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REVISITING OLD HABITS: THERE IS NO BENEFIT IN PRESCRIBING METHYLPREDNISOLONE ADMINISTRATION DURING EUPLOID EMBRYO TRANSFERS IN THE GENERAL INFERTILE POPULATION

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OBJECTIVE: Two decades ago, a small RCT concluded that embryos with an incision in the *zona pellucida* could be protected from an immune response by administering systemic corticosteroids¹. The utilization of corticosteroids remains a standard practice at many ART centers^{2,3}. In early 2020, during the peak of the Sars-Cov-2 pandemic, some reports showed that corticosteroid intake associated with an extended time of viral shedding which associated to higher mortality among patients with coronavirus pneumonia⁴. Our center therefore discontinued standard of methylprednisolone in frozen embryo transfer (FET) cycles. Our study aims to evaluate IVF pregnancy outcomes of patients who underwent a short course of oral steroids compared to those that were not treated with corticosteroids.

MATERIALS AND METHODS:

All patients who underwent IVF from 2016 – 2021 were included. All cases underwent PGT-A with NGS. Only patients who underwent a single euploid FET under a synthetic endometrial preparation cycle were included. Cohorts were separated by use of steroids prior to ET (Group A: Oral methylprednisolone Treatment (16mg for 7 days); Group B: non-treatment controls). Patients with RPL, implantation failure and uterine factor were excluded. Baseline, demographic characteristics and cycle outcomes were recorded. Comparative statistics and a multivariate regression analysis fitted with a GEE were utilized for statistical analysis. A sample size of 1,437 FET's per group was calculated to have an 80% power to detect a difference of 5% on implantation rates, $\alpha=0.05$.

RESULTS:

A total of 7,172 cycles were included in the analysis, 5,002 cycles with methylprednisolone utilization were compared against 2,170 controls. No differences were found in oocyte age, age at FET, BMI, AMH, FSH, previous cycles, days of endometrial preparation, endometrial thickness at FET and embryo quality at FET among cohorts. When comparing IVF outcomes, in an unadjusted-analysis a difference was found in implantation rates among patients that used methylprednisolone compared with controls (75.8% vs 72.8%, $p=0.008$), clinical pregnancy, ongoing pregnancy and clinical pregnancy loss rates were comparable among groups. In a multivariate analysis after adjusting for oocyte age, day of biopsy, embryo quality, BMI, AMH, and endometrial thickness at ET, no association was found with the utilization of Methylprednisolone and higher implantation (OR 1.1 CI95% 0.9-1.2), clinical pregnancy (OR1.02; 0.9-1.1), ongoing pregnancy (OR 0.9; 0.8-1.08) or higher odds of clinical pregnancy loss (OR 1.1; 0.9-1.4)

CONCLUSIONS:

Systemic corticosteroids use continues to be a controversial, yet widespread, adjuvant treatment during IVF cycles in many modern ART centers. Our study demonstrated the utilization of



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methyprednisolone is not associated with increased odds of implantation, ongoing pregnancy or decreased odds of pregnancy loss after a single euploid FET.

IMPACT STATEMENT:

Our findings add to the growing body of evidence suggesting that the standard use of peri-implantation corticosteroids does not enhance nor impact reproductive outcomes in FET cycles

REFERENCES:

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