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CLOMIPHENE CITRATE EXPOSURE DOES NOT ADVERSELY AFFECT CLINICAL OUTCOMES IN SINGLE, EUPLOID FET CYCLES

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OBJECTIVE:

Clomiphene citrate (CC) is a selective estrogen receptor modulator utilized for OI and COH. Pharmacologically, CC has a half-life of 5 days; yet, it can be excreted after 6 weeks after initial administration[1]. CC is known to have antioestrogenic side effects which had been associated to a reduction in implantation rates for patients who undergo fresh IVF cycles[2]. However, evidence is scarce about the effect of CC on implantation potential in FET cycles. One study showed that patients who undergo a FET within 90 days after CC treatment had lower pregnancy rates compared with FET cycles that occur after 90 days of CC treatment [3]. Conversely, another study did not find lower implantation rates in patients who undergo FET cycles, regardless of the time of CC administration [4]. To date, no study has analyzed CC exposure and subsequent transfer of euploid embryos. The objective of this study is to analyze implantation rates in patients exposed to CC prior to a single, euploid FET cycle.

DESIGN:

Retrospective analysis.

MATERIALS AND METHODS:

The study included patients who underwent a single, euploid FET from 2016 to 2020. PGT-A was performed by NGS. Cohorts were segregated in 2 groups according to duration between the last day of CC administration and FET day (Group 1: ≤90 days, Group 2: patients unexposed to CC or when exposure elapsed > 90 days). Patients with genetic translocations, uterine factor,

hydrosalpinx and RPL diagnosis were excluded from the analysis. Demographic characteristics and IVF outcomes were assessed. Comparative statistics and an adjusted multivariate analysis with a GEE framework were used for analysis. A sample size of 355 FET cycles per group was calculated to have an 80% power to detect a difference of 10% on implantation rates (α=0.05).

RESULTS:

433 FET cycles in which patients were exposed to CC within 90 days (Group 1) were compared with 5723 control cycles (Group 2). AMH levels were different among groups (3.5± 4 vs 3.5±3, p=0.02). The remaining demographic characteristics, including endometrial thickness at ET, were comparable among groups. Clinical pregnancy rate (CPR) (67.2% vs 61.4%, p=0.01) and ongoing pregnancy rate (OPR) (57.7% vs 51.5%, p=0.01) were significantly different among groups. No differences were found in implantation or clinical pregnancy loss (CPL) rates among groups. After adjusting for age, BMI, AMH, endometrial thickness at ET, embryo quality, and day of biopsy, there was no association with CC exposure and lower odds of implantation (OR 1.12,CI 95% 0.8-1.4,p=0.36), CPR (OR 1.21,CI 95% 0.9-1.5,p=0.09), OPR (OR 1.18,CI 95% 0.9-1.4,p=0.12), or higher odds of CPL (OR 0.96,CI 95% 0.6-1.3,p=0.85), when compared with controls. On a sensitivity analysis we also found no association within shorter CC exposure times (30 & 60 days) and IVF outcomes.

CONCLUSIONS:

Although CC is a safe oral agent for ovarian stimulation, unfavorable effects on endometrial thickness are possible and could result in implantation failure during fresh IVF cycles. However, our study demonstrated no association between exposure to CC and adverse effect on IVF outcomes in patients undergoing a single, euploid FET cycle.