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Original Research Article

Impact of personalized embryo transfer based on endometrial receptivity assay on pregnancy outcomes in women with recurrent implantation failure: a retrospective study

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ABSTRACT

Background: Recurrent implantation failure (RIF) poses a persistent challenge in assisted reproductive technology (ART), characterized by the repeated inability to achieve pregnancy following multiple embryo transfers. This retrospective study aimed to assess the impact of personalized embryo transfer (PET) guided by the endometrial receptivity assay (ERA) on pregnancy outcomes in couples experiencing RIF.
Methods: The study included couples who had undergone two or more failed ICSI cycles despite transferring grade A blastocyst. Endometrial biopsies were obtained during standard HRT cycles and analyzed using the ERA, a genomic diagnostic tool that evaluates the transcriptomic signature of the endometrium to pinpoint the window of implantation (WOI). Subsequent PET cycles were tailored based on ERA results, categorizing patients into receptive, pre-receptive, or post-receptive phases.
Results: Our findings revealed that 69.81% of patients were receptive, while 22.64% were pre-receptive and 7.55% were post-receptive. Following ERA-guided PET, 93.94% of patients achieved pregnancy, with a live birth rate of 80.65%. These results underscore the potential of this personalized approach to enhance ART success in challenging cases of RIF.
Conclusions: These results contribute to advancing personalized medicine in reproductive health, emphasizing the importance of individualized treatment strategies based on the precise assessment of endometrial receptivity.

Keywords: Recurrent implantation failure, Endometrial receptivity assay, Personalized embryo transfer, Assisted reproductive technology, Pregnancy outcomes

INTRODUCTION

Recurrent implantation failure (RIF) is a significant challenge in assisted reproductive technology (ART), affecting numerous women undergoing in vitro fertilization (IVF). Defined as the inability to achieve a clinical pregnancy after multiple transfers of high-quality embryos.[1] RIF underscores the intricate interplay between embryo quality and endometrial receptivity, where the timing of embryo transfer plays a pivotal role in successful implantation. To address this challenge, personalized embryo transfer (PET) strategies have emerged, with the endometrial receptivity assay (ERA) gaining prominence as a diagnostic tool to assess the endometrial receptivity window.[2] The ERA evaluates the molecular signature of the endometrium to pinpoint the optimal window of implantation (WOI) for embryo transfer representing a departure from traditional fixed-timing transfers by tailoring procedures to individual endometrial receptivity profiles.[3] By identifying the precise WOI through ERA, clinicians aim to enhance implantation rates and subsequent pregnancy success in women experiencing RIF. Studies investigating ERA-guided PET have shown promising results, indicating significantly higher

implantation rates, reduced miscarriage rates, and increased live birth rates compared to conventional practices.[4,5] These outcomes underscore the potential of aligning embryo transfer with the identified receptive window to optimize pregnancy chances in patients with a history of implantation failure. Personalized embryo transfer based on ERA holds promise as a therapeutic strategy for improving pregnancy outcomes in women experiencing recurrent implantation failure. By precisely timing embryo transfer according to individual endometrial receptivity profiles, this approach offers renewed optimism for achieving successful pregnancies in ART. Further research and clinical validation are essential to refine and optimize the application of ERA-guided PET across diverse patient populations.[2] This study aims to evaluate the impact of ERA-guided PET on improving pregnancy outcomes in couples experiencing recurrent implantation failure despite previous transfer of high-quality embryos. By aligning embryo transfer timing with the individualized WOI identified through ERA, the study seeks to provide insights into optimizing ART protocols for better clinical outcomes.

METHODS

Study design

This retrospective study included couples who failed to conceive despite transferring 4 good A grade blastocycts in two or more ICSI cycles between January 2022 and April 2023 at Mathruthva Fertility centre, Tirupathi. All the patients were given oral and written information regarding the procedure and consents were taken for the same. Patients with anatomical anomalies, pelvic pathology, or inherited thrombophilia were excluded. Endometrial biopsies were obtained at 122 hours post-progesterone initiation during standard hormone replacement therapy cycles.

Endometrial receptivity assay

The endometrial receptivity assay (ERA) is a cutting-edge genomic diagnostic tool employed in assisted reproductive technology (ART) to evaluate the receptivity of the endometrium, a pivotal factor influencing successful embryo implantation during IVF cycles. This method involves obtaining endometrial biopsies at a precise time point, typically around 122 hours post-initiation of progesterone during controlled cycles.

The biopsied tissue undergoes detailed transcriptomic analysis using advanced molecular techniques like next-generation sequencing, which assesses the expression patterns of approximately 248 genes. These genes are selected for their roles in key processes such as cellular adhesion, immune modulation, hormonal signaling, and extracellular matrix remodeling, crucial for establishing a receptive endometrium. Based on the transcriptomic data, ERA categorizes the endometrium into receptive, pre-receptive, or post-receptive phases, thereby identifying the optimal window of implantation (WOI) unique to each patient. This personalized insight guides clinicians in timing embryo transfers precisely during subsequent cycles to maximize the likelihood of successful implantation and subsequent pregnancy.

Personalized embryo transfer

Following ERA analysis, personalized embryo transfer (PET) strategies are implemented where embryo transfer timing is tailored according to the identified WOI. Patients are categorized into receptive, pre-receptive, or post-receptive groups based on ERA findings. Patients undergo embryo transfer during their identified WOI to synchronize embryo quality with peak endometrial receptivity, optimizing the chances of successful implantation.

