovarian syndrome & male factor infertility. The aim of this modality of treating infertile patients is to increase the number of available ova to the spermatozoa at the site of fertilization.

Various approaches have been suggested to increase the pregnancy rate in IUI cycles. These include: double

insemination, identification of conception cycles with use of colour Doppler sonography and prevention of premature LH surge and use of different ovarian stimulation protocols.

Several studies have proven that neovascularization occurs during the growth and selection of ovulatory follicles. Capillary permeability is also increased during follicular development. Neovascularisation also plays a great role in the corpus luteum development and function. The preovulatory follicles have an extensive capillary network in comparison to other follicles.⁽¹⁾ So it has been proposed that initiation and maintenance of follicular growth depends on the follicular microvasculature development.

Due to the extensive capillary network a greater level of the intrafollicular level of oxygen and vascular endothelial growth factor (VEGF) is available to the dominant follicle. The health of the developing oocyte is thus influenced. Studies have shown that the vascularity of the follicle from which the oocyte is retrieved during IVF influences the viability of the embryo.⁽²⁾ Colour Doppler can be used to assess follicular vascularity.⁽³⁾ But the drawback of Colour Doppler is that any flow perpendicular to the probe would not be displayed. To

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overcome this problem Power Doppler has been introduced. In Power Doppler, the intensity or amplitude of the Doppler signal is assessed. The amplitude of Doppler signal is generated by the signal intensity of the red blood cells within a vessel, which is almost independent of angle of insemination. As a result, Power Doppler can display flows with lower velocities and volumes. Another advantage of Power Doppler is that unlike conventional Colour Doppler it is not affected by aliasing and can display perfused regions where the mean velocity is zero.⁽⁴⁾ Visualization of small vessels is improved by these factors. Therefore several studies have used the information obtained by use of power Doppler for assessing perfollicular blood flow to determine the quality of the oocyte and to predict the potential success of ART cycles.^(5,6)

Objective

The aim of this study was to assess if we can use perfollicular vascularity in a follicle in IUI cycles to predict treatment outcome.

MATERIALS AND METHODS

The study was conducted at Ray Hospital & Test Tube Baby Centre from January 2015 to December 2015. One hundred seventy-eight infertile couples meeting the inclusion criteria were included in the study. Written informed consent was obtained from all couples. The study was approved by the local ethics committee. Inclusion criteria was-

- At least 5 million/mL sperm count and 5% normal morphology according to strict Kruger's criteria.
- Unexplained infertility.
- Minimal or mild endometriosis.
- Bilateral tubal patency and normal uterine cavity as confirmed by either Hysterosalpingography or diagnostic hysteroscopy & laparoscopy.
- Previous maximum 2 cycles of IUI.
- Regular menstrual cycle.
- Day 2 FSH ≤ 10 IU/L.
- Normal levels of prolactin and thyroid stimulating hormone.
- Patients with following conditions were excluded from the study.
- Age ≥ 35 years.
- Endometriosis Stage III/IV.
- PCOS.
- Tubal factor like unilateral tubal patency or hydrosalpinx.

Basal scan was done in all cases on second day of cycle to rule out presence of ovarian cyst before starting ovarian stimulation. Clomiphene citrate 50 mg was started from 2nd day of periods and continued for 5 days. It was followed by HMG (human menopausal gonadotropin) 75 IU intramuscular injections. All patients were followed up with serial ultrasounds on alternate day starting from day 7, till administration of hCG (Human chorionic gonadotropin) injection. Transvaginal ultrasound was performed in each case with a ultrasound machine having power Doppler facility (Voluson P8, Wipro GE). The follicle was measured in two maximum diameters and mean was calculated. Power Doppler color was placed over each ovarian follicle measuring ≥ 17 mm. Perfollicular blood flows were studied.

According to the perfollicular blood flow in the dominant follicle, the patients were divided into 3 groups. Group A consisted of patients with a perfollicular blood flow of 76% to 100%. Group B with a perfollicular blood flow of 51% to 75% & Group C with a perfollicular blood flow of 0% to 50%. When the dominant follicle reached 17 mm in diameter, triggering of ovulation was done by injection HCG 5000 I.U.

Single intra uterine insemination was performed after preparing the semen by double density gradient technique. IUI was done 36-38 hrs. after hCG injection. Micronized vaginal progesterone 400 mg. twice daily was used for luteal support in all groups. Presence of gestational sac was confirmed by transvaginal sonography after 20-25 days of IUI. TVS was repeated at appropriate time to confirm viability. We defined clinical pregnancy as ultrasound visualization of at least one gestational sac with or without cardiac activity. Luteal support continued till 12 weeks.

Primary Outcome Measure was Clinical Pregnancy rate.

