

# COMPARISON OF THE EFFECTS OF ORAL 17β-ESTRADIOL AND ESTRADIOL VALERATE ON ENDOMETRIAL PREPARATION IN FROZEN-THAWED EMBRYO TRANSFER CYCLES AT REPRODUCTIVE-AGED WOMEN WITH REPEATED ART FAILURE

# Anna Sulima, Viktoriya Voronaya

Medical Academy named after S. I. Georgievsky of Vernadsky CFU, Department of Obstetrics, Gynecology and Perinatology № 1, Simferopol, Russia C.I.S.

# What is known already

Failure of frozen-thawed selective blastocyst transfer is often associated with the problems with endometrium. The key factor in determining the ART effectiveness during frozen-thawed selective blastocyst transfer is its adequate preparation. According to existing literature, a subsequent hysteroscopic control scraping of the uterine cavity and histological examination of these patients shows changes of endometrium in 91.4% of cases. Often the inability to overcome the so-called "thin endometrium" leads necessitates surrogate motherhood assistance.

2010 Nobel prize winner R. Edwards: 'Embryo's implantation is the last barrier of an ART' (2006)



### Study question:

Our study aims at comparing the clinical usage effectiveness of oral 17β-estradiol (Femoston® 2/10) 4 mg and estradiol valerate (Proginova®) 4 mg in the course of endometrium preparation for frozen-thawed selective blastocyst transfer.

# Study design & Main results

Study design, size, duration:

The study draws its findings from 220 protocols of frozen-thawed embryo transfer cycles at reproductive age women, where the participating women were divided into two groups. All the patients underwent diagnostic hysteroscopy. Histologically, endometrial pathology was diagnosed in 89.6% of cases.

### Participants/materials, setting, methods:

Group 1 comprised 110 women, who received HRT - estradiol valerate (Proginova®) 4 mg during the endometrium preparation starting from the 2nd day of menstrual cycle and were exposed to two or more frozen-thawed embryo transfer cycles, which ended in failure. Group 2 included the 110 women, which earlier were in Group 1. Group 2 received HRT – oral 17 $\beta$ - estradiol (Femoston® 2/10) 4 mg in the course of the following frozen-thawed embryo transfer cycle staring from the 2nd day of menstrual cycle.

### Limitations, reasons for caution:

Group inclusion criteria: aged between 24 and 45 years; 5 or more years of infertility; clinical history (2 times or more) of ineffective frozen-thawed embryo transfer cycles on HRT - estradiol valerate (Proginova®); selective single blastocyst transfer.

Group exclusion criteria: contraindications for ART and estrogen prescription.

# Main results and the role of chance:

First results coming from the groups under investigation and carried out with the help of transvaginal ultrasound on the 10th and 14th days showed a statistically significant difference in endometrium thickness among the women treated with oral  $17\beta$ -estradiol (Femoston® 2/10) (p>0,05). Group 1 displayed the endometrial thickness of  $6.8 \pm 0.3$  mm on 10th day, while in Group 2 it reached  $8.2 \pm 0.5$  mm. On 14th day of the study endometrial thickness was equal to  $7.3 \pm 0.1$  mm and  $9.2 \pm 0.2$  mm respectively. Clinical pregnancy came about in 32.7% of cases (36 out of 110 patients became pregnant) when oral  $17\beta$ -estradiol (Femoston® 2/10) was used during the endometrial preparation for frozen-thawed embryo transfer cycles among women of the 2nd group.

