IMPACT OF THIN ENDOMETRIUM ON IVF

R. Frydman, F. Lamazou

Univ Paris-Sud, Clamart

AP-HP, Service de Gynécologie-Obstétrique et Médecine de la Reproduction, Hôpital Antoine Béclère, Clamart, France

Thin endometrium defined is frequent problem observed in ART. In different studies, a thin endometrium is defined by a thickness inferior to 5 to 8 mm and should be a possible complication of surgical curettage (Shufaro et al. 2008). Thin endometrium reduced PRs in relatively young patients (<38 years old), in patients who required more than 10 days of gonadotropin stimulation, or in patients whose embryo transfers consisted of poor quality embryos (Zhang et al 2005, Hassan et al. 1996, Dix et al. 2009). Basir et al. (2002) report an important intercycle reliability that should offer the possibility to determine before the IVF-ET the implantation failure.

Different treatments have been proposed to improve the ART outcomes like the use of triptorelin 0.1 mg on the day of ovum pickup (OPU), on the day of embryo transfer (ET) and three days thereafter (Qublan 2008), or extended estrogen therapy for 14 to 82 days (Chen et al. 2006), or Vitamin E, larginine, or sildenafil citrate treatment (Takasaki et al. 2010, Sher 2000, 2002). But the impact of sildenafil acetate remain discussed (Check et al. 2004). A thin endometruim is also the actual hypothesis explaining the lower implantation rate in In Vitro Maturation (IVM) (Holzer 2007, Child 2003) but the use of HMG or oestradiol didn't improve the pregnancy rate during the ovum pickup cycle (Elizur et al. 2009).

However the good question is there a thin endometrium or a low endometrium volume? The new trend of 3-dimensionnal ultrasound offers new possibilities in endometrium exploration. A low endometrial volume is defined by < 2.5 ml. The global idea concerning the endometrium development is that endometrium growth is dependant of its vascularity. Ng et al. (2009) have show that endometrial and subendometrial vascularity measured by 3D power Doppler ultrasound was significantly lower (P <or= 0.003) in patients with low volume endometrium, but not in those with thin endometrium. And Merce et al. (2008) conclude that Endometrial volume and 3D power Doppler indexes are statistically significant in predicting the cycle outcome. But this point needs several studies to be confirmed.

The next step will be to understand the physiology of this type of endometruim: their implantation rates are weak but not to zero. The study of cytokines environment should be explored more further to conclude to the receptivity potential of these patients (Ledee et al. 2008, 2007, Dekel et al. 2010) as the genetic aspect (Munro et al. 2010).

Basir GS, O WS, So WW, Ng EH, Ho PC. Evaluation of cycle-to-cycle variation of endometrial responsiveness using transvaginal sonography in women undergoing assisted reproduction. Ultrasound Obstet Gynecol. 2002 May;19(5):484-9. • Check JH, Graziano V, Lee G, Nazari A, Choe JK, Dietterich C. Neither sildenafil nor vaginal estradiol improves endometrial thickness in women with thin endometria after taking oral estradiol in graduating dosages. Clin Exp Obstet Gynecol. 2004;31(2):99-102. • Chen MJ, Yang JH, Peng FH, Chen SU, Ho HN, Yang YS. Extended estrogen administration for women with thin endometrium in frozen-thawed in-vitro fertilization programs. J Assist Reprod Genet. 2006 Jul-Aug;23(7-8):337-42. • Child TJ, Gulekli B, Sylvestre C, Tan SL. Ultrasonographic assessment of endometrial receptivity at embryo transfer in an in vitro maturation of oocyte program. Fertil Steril. 2003 Mar;79(3):656-8. Dekel N, Gnainsky Y, Granot I, Mor G. Inflammation and implantation. Am J Reprod Immunol. 2010 Jan;63(1):17-21. • Dix E, Check JH. Successful pregnancies following embryo transfer despite very thin late proliferative endometrium. Clin Exp Obstet Gynecol. 2010;37(1):15-6. Elizur SE, Son WY, Yap R, Gidoni Y, Levin D, Demirtas E, Tan SL. Comparison of low-dose human menopausal gonadotropin and micronized 17beta-estradiol supplementation in in vitro maturation cycles with thin endometrial lining. Fertil Steril. 2009 Sep;92(3):907-12. • Hassan HA, Saleh HA. Endometrial unresponsiveness: a novel approach to assessment and prognosis in in vitro fertilization cycles. Fertil Steril. 1996 Oct;66(4):604-7. • Holzer H, Scharf E, Chian RC, Demirtas E, Buckett W, Tan SL. In vitro maturation of oocytes collected from unstimulated ovaries for oocyte donation. Fertil Steril. 2007 Jul;88(1):62-7. • Lédée N, Dubanchet S, Oger P, Meynant C, Lombroso R, Ville Y, Chaouat G. Uterine receptivity and cytokines: new concepts and new applications. Gynecol Obstet Invest. 2007;64(3):138-43. • Lédée N, Chaouat G, Serazin V, Lombroso R, Dubanchet S, Oger P, Louafi N, Ville Y. Endometrial vascularity by three-dimensional power Doppler ultrasound and cytokines: a complementary approach to assess uterine receptivity. J Reprod Immunol. 2008 Jan;77(1):57-62. • Mercé LT, Barco MJ, Bau S, Troyano J. Are endometrial parameters by three-dimensional ultrasound and power Doppler angiography related to in vitro fertilization/embryo transfer outcome? Fertil Steril. 2008 Jan;89(1):111-7. Munro SK, Farquhar CM, Mitchell MD, Ponnampalam AP. Epigenetic regulation of endometrium during the menstrual cycle. Mol Hum Reprod. 2010 May;16(5):297-310. • Ng EH, Yeung WS, Ho PC. Endometrial and subendometrial vascularity are significantly lower in patients with endometrial volume 2.5 ml or less. Reprod Biomed Online. 2009 Feb;18(2):262-8. • Qublan H, Amarin Z, Al-Qudah M, Diab F, Nawasreh M, Malkawi S, Balawneh M. Luteal phase support with GnRH-a improves implantation and pregnancy rates in IVF cycles with endometrium of <or=7 mm on day of egg retrieval. Hum Fertil (Camb). 2008 Mar;11(1):43-7. • Senturk LM, Erel CT. Thin endometrium in assisted reproductive technology. Curr Opin Obstet Gynecol. 2008 Jun;20(3):221-8. Sher G, Fisch JD. Effect of vaginal sildenafil on the outcome of in vitro fertilization (IVF) after multiple IVF failures attributed to poor endometrial development. Fertil Steril. 2002 Nov;78(5):1073-6. • Sher G, Fisch JD. Vaginal

sildenafil (Viagra): a preliminary report of a novel method to improve uterine artery blood flow and endometrial development in patients undergoing IVF. Hum Reprod. 2000 Apr;15(4):806-9. • Shufaro Y, Simon A, Laufer N, Fatum M. Thin unresponsive endometrium--a possible complication of surgical curettage compromising ART outcome. J Assist Reprod Genet. 2008 Aug;25(8):421-5. • Takasaki A, Tamura H, Miwa I, Taketani T, Shimamura K, Sugino N. Endometrial growth and uterine blood flow: a pilot study for improving endometrial thickness in the patients with a thin endometrium. Fertil Steril. 2010 Apr;93(6):1851-8. • Zhang X, Chen CH, Confino E, Barnes R, Milad M, Kazer RR. Increased endometrial thickness is associated with improved treatment outcome for selected patients undergoing in vitro fertilization-embryo transfer. Fertil Steril. 2005 Feb;83(2):336-40.