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The Impact of Three-Dimensional Ultrasound of Endometrial Thickness and Volume on ICSI Outcome

[1]M.D. Mahtab Zeinalzadeh, [1]M.D. Yousefreza Yousefnia-Pasha, [2]M.D. Zinatossadat Bouzari, [3]M.D. Ashraf Mahbobi, [1]Maedeh Mohammadnetaj and [4]Masoumeh Golsorkhtabar-Amiri

[1]Fatemezahra Infertility and Reproductive Health Research Center
[2]Cellular and Molecular Biology Research Center, Babol University of Medical Sciences, Babol, Iran
[3]Radiology and Sonography Department, Babol University of Medical Sciences, Babol, Iran
[4] Mazandaran University, Iran

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Abstract: Objectives: One of the most effective elements in the success of Intra Cytoplasmic Sperm Injection (ICSI) is favorable endometer. Our study was designed to find the correlation of three-dimensionally measured endometrial volume and thickness and pregnancy outcome in the women undergone ICSI. *Methods and materials:* This cross-sectional study was conducted by reviewing 62 patients' obstetric records undergone ICSI in age <37 yr. The endometrial thickness and volume were assessed by 3D transvaginal ultrasound at the day of Human chorionic Gonadotropin(HCG) injection. Correlation between the endometrial thickness and volume with outcome of pregnancy were evaluated and the data was analyzed. Results: The overall pregnancy rate was 26%. Mean of the endometrial thickness and volume at the day of HCG administration in the women who conceived were 11.31±2.49mm, 6.62±4.23ml respectively. Multivariate logistic regression analysis was shown that there were no significantly associations between endometrial thickness and volume with the pregnancy outcome. Conclusion: The results of the present study reveal that at least 11mm endometrial thickness and 5ml endometrial volume require achieving conception at ICSI cycles.

Key words: Intracytoplasmic sperm injection · Three-dimensional ultrasound · Endometer · Pregnancy rate

INTRODUCTION

Although assisted reproductive technology (ART) such as In Vitro Fertilization (IVF) and Intracytoplasmic Sperm Injection (ICSI) have been developed, however, implantation rates per embryo transfer have remained in the low range [1-2]. Some researchers believed happening a pregnancy depends on the coordination between endometrial receptivity and embryo factors [3]. The assessment of embryo quality and proper grading of embryos for transfer is easily determined by ART lab, while the evaluation of endometrial receptivity is complicated [1]. Transvaginal ultrasonography has enhanced the visualization of the endometer to evaluate its improvement. [4] It is an ideal non- invasive method but lack of specificity [1, 5]. A study reported using 3D ultrasonography to estimate endometrial volume and thickness at the day of HCG injection can be a good predictor of IVF outcome [1].

In this query, we investigated the role of three dimensionally measured endometrial volume and thickness as a predictor of endometrial receptivity on the ICSI outcome.

METHODS AND MATERIAL

This cross-sectional observational study was conducted by reviewing 62 patients' obstetric records undergone ICSI at Fatemezahra Infertility and Reproductive Health Research Center in northern Iran from March 2008 to September 2009.The study was approved by the Ethics Committee of Babol University of Medical Science. Inclusion criteria included all healthy ART candidate women = 37 years old with the infertility

Corresponding Author: Bouzari Zinat, M.D., Ganjafrouz st, Babol University of Medical Science, Babol, Iran.
Tel: +98-9111131229.

causes; male factor, unovulatory cycles and unexplained infertility. Patients with endometriosis, tubal or uterine abnormality, the women with ovarian hyperstimulation syndrome (OHSS) during treatment, the women without mature oocytes after ovulation stimulation (poor responders) and the women with fetus in grade except A and B were excluded from the study. Participants underwent long protocol regime for ovulation stimulation. At the time of HCG injection, a 3 dimentional transvaginal sonography and scaning (combined 530D, kretz-technic, zipf, Austria) were done to measure the endometrial thickness and volume.