# Conclusion

Difference at the endometrial

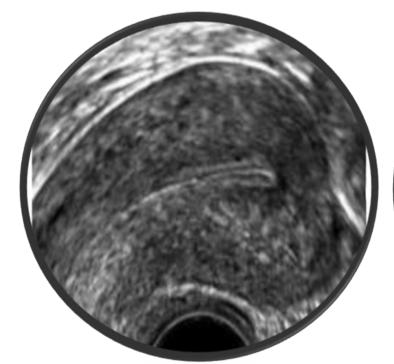
ultrasound structure when taking

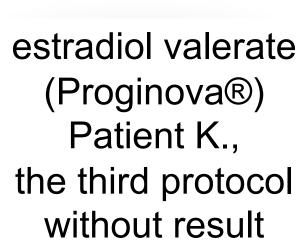
17β-estradiol (Femoston® 2/10) and

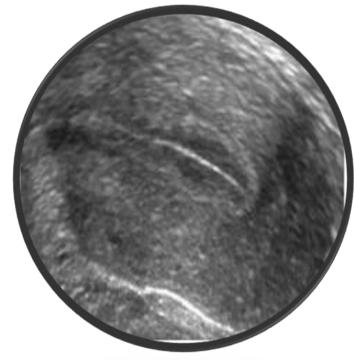
estradiol valerate (Proginova®) on the

18th day of the menstrual cycle

(embryotransfer day)







17β-estradiol
(Femoston® 2/10)
The same patient K.,
the first successful
protocol

Wider implications of the findings:

Using of oral  $17\beta$ -estradiol (Femoston® 2/10) in the course of the endometrium preparation for frozen-thawed cycles at reproductive age women with repeated ART failure on HRT-estradiol valerate (Proginova®) enables to reach a clinical pregnancy in 32.7% of cases. The result may be associated with the increase in endometrium receptivity to the oral  $17\beta$ -estradiol molecule.

Trial registration number:

Case control study.

### References

- Freeze-All Policy: Fresh vs Frozen-Thawed Embryo Transfer / M. Roque,
   M. Valle, F. Guimarães [et al.] // Fertility and sterility. 2015. Vol. 103. P. 1190- 1193.
- 2. Impact of office hysteroscopy in repeated implantation failure: Experience of a single center / E. G. Pabuçcu, İ. Yalçın, T. Bodur [et al.] //J Turk Ger Gynecol Assoc. 2016. –Vol. 17, No 4. P. 197-200.
- 3. Local injury of the endometrium induces an inflammatory response that promotes successful implantation / Y. Gnainsky, I. Granot, P. B. Aldo [et al.] // Fertility and sterility. 2010. Vol. 94, No 6. P. 2030–2036.
- 4. Mazur, M. T. Diagnostic of endometrial biopsies and curreting: A practical approach / M. T. Mazur, R. J. Kurman // New York: Springer, 2005. 296 p.
- 5. Outcomes of vitrified early cleavage-stage and blastocyst-stage embryos in a cryopreservation program: evaluation of 3,150 warming cycles / A. Cobo, M. J. de los Santos, D. Castello [et al.] // Fertility and sterility. 2012. Vol. 98, No 5. P. 1138- 1146.
- 6. Pierson, R. A. Imaging the endometrium: are there predictors of uterine receptivity? / R. A. Pierson // Journal of Obstetrics and Gynaecology Canada. 2003. Vol. 25. P. 360-368.
- 7. The European IVF-monitoring (EIM) Consortium for the European Society of Human Reproduction and Embryology (ESHRE) Assisted reproductive technology in Europe, 2011: results generated from European registers by ESHRE / M. S. Kupka, T. D'Hooghe, A. P. Ferraretti [et al.] // Human Reproduction. 2016. Vol. 31, No 2. P. 233-248.
- 8. Trans dermal estrogen (oestrogel) for endometrial preparation in freeze embryo transfer cycle: An RCT / E. S. Tehraninejad, R. Kabodmehri, B. H. Rashidi [et al.] // Int J Reprod Biomed (Yazd). 2018. Vol. 16, No 1. P. 51-56
- 9. Zhioua, A. Morphometric analysis of the human endometrium during the implantation window. Light and transmission electron microscopy study / A. Zhioua, H. Elloumi, S. Fourati // European J. Obstetrics & Gynecology and Reproductive Biology. 2012. Vol. 41, No 3. P. 235-242.

# **Contact**

Anna N. Sulima – MD, Dr Sci Med, Professor, Department of Obstetrics, Gynecology and Perinatology No 1, Medical Academy named after S. I. Georgievsky, V. I. Vernadsky Crimean Federal University, Simferopol, Russia. E-mail: gsulima@yandex.ru.

ORCID: https://orcid.org/0000-0002-2671-6985.