Secondary Outcome Measures were-

1. Endometrial thickness.
2. Number of dominant follicles.

Statistical Analysis

Statistical analysis was done using MEDCALC software. Data were statistically analysed by using by Student's t test. Proportions were analysed using the chi-square test. Results were expressed as mean and standard error of the mean. $P < .05$ was considered a statistically significant difference.

RESULTS

We studied a total of 178 women undergoing consecutive IUI cycles. Group A consisted of 81 patients, whereas Group B consisted of 61 patients and Group C consisted of 36 patients. No statistically significant difference was observed between the three groups as regarding age, body mass index (BMI). We could not find any statistically significant difference between the three groups as regarding number of follicles, diameter of follicles, endometrial thickness on the day of hCG administration (Tables 1, 2, 3) and the number of days from starting stimulation till day of IUI.

In our study, clinical pregnancy occurred in 17 patients in Group A with a clinical pregnancy rate of 21% whereas 4 cases had a clinical pregnancy in Group B with a clinical pregnancy rate of 6.6%. No clinical pregnancy was reported in Group C.

There was statistically significant difference between the 3 groups as regarding the pregnancy rate. (Tables 4, 5).

	Group A	Group B	p-Value
Age	27.8 $\pm$ 4.6	27.5 $\pm$ 4.1	0.68
BMI	27.1 $\pm$ 2.1	27.2 $\pm$ 2.4	0.79
No. of Follicles	1.8 $\pm$ 0.7	1.7 $\pm$ 0.4	0.31
Size of Follicles	19.8 $\pm$ 3.8	18.7 $\pm$ 3.1	0.07
Endometrial Thickness	9.7 $\pm$ 1.1	9.5 $\pm$ 1.3	0.32
Day of IUI	14.5 $\pm$ 1.6	14.3 $\pm$ 1.8	0.48
Table 1			

	Group A	Group C	p-Value
Age	27.8 ± 4.6	28.5 ± 4.5	0.45
BMI	27.1 ± 2.1	26.4 ± 2.1	0.1
No.of Follicles	1.8 ± 0.7	1.6 ± 0.7	0.16
Size of Follicles	19.8 ± 3.8	19.2 ± 3.0	0.040
Endometrial Thickness	9.7 ± 1.1	9.4 ± 1.3	0.20
Day of IUI	14.5 ± 1.6	14.4 ± 1.2	0.73

Table 2

	Group B	Group C	p-Value
Age	27.5 ± 4.1	28.5 ± 4.5	0.26
BMI	27.2 ± 2.4	26.4 ± 2.1	0.1
No.of Follicles	1.7 ± 0.4	1.6 ± 0.7	0.37
Size of Follicles	18.7 ± 3.1	19.2 ± 3.0	0.43
Endometrial Thickness	9.5 ± 1.3	9.4 ± 1.3	0.71
Day of IUI	14.3 ± 1.8	14.4 ± 1.2	0.76

Table 3

	Group A	Group B	p-Value
n	81	61	
Clinical Pregnancy	17	4	
Pregnancy Rate/Cycle (%)	21	6.6	0.017

Table 4

	Group A	Group C	p-Value
n	81	36	
Clinical Pregnancy	17	0	
Pregnancy Rate/Cycle (%)	21	0	0.003

Table 5

DISCUSSION

In our study, clinical pregnancy occurred in 17 patients in Group A with high grade vascularity with a clinical pregnancy rate of 21% whereas 4 cases had a clinical pregnancy in Group B with medium grade vascularity with a clinical pregnancy rate of 6.6%. No clinical pregnancy was reported in Group C. There is a statistically significant difference in pregnancy rates. Intrafollicular oxygen levels provided by adequate blood supply determines the quality of oocyte. Several studies have demonstrated that the developmental competence of oocytes⁽⁷⁾ and subsequent embryos,^(2,8) have been associated with follicular vascularity. This could be the cause for the differences in pregnancy rates between the vascularity groups.

Our study correlates well with previous studies, who have demonstrated a better pregnancy rate with increase in perifollicular vascularity.^(9,10,11) The underlying mechanism may be a better quality oocyte associated with a follicle having >75% peripheral blood flow on power Doppler. Hence, PFBF may be used as a valid indirect marker of oocyte quality.⁽¹²⁾

The low perifollicular vascularity is the cause of hypoxia which is responsible for an increased incidence of aneuploidal oocytes. Studies have confirmed this phenomenon by finding that oocytes derived from follicles with low grade vascularity resulted in a significantly higher proportion of aneuploid embryos when compared to those derived from follicles with high grade vascularity.^(13,14)

Perifollicular blood flow appears to be an important factor in determining the outcome of stimulated IUI cycles. We have found no pregnancy in the women with low grade vascularity. So, the identification of these cycles would be very helpful in counselling the couple regarding the outcome of the treatment.

CONCLUSION

Perifollicular vascularity assessment by transvaginal power Doppler ultrasonography plays a great role in predicting the outcome of stimulated IUI cycles.

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