הכינוס השנתי ה-67 של
האגודה הישראלית לחקר הפוריות (איל"ה)
12 במאי 2025, מלון דיוויד אינטרקונטיננטל, תל אביב
האגודה הישראלית לחקר הפוריות (איל"ה)
THE ISRAEL FERTILITY ASSOCIATION (IFA)
الجمعية الإسرائيلية لأبحاث الخصوبة

Natural- versus modified natural cycle in patients undergoing frozen embryo transfer: a retrospective study

Gal Bachar[1,2], Omer Sheskin[2], Ofer Fainaru[1,2]

[1]IVF Unit, Rambam Medical Center, Haifa, Israel
[2]Rappaport School of Medicine, Technion – Israel Institute of Technology, Haifa, Israel

INTRODUCTION

NC and mNC protocols offer potential advantages for FET as compared to hormonal endometrial preparation. NC may better mimic the physiological conditions that support successful implantation and placentation, potentially leading to improved pregnancy outcomes. These advantages have been attributed to the presence of a corpus luteum. Study's objective was to compare the efficacy of NC and mNC FET cycles.

METHODS

Retrospective study of patients undergoing FET at a tertiary fertility clinic (2023-2024). Each was monitored during the cycle through blood tests (E2, LH and progesterone) and transvaginal ultrasounds. For mNC cycle: when dominant follicle was >14 mm and endometrial thickness >7 mm, a trigger of hCG was administered to induce ovulation. If a spontaneous LH surge was detected with similar follicle and endometrial parameters, the patient was allocated to NC group. Both received progesterone supplementation.

Included were women aged 18-45 with regular menstrual cycles and at least one available high-quality frozen embryo. Data analyzed included demographic characteristics, hormonal profiles, endometrial thickness. Primary outcomes were biochemical- and clinical pregnancy rates.

RESULTS

82 patients were included in the analysis: 17 underwent NC and 65 mNC. Baseline characteristics were similar between study groups, including age, BMI, parity and baseline hormonal profile.

Endometrial thickness and maximal follicle size at trigger day were similar between the NC and mNC groups (8.2±1.3 vs. 8.6±1.6 mm, p=0.32 and 17.3±3.3 vs. 17.0±2.7 mm, p=0.70, respectively). Patients in the NC group demonstrated significantly higher LH and progesterone levels at the end follicular phase as compared to those in mNC group (27.9±18.8 vs. 9.9±10.9 IU/L, p<0.001 and 2.3±1.3 vs. 1.6±1.0 nmol/L, p=0.023, respectively). Comparable biochemical- and clinical pregnancy rates between NC and mNC groups were observed (41.1% vs. 41.5%, p=0.98; 29.4% vs. 24.6%, p=0.68, respectively).

A model for predicting clinical pregnancy versus no clinical pregnancy, demonstrated that the significant parameters that favored clinical pregnancy were blastocyst transfer (90% vs. 66.2%, p=0.046) and grade A blastocyst transfer (75% vs. 32.2%, p=0.003). Interestingly, neither the number of embryos transferred (p=0.80) nor the protocol used (p=0.68) predicted clinical pregnancy in this model.

CONCLUSION

These findings suggest that both NC and mNC protocols are similarly effective regarding biochemical and clinical pregnancy rates in FET cycles. Further randomized controlled trials are needed to confirm these findings and guide clinical practice.

Table 1: FET characteristics and pregnancy outcome

	Modified natural cycle n=65	Natural cycle n=17	P value
Endometrial thickness, mm, mean±SD	8.58±1.57	8.17±1.31	0.32
Max size of dominant follicle. Mean±SD	17.0±2.69	17.3±3.30	0.70
E2 level at trigger day, (pmol/L), median IQR	735 [494-998]	912 [533-1464]	0.40
LH level at trigger day, (pmol/L), mean±SD	9.9±10.9	27.9±18.8	<0.01
Progesterone level at trigger day, (pmol/L), mean±SD	1.61±1.04	2.30±1.27	0.023
Embryonic day, n(%)			
3-4	17 (27.0)	5 (31.3)	0.76
5-6	46 (73.0)	11 (68.9)	
Chemical pregnancy, n(%)	41.5	41.1	0.98
Clinical pregnancy, n(%)	16	29.4	0.68

Table 2: Predictive parameters for clinical pregnancy

	Non-clinical pregnancy n=61	Clinical pregnancy n=21	P value
Day of HCG trigger, mean+SD	12.6±3.8	14.1±4.3	0.13
Spontaneous LH surge day, Mean+SD	10.6±5.04	14.6±2.9	0.12
Endometrial thickness, mm, mean+SD	8.4±1.6	8.8±1.4	0.30
Max size of dominant follicle, mm, Mean+SD	16.9±2.7	17.4±3.2	0.58
E2 level at trigger day, (pmol/L), median IQR	700 [526-971]	852 [401-2571]	0.17
LH level at trigger day, (pmol/L), mean±SD	15.2±15.8	9.2±9.9	0.10
LH level at trigger day, (pmol/L), Median IQR	9.1 [6.5-13.5]	4.7 [3.4-16.6]	0.003
P level at trigger day, (pmol/L), mean±SD	1.75±1.15	1.74±1.07	0.97
Embryonic day, n (%)			
2+3+4	20 (33.8)	2 (10)	0.046
5+6	39 (66.2)	18 (90)	
Blast scoring, n (%)			
A	19 (32.2)	15 (75)	0.003
B	21 (35.6)	4 (20)	
C	19 (32.2)	1 (5)	
# embryo transferred. n (%)			
1	52 (86.7)	18 (85.7)	0.80
2	7 (11.7)	3 (14.3)	
3	1 (1.7)	0	
Protocol used, n (%)			
mNC	49 (75.4)	16 (24.6)	0.68
NC	12 (70.6)	5 (29.4)	