The Measurement Method in Sonography: After taking a full longitudinal observation, the endometrial thickness was measured at the point of maximum thickness; endometrial-myometrial junction. Measurement involved both layers of endumetrium (covering layer with Low-amplitude considered exception). On the B mode, the 3dimentional volume and area point was determined by a movable probe (7.5 MHZ transducer). The section was an incomplete pyramidal shape which was not adjusted automatically to determine the whole endometrial cavity volume in minimum time, so we set it manually. Then, the slow volume acquisition setting using high resolution was activated. All the sonographic measurements were done by the same radiologist for volume calculation. The total information was compared with a predetermined image. Page A, B, C showed respectively a transverse, longitudinal and frontal image.

The time of embryo transfer, the number of bastosyst and the morphologic grade of each embryo were recorded. 48 hours after picking up the oocytes, 2-3 embryos in good quality were transferred. Progesterone vaginal suppositories (Cyclogest 400mg, Actavis Group, Iceland) twice a day were daily prescribed for 16 days (Actavis Group, Iceland). The criterion for implantation was defined according to a positive β HCG (> 10 IU) 16 days after embryo transfer and also its rising level at 2 following days. Additionally, Clinical pregnancies were defined by β HCG value > 100 UI and visualization of a gestational sac on ultrasound examination 4-6 weeks after oocyte retrieval.

Data were collected and analyzed by software version 18. Statistical analysis performed with the fisher exact test, chi-square test and Student T-test. Statistical significance was considered at $p \leq 0.05$. Multivariate logistic regression analysis was performed to predict the favorable level of endometrial thickness and volume in the pregnancy outcome.

RESULTS

Out of 62 participants in this study, 7 women were excluded; 1 because of having no mature oocytes, 2 having low grade embryos and 5 women involved OHSS during the treatment. Finally, 50 patients followed up. From the investigated cases, only 26% [13] patients were pregnant and 74% [37] patients failed in pregnancy. The etiology of infertility of the patients included male factors (44%), female factors (36%), both female and male factors (16%) and unexplained infertility (4%). Sperm analysis of the partners of women showed the mean concentration of spermatozoa was 41.9±39.99 million/ml and the mean of motility of spermatozoa was 56.30± 39.36.

Table 1 shows demographics, stimulation parameters and embryo transferred in ICSI cycles of the pregnant and nonpregnant groups.

Comparison of the mean endometrial thickness and endometrial volume in the pregnant with the non pregnant women demonstrated in Table 2. There is no significant difference between the two groups.

Table1: Comparison of demographic, stimulation and embryo parameters in pregnant and nonpregnant women conceived by ICSI

Parameter	Mean±SD	Mean±SD	p
Age(yr)	27.54±5.25	29.19±5.84	0.374
No. of previous ART cycle	1.85±1.67	1.59±1.49	0.616
Days of stimulation	10.85±2.23	10.43±2.46	0.597
No. of FSH(ampoules)	31.31±9.84	33.05±15.92	0.713
Endometrial thickness at HCG day (mm)	11. 31±2.49	10.57±2.65	0.384
Endometrial volume at HCG day (ml)	6.62±4.32	6.01±4.07	0.649
No. of transferred embryos	0.44	1	0.742

FSH= Follicular Stimulating Hormone, ICSI= Intracytoplasmis Sperm Injection

Table 2: Comparison of endometrial thickness and volume in the pregnant and non pregnant women

Parameter	Pregnant	Non pregnant	P-value
Endometrial thickness	11.31±2.49	10.57±2.65	0.64
Endometrial volume	6.61±4.23	6±4.07	0.38

Table 3: Rate of pregnancy at different endometrial thicknesses in our groups under study

Endometrial thickness on the day of HCG	Pregnant(n)	Non pregnant(n)	Pregnancy rate (%)	P	OR	95%CI
<9 mm	3	15	0.17	0.32	2.27	0.53- 9.66
9 mm≥	10	22	0.31			
10mm<	6	18	0.25	0.87	1.1	0.31- 3.9
10mm≥	7	19	0.27			
11mm<	6	28	0.18	0.08	3.63	0.96- 13.64
11mm≥	7	9	0.44			

Table 4: Pregnancy rates at different endometrial volumes in the groups under study

