Early endometrial changes following successful implantation: 2 and 3-dimensional ultrasound study

E. Zohav, *M.D.*; **I. Bar-Hava,** *M.D.*; **S. Meltcer,** *M.D.*; **J. Rabinson,** *M.D.*; **E.Y Anteby,** *M.D.*; **R. Orvieto,** *M.D., MMSc*

Department of Obstetrics and Gynecology, Barzilai Medical Center, Ashkelon, Israel, and Ben-Gurion University, Beer Sheva (Israel)

Summary

Objective: To study of the possible role of ultrasound (US) measurements of the endometrium in the prediction of IVF outcome. *Patients and Methods:* 28 infertile women underwent US measurements of endometrial thickness and volume on day of ET and two weeks later. US measurements were compared between day of ET and two weeks later, and between those who conceived and those who did not. *Results:* While in the group of patients who conceived (n = 7) endometrial thickness and volume rose significantly between day of hCG and two weeks later, no differences were observed in patients (n = 21) who did not. *Conclusion:* The dynamic changes in endometrial volume and thickness between day of ET and two weeks later may predict IVF treatment outcome.

Key words: Endometrial volume; 3-D ultrasonography, Prediction; ET; IVF.

Introduction

Pelvic ultrasound (US) imaging [1] and serum hCG measurements [2, 3] are part of the routine follow-up after in-vitro fertilization (IVF) or intracytoplasmic sperm injection (ICSI) treatments. While hCG measurements are reliable as early as 11 or 12 days after embryo transfer (ET), pelvic US may visualize a gestational sac only 17-21 days after ET.

The recent advent of computerized three-dimensional (3D) US systems has led to improvement in the quality and precision of US examination. Moreover, this tool allowed endometrial volume estimation with a high degree of reproducibility [4]. While, few studies have examined the role of 3D endometrial volume on the day of hCG administration [5], oocyte pick-up (OPU) [6], embryo transfer (ET) [7] or one week later (mid-luteal phase) [8] in the prediction of IVF outcome, only one study has assessed its role during early pregnancy [9].

We therefore aimed to evaluate whether US measurements of endometrial thickness and volume differ between day of ET and two weeks later and whether this difference may predict IVF outcome.

Patients and Methods

The study population included 28 infertile women who have been treated in our IVF unit. During the routine follow-up patients underwent 2D and 3D US (VDW5-8B Probe, Volusone 530D MT, Medison-Kretz) transvaginal measurements of endometrial thickness and volume on day of ET and two weeks later. The study was approved by the institutional Clinical Research Committee.

Patients were classified according to hCG results into two further groups, those who conceived and those who did not. US measurements were compared between day of ET and two weeks later, and between those who conceived and those who did not.

The results are expressed as means and standard deviations. The statistical analysis was performed with the Student's *t*-test; $p < 0.05$ was considered significant.

Results

Twenty-eight patients were included in the study. In the whole study group no differences were observed in endometrial volume and thickness between day of ET and two weeks later.

Of the 28 patients, seven conceived. While in the group of patients who conceived endometrial volume and thickness rose significantly ($p < 0.02$, for both) between day of ET and two weeks later, no differences were observed in patients who did not (Table 1). Moreover, while comparing the mean differences in endometrial volume and thickness between day of ET and two weeks later, patients who conceived showed a significantly ($p < 0.002$) higher mean difference as compared to those who did not (Table 1).

In addition, while endometrial volume and thickness measurements two weeks following ET, were significantly higher in those who conceived as compared to those who did not ($p < 0.0.1$ for all), no between-group differences were observed on day of ET (Table 1).

Discussion

In the present study, in patients undergoing IVF, US measurements of the endometrium between day of ET and two weeks later, showed dynamic changes, which were unique only to patients who conceived. These changes reflect successful implantation, and the subse-

Revised manuscript accepted for publication March 20, 2008

Table 1. — *US measurements of endometrial thickness and volume (mean ± SD) in patients who conceived and those who did not.*

	Patients who conceived (n = 7)			Patients who did not conceive (n = 21		
	Day of ET	2 weeks following ET	Mean differences	Day of ET	2 weeks following ET	Mean differences
US endometrial thickness (mm)	11.7±1.2	15.7±3.7[a]	4.5±3.08[c]	10.2±3.01	8.7±3.5[b]	-1.31±3.9
(range)	(10-13)	(9.5-20)	(-0.5-7)	(5.1-13.5)	(3-13.3)	(-7.5-3.6)
US endometrial volume (ml)	4.5±2.9	8.9+2.9[a]	5.7±3.09[c]	3.0±2.0	2.7±2.0[b]	-0.09±2.4
(range)	(2.5-10.1)	(4.25-12.2)	(1.66-8.5)	(0.83-5.5)	(0.27-8.4)	(-2.6-3.5)

[a]$p < 0.02$ when compared to day of ET; [b]Non significant difference, when compared to day of ET; [c]$p < 0.002$ when compared to patients who did not conceive.

quent induced changes at the endometrial level. Although endometrial thickness rose as well, the most significant change was found in endometrial volume, which doubled from an average of 4.7 ml on the day of ET to 8.9 ml, two weeks later.

