Can modified natural cycle equalize the risks for patients over 40 years old to those for younger patients? Perinatal outcomes of 268 euploid single blastocyst cryotransfers

Garcia-Faura A [1,2], Benigna M [1,2], Milani V [1,2], Parastie S [1,2], Pagnini G [1,2], Garcia F [1,2], Montalvo V [1,2], Marques B [1,2]
[1] Institut Marquès, Reproductive Medicine Service, Barcelona, Spain; [2] FutureLife Group

Introduction

The increase in advance maternal age patients in Artificial Reproductive Techniques (ART) is becoming a challenging issue for clinicians, facing higher obstetric risks such as gestational diabetes, preeclampsia, intra-uterine growth restriction, and preterm birth. Several studies on FET in ovulatory patients have shown that mNC and the presence of a corpus luteum can reduce some obstetric risks, such as preeclampsia and preterm birth, when compared to hormonal replacement treatment protocols. Even so, few data are available regarding the obstetric risk reduction of mNC-FET in ovulatory patients up to 50y, where those risks due to advanced maternal age could potentially be reduced.

Objectives

Retrospective single-centre comparative clinical study, including 268 euploid single blastocyst (≥3BB, Gardner score) mNC-FET in regular ovulatory patients between Jan-2018 and Dec-2022: 112 patients (42%) >40y (x^{-} =43,8+2,4y, range 41-50y) and 156 patients (58%) ≤40y (x^{-} =36,5+3,0y, range 28-40y). Both >40y and ≤40y groups were homogeneous for body mass index (22,6+4,5 Vs 22,9+3,1), egg donor's age (31,0+5,9y Vs 32,1+5,0y), the need for sperm donation (31,2% Vs 28,1%), and the average trophoectoderm embryo quality (A=32,2% Vs A=33,0%). We studied the clinical, obstetric and perinatal outcomes of the 268 mNC-FET, comparing >40y to ≤40y group for: pregnancy rate, miscarriage rate, Live Birth Rate (LBR), severe preeclampsia, preterm birth rate <37 weeks and neonatal weight. FET cancellation rate for medical reasons such as thin endometrium, spontaneous ovulation and abnormal endometrial pattern was used to adjust LBR and term LBR per started cycle. We used Chi-square and T-test to compare groups ($p<.05$).

Results

There were no statistically significant differences between >40y and ≤40y when comparing FET cancellation rate (8,1% Vs 8,7%, p=.81) and the reason why FET was cancelled: thin endometrium (44% Vs 49%, p=.77), spontaneous ovulation (26% Vs 19%, p=.57) nor abnormal endometrial pattern (36% Vs 26%, p=.33). When comparing implantation and obstetric results, there were no differences between the >40y and ≤40y groups in terms of pregnancy rate (56% Vs 56%, p=.98), miscarriage rate (15% Vs 15%, p=.87) and live-birth rate (45% Vs 47%, p=.70). Obstetric risks were non-significantly higher in >40y group, almost doubling the risks seen in the ≤40y group: severe preeclampsia (1,8% Vs 0,9%, p=.53) and preterm birth rate <37 weeks (8,7% Vs 4,5%, p=.36). Neonatal weight was significantly lower in the >40y group (x^{-} =3145±613g Vs x^{-} =3347±419g, p=.028). When adjusting results per started cycle, no significant differences were found between the >40y and ≤40y groups: LBR (41% Vs 43%, p=.76) and term LBR (38% Vs 41%, p=.56).

Conclusions

mNC should be encouraged for FET in ovulatory patients up to 50y because of its comparable success rates when using the same protocol in younger patients, such as LBR, even when adjusted per started cycle. However, obstetric risks when using mNC thaw cycles remain high in advanced maternal age patients.

Recommended reading

- *Busnelli A, Schirripa I, Fedele F, et al. Obstetric and perinatal outcomes following programmed compared to natural frozen-thawed embryo transfer cycles: a systematic review and meta- analysis. Hum Reprod. 2022;37(7):1619-41.*
- *Singh B, Reschke L, Segars J, Baker VL. Frozen-thawed embryo transfer: the potential importance of the corpus luteum in preventing obstetrical complications. Fertil Steril. 2020;113(2):252-7.*
- *Von Versen-Höynck F, Griesinger G. Should any use of artificial cycle regimen for frozen-thawed embryo transfer in women capable of ovulation be abandoned: yes, but what's next for FET cycle practice and research? Hum Reprod. 2022;37(8):1697-703.*