

UNEXPLAINED EUPLOID EMBRYO TRANSFER FAILURE: TESTING AND TREATMENT OPTIONS

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Background

Endometriosis affects 5-10% of women of reproductive age and up to 50% of these women experience infertility (1). Despite advances in Assisted Reproductive Technology (ART), the overall mean success rate for IVF rarely exceeds 70%, even with preimplantation genetic testing (PGT-A) (2). Endometriosis may be an underlying cause of unexplained euploid embryo transfer failure (UEETF). If this hypothesis is true, medical suppression of ovulation could potentially be a therapeutic option to improve outcomes for those with unexplained implantation failure (3,4).

Objective

The purpose of this study was to compare success rates among first time IVF patients using preimplantation genetic tested (PGT-A) embryos, women with UEETF who underwent 2 months of ovulation suppression with GnRH agonist (GnRHa) or controls receiving no treatment (NoTx). A subset of UEETF subjects underwent endometrial biopsy and testing for endometriosis biomarkers, BCL6 and SIRT1 (3,5).

Materials and Methods

Electronic records of 205 frozen embryo transfer (FET) cycles using euploid embryos between 2019 and 2023 were examined. A total of 127 first IVF attempt (FirstPGTA) were evaluated and compared to 61 with prior UEETF: 47 were treated with GnRHa for 2 months of ovulation suppression (GnRHa) and 14 received no treatment (NoTx) prior to the next FET. Pregnancy success was defined as live birth or ongoing pregnancy (heartbeat after 12 weeks). We performed endometrial biopsies on 48 women with prior UEETF, using standard immunohistochemistry (IHC) staining for BCL-6 and SIRT1. Hscore was performed for IHC analysis by a blinded observer. A cut-off of 1.4 and 2.0 (out of 4.0) was considered positive for BCL-6 and SIRT1, respectively. Pregnancy success rates are reported as a 95%CI and compared using *chi*-squared for trend testing.

Results

Pregnancy success was higher in FirstPGTA, and GnRHa groups compared to NoTx (Chi-square for trend, $p=0.02$) (Fig 1). Immunohistochemistry for BCL6 testing was positive in 42 of 48 cases (87.5%), while SIRT1 was positive in 39 of 45 cases (88.8%).

Conclusion(s): Unexplained failure with euploid embryo transfer is common and may be associated with defective endometrial receptivity and undiagnosed endometriosis. Biomarkers for endometriosis (BCL6 and SIRT1) were positive for a majority of subjects tested with UEETF. Endometrial suppression for 2 months with GnRHa was superior to no treatment, providing similar outcomes to overall first time PGT-A FET success rates.

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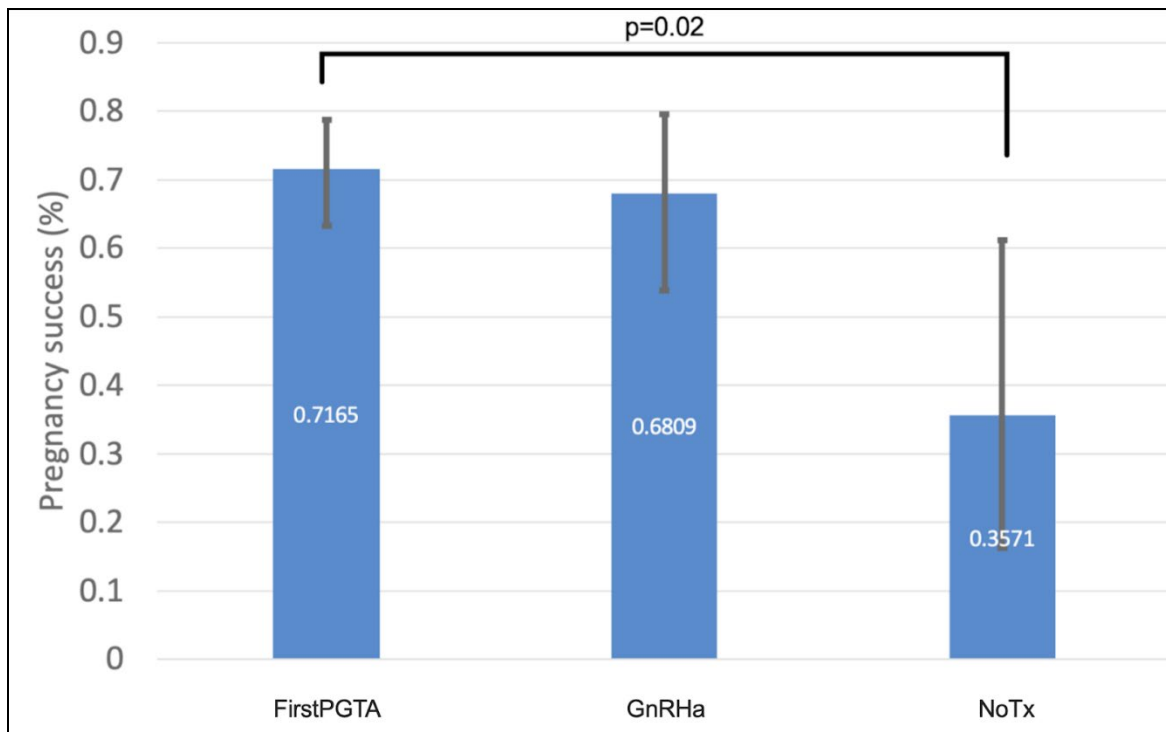


Figure 1: Pregnancy success rates (live birth/ongoing pregnancy) is first attempt PGT-A (FirstPGTA) compared to those with prior failure treated with GnRH agonist suppression (GnRHa) or no further treatment (NoTx).