Rabinowitz *et al.* [10] observed a slower linear growth of the endometrium through the luteal phase of an IVF cycle, with a subsequent accelerated growth in conception cycles as compared with non-conception cycles. However, in their excellent review of the literature, Friedler *et al.* [11] have comprehensively described the controversy between studies comparing the mean endometrial thickness in conception and non-conception cycles and concluded that at present, insufficient data exist describing a linear correlation between endometrial thickness and the probability of conception.

To the best of our knowledge, we present the first report demonstrating dynamic changes in US measurement of endometrial thickness and volume between day of ET and two weeks later and before the appearance of a visible gestational sac. Moreover, these changes could predict IVF outcome. Further studies are needed to evaluate the role of US measurements of endometrium at different stages of IVF treatment and their role in the prediction of treatment outcome.

References

[1] Cacciatore B., Tiitinen A., Stenman U.H., Ylostalo P.: "Normal early pregnancy: serum hCG levels and vaginal ultrasonography findings". *Br. J. Obstet. Gynaecol.*, 1990, *97,* 899.

[2] Sugantha S.E., Webster S., Sundar E., Lenton E.A.: "Predictive value of plasma human chorionic gonadotrophin following assisted conception treatment". *Hum. Reprod.,* 2000, *15,* 469.

[3] Poikkeus P., Hiilesmaa V., Tiitinen A.: "Serum HCG 12 days after embryo transfer in predicting pregnancy outcome". *Hum. Reprod.*, 2002, *17,* 1901.

[4] Kyei-Mensah A., Maconochie N., Zaidi J., Pittrof R., Campbell S., Tan S.L.: "Transvaginal three dimensional ultrasound: reproducibility of ovarian and endometrial volume measurements". *Fertil. Steril.*, 1996, *66,* 718.

[5] Yaman C., Ebner T., Sommergruber M., Polz W., Tews G.: "Role of three-dimensional ultrasonographic measurement of endometrium volume as a predictor of pregnancy outcome in an IVF-ET program: a preliminary study measurement". *Fertil. Steril.,* 2000, *74*, 797.

[6] Schild R.L., Indefrei D., Eschweiler S., van der Ven H., Fimmers R., Hansmann M.: "Three dimensional endometrial volume calculation and pregnancy rate in an in-vitro fertilization program". *Hum. Reprod.*, 1999, *14*, 1255.

[7] Raga F., Bonila-Musoles F., Casan E.M., Klein O., Bonilla F.: "Assessment of endometrial volume by three-dimensional ultrasound prior to embryo transfer: clues to endometrial receptivity". *Hum. Reprod.*, 1999, *14,* 2851.

[8] Martins W.P., Ferriani R.A., dos Reis R.M., Nastri C.O., Filho F.M.: "Endometrial thickness and volume by three-dimensional ultrasound one week after embryo transfer to detect pregnancy". *J. Assist. Reprod. Genet.,* 2007, *24,* 155.

[9] Zohav E., Orvieto R., Anteby E.Y., Segal O., Meltcer S., Tur-Kaspa I.: "Low endometrial volume may predict early pregnancy loss in women undergoing in vitro fertilization". *J. Assist. Reprod. Genet.*, 2007, *24,* 259.

[10] Rabinowitz R., Laufer N., Lewin A., Navot D., Bar I., Margalioth E.J., Schenker J.J.: "The value of ultrasonographic endometrial measurement in the prediction of pregnancy following in-vitro fertilization". *Fertil. Steril.*, 1986, *45,* 824.

[11] Friedler S., Schenker J.G., Herman A., Lewin A.: "The role of ultrasonography in the evaluation of endometrial receptivity following assisted reproductive treatments: a critical review". *Hum. Reprod. Update*, 1996, *2,* 323.

Address reprint requests to:
E. ZOHAV, M.D.
Department of Obstetrics and Gynecology
Barzilai Medical Center,
78278 Ashkelon (Israel)
e-mail: zohav@barzi.health.gov.il