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Title:

IS A THIN ENDOMETRIAL LINING ASSOCIATED WITH A HIGHER INCIDENCE OF ECTOPIC PREGNANCIES IN OVULATION INDUCTION CYCLES?

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Objective:

Clinicians continue to explore risk factors and apply clinical pathways to prevent the occurrence of an ectopic pregnancy during assisted reproduction technologies treatment. Rombauts et al. published a report that demonstrated a 4-fold increased risk of ectopic pregnancy in women who underwent a fresh in vitro fertilization cycle with an endometrial thickness (EnT) of <9mm as compared to >12mm.[1] No studies to date have evaluated whether there is a similar association in ovulation induction (OI) cycles. This study aimed to determine the value of EnT at time of surge to predict ectopic pregnancies in OI cycles.

Design:

Retrospective, cohort study

Materials and Methods:

The study included patients who underwent an OI cycle from 2001-2018 using clomiphene citrate (CC) or letrozole. Gonadotropin cycles were excluded. OI cycles were separated into groups based on outcome (ectopic pregnancy (EP) and no EP). EnT was treated as a continuous variable. A sub-analysis was performed treating EnT as a dichotomous variable, thin (<7mm) or not thin (≥7mm). Age, body mass index (BMI), EnT and endometrial pattern (EnP) at time of surge, gravidity, parity, and anti-mullerian hormone level (AMH) were collected. Data were analyzed using t-tests, Chi square analysis, and binary logistic regressions with a general estimate equation (GEE) model with an exchangeable working correlation structure to account for repeated measures.

Results:

A total of 22,956 OI cycles from 11,043 patients were included. Baseline characteristics were similar between cycle outcome groups (Table 1). There was a significant difference in the number of CC cycles that resulted in a thin lining (<7mm) compared to letrozole (18.6% vs. 13.4%, p=0.0001). The overall rate of EP in the study was 1.13% (n=259). There was no difference in the rate of EP between CC or letrozole cycles (1.15% vs. 1.07%, p=0.65). Controlling for age, gravidity BMI, EnP, and type of cycle (CC vs. letrozole), there was no significant increase in likelihood of patients experiencing an EP based on EnT at time of surge (OR 0.96, [95% CI 0.96-1.05], p= 0.43). When EnT was treated as a dichotomous variable, there was still no significant difference in incidence of EP with an EnT <7mm, compared to ≥7mm (OR 0.75, [95% CI -1.00-0.42], p= 0.42). Similarly, a suboptimal EnP was not associated with risk of EP (OR 1.30, [95% CI -0.18 - 0.71], p=0.25).

Conclusions:

In contrast to recent reports that EnT is an independent risk factor for EP in IVF cycles, this study demonstrated that there is no association between EnT and EP in OI cycles. Although CC predisposes a patient to having a thin endometrium, there was no increase in the risk of an EP, as compared to patients exposed to letrozole. Clinicians can be reassured that patients do not have a greater risk of experiencing an EP during OI, even in the presence of a thin endometrial lining.

References:

1. Rombauts L, McMaster R, Motteram C. Risk of ectopic pregnancy is linked to endometrial thickness in a retrospective cohort study of 8120 assisted reproduction technology cycles. Hum Reprod 2015; 30(12):2846-2852.

Table 1:

Patient demographics

	Ectopic pregnancy (N=259)	No ectopic pregnancy (N=22,698)	P value
Age	34.89 ± 4.38	35.02 ± 5.05	0.66
BMI	24.92 ± 5.28	24.30 ± 5.06	0.10
EnT at surge	8.34 ± 1.89	8.12 ± 1.88	0.06
Endometrial type	1- 109 (42.9%) 2- 115 (45.3%) 3- 30 (11.8%)	1- 10501 (46.1%) 2- 9299 (40.8%) 3- 2720 (11.9%)	0.42
AMH	4.48 ± 7.68	4.18 ± 5.31	0.70
Gravidity	1.37 ± 1.53	0.81 ± 1.19	0.00
Parity	0.33 ± 0.59	0.26 ± 0.59	0.28
Cycle Type	Clomid: 73.0% Letrozole: 27.0%	Clomid: 71.5% Letrozole: 28.5%	0.60

Table 2:

Chi square analysis results comparing lining thickness and cycle type

	Clompihene Citrate	Letorozole	P value
EnT <7 mm	3,057 (18.6%)	876 (13.4%)	0.0001
EnT ≥7 mm	13,356 (81.4%)	5,667 (86.6%)	