Endometrial volume on the day of HCG	Pregnant(n)	Non pregnant(n)	Pregnancy rate (%)	P	OR	95%CI
<5 ml	4	15	0.21	0.74	1.53	0.39±5.9
≥5 ml	9	22	0.29			
6ml<	8	23	0.25	1	1.02	0.28±3.76
≥6ml	5	14	0.26			
7ml<	9	27	0.25	1	1.2	0.3±4.78
≥7ml	4	10	0.28			

Multivariate logistic regression analysis showed the pregnancy rate improved with endometrial thickness; although, there were no significantly correlation between the endometrial thickness and volume with the pregnancy outcome. The estimated odds ratio (OR) for the successful pregnancy with each additional millimeter of endometrial thickness was 1.16 (95%CI 0.8- 1.69; P = 0.41) and for the successful pregnancy with each additional milliliter of endometrial volume was 0.96 995% CI 0.76- 1.21; P= 0.73). The pregnancy rates improved when the endometrial thickness was = 11mm and also, the endometrial volume was =5ml respectively (Table 3, 4).

DISCUSSION

We failed to find a relationship between endometrial thickness and endometrial volume in the pregnant compared with non pregnant women.

Although, Yaman reported in a quest that two-dimensional ultrasound is a reliable method for evaluation of the female pelvic, but a mean absolute error rate of 12.6% for two-dimensional volume measurement has been reported [6].

Some studies are not consistent with our study and have shown that three dimensional ultrasound measurements of endometrial thickness and endometrial volume can be a predictor of pregnancy in ART cycles [4, 7]. Martins *et al* investigated the endometrial volume and thicknesses were significant higher in the pregnant women. No pregnancy was achieved in women who had an endometrial volume <3.8 ml or endometrial thickness < 7.9 mm in his study [7]. Maybe the difference in the results of his study and us are related to our study samples which were greater than Martins' query.

Also, Alghamdi *et al* found a correlation between endometrial thickness and pregnancy outcome and demonstrated these factors can be work as the prognostic factors [10].

Kovacs *et al* concluded that the improving thickness of endometer is correlated with pregnancy outcome and can be a reliable prognosis singly. This inconsistency between our study and Kovacs' and alghamdi' researches may be due to the further number of ICSI cycles in their studies which were not matched in some variables. In our study, the cases were matched according to infertility causes, age and quality of embryo, so they seem limited. Despite Kovacs, Hartman reported the endometer volume is more valuable predictor versus the endometer thickness for pregnancy outcome. He recommended the embryo

transfer should be cancelled in volume <2mm and thickness <8mm. Hence, the embryo should be freeze and maintain for the following cycles. [11] Our main difference with Hartman is choosing of two diverse days for sonograghy. It should be mentioned we chose the day of sonograghy at the day of HCG injection, because, we could easily evaluate and manage mature endometer at the day of HCG injection, while it could not be possible at the day of oocyte retrieval.

Some studies are in consistent with our research. Aboulghar studied on 103 women and divided them according to endometrial volume in the 3 subgroups; < 2ml, 2-4ml and >4 ml and also, endometrial thickness in the 3 groups; <8mm, 8-12mm and >12mm. No significant differences were seen in the pregnancy rates among all groups regarding to the endometrial volume and thickness [1].

It appeared the use of endometrial thickness was more reliable than endometrial volume to predict pregnancy, although we found statistical significant differences between neither endometrial thickness nor endometrial volume with the rate of pregnancy in our cases. Our mean endometrial thickness and volume in the pregnant women were 11.31±2.49mm, 6.62±4.23 ml respectively. Schild and colleague in their study on 47 patients showed mean endometrial thickness and volume (±SD) in the pregnant women were 10.8±2.3mm, 4.9±2.2ml respectively [8]. However, these differences may be in the result of the diversity of the days of sonography in two studies. It should be mentioned that Aboulghar *et al* and Schild *et al* demonstrated measurements of the endometrial thickness and volume at the day of HCG administration, oocyte retrieval and also the day of embryo transfer can anticipate the pregnancy outcome. [1, 2].

CONCLUSION

Although, we found no correlation between 3-dimensionally ultrasound measured endometrial thickness and volume at the day of HCG administration but the present study identified at least 11mm endometrial thickness and 5ml endometrial volume require to occur a successful pregnancy at the ICSI cycles.

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