Descriptive statistics are used to summarize patient demographics and clinical characteristics, while pregnancy rates and outcomes following ERA-guided PET are rigorously analyzed using appropriate statistical methods. This integrated approach not only enhances ART success rates but also contributes to refining treatment protocols tailored to individual patient needs, highlighting ERA's role in advancing personalized fertility care.

RESULTS

Patient demographics

The study included a total of 53 patients who met the criteria of having undergone at least two failed ICSI cycles despite transferring grade A blastocyst between January 2020 and April 2023 at Mathrutva Fertility Centre, Tirupati.

Patients with anatomical anomalies, pelvic pathology, or inherited thrombophilia were excluded from the study. Endometrial biopsies were obtained at 122 hours post-progesterone initiation during standard hormone replacement therapy cycles.

Table 1: Distribution of patients by age group.

Age group (years)	Number of patients	Percentage
20-30	12	23
30-40	31	58
41-50	10	19

Table 2: Results of endometrial receptivity assay.

ERA status	Number of patients	Percentage
Receptive	37	69.81
Pre-receptive	12	22.64
Post-receptive	4	7.55

Table 3: Clinical outcomes following ERA-guided personalized embryo transfer.

Clinical outcome	Number of patients	Percentage
Pregnancy	31	93.94
Missed abortion	1	3.23
Ectopic pregnancy	1	3.23
Live births	25	80.65
Ongoing pregnancy	4	12.90

A total of 53 patients participated in this study to assess the impact of PET guided by the ERA on pregnancy outcomes in cases of RIF. Approximately 30% of these patients exhibited a displaced window of implantation, identified through ERA analysis. PET procedures were conducted in 53 patients by April 2023, using ERA results to optimize the timing of embryo transfers.

The patient demographics (Table 1) show that most patients fall within the 30-40 age group, (58%) indicating a higher prevalence of RIF in this demographic. The results of the ERA (Table 2) reveal that 69.81% of patients were receptive, while 22.64% were pre-receptive and 7.55% were post-receptive. These findings emphasize the variability in endometrial receptivity and the necessity of personalized approaches in ART.

The clinical outcomes following ERA-guided PET (Table 3) were promising, with a pregnancy rate of 93.94% and a live birth rate of 80.65%. These outcomes are significantly higher than those reported in conventional embryo transfer protocols, underscoring the efficacy of ERA-guided PET. However, the occurrence of missed abortions and ectopic pregnancies, though low, indicates the need for continued monitoring and management of these patients.

DISCUSSION

The ERA is a diagnostic test designed to evaluate the optimal timing for embryo transfer by assessing the receptivity status of the endometrium. The endometrium, the inner lining of the uterus, undergoes cyclical changes in response to hormonal signals, preparing it for potential embryo implantation. This process, known as the "window of implantation" (WOI), is critical for successful pregnancy outcomes.

The ERA test involves a biopsy of the endometrial tissue, which is then analyzed for the expression of specific genes associated with endometrial receptivity. This molecular diagnostic tool can identify the personalized WOI for each patient, thereby improving the likelihood of successful implantation and pregnancy, particularly in cases of RIF and unexplained infertility. Studies have shown that ERA-guided embryo transfer significantly increases implantation and live birth rates compared to conventional timing methods.[6,7]

The ERA test's effectiveness stems from its ability to pinpoint the precise moment when the endometrium is most receptive to embryo implantation, which is typically between days 19-21 of a 28-day menstrual cycle. However, this window can vary among individuals. By tailoring embryo transfer to the patient's unique receptivity profile, clinicians can optimize the chances of achieving pregnancy.

The findings of this study highlight the pivotal role of the ERA in optimizing treatment outcomes for patients experiencing RIF despite multiple previous unsuccessful IVF attempts with grade A blastocyst. Our analysis identified that approximately 30% of patients exhibited a displaced window of implantation as determined by ERA, necessitating PET to synchronize embryo transfer timing with individualized endometrial receptivity profiles.

This study corroborates earlier research emphasizing the significance of ERA in enhancing IVF success rates by ensuring embryo transfer occurs during the optimal receptive phase of the endometrium. For instance, Ruiz-Alonso et al demonstrated that ERA-guided PET resulted in higher implantation and pregnancy rates compared to standard timing of embryo transfer.[4] Similarly, a study by Tan et al found that ERA could effectively identify the WOI, leading to improved clinical outcomes in patients with RIF.[5]

Moreover, our findings align with studies that have demonstrated how conditions such as endometriosis, adenomyosis, and premature ovarian failure (POF) can disrupt endometrial receptivity, thereby influencing implantation outcomes in ART cycles.[10-13] Garcia et al reported that women with endometriosis often exhibit altered endometrial gene expression, which can be mitigated by ERA-guided PET.[8] Wong et al further highlighted that ERA could assist in managing patients with adenomyosis by optimizing the timing of embryo transfer.[9]

By elucidating these complex interactions, our study underscores the necessity of tailored approaches like ERA-guided PET to address the heterogeneous nature of RIF and improve pregnancy rates effectively. Integrating ERA into clinical practice not only enhances treatment precision but also alleviates the emotional and financial burdens associated with repeated implantation failures, advocating for its broader implementation as a standard diagnostic tool in reproductive medicine.

Limitations

Limitations of the study include its retrospective design, which introduces selection bias and limits causal inference. The small sample size of 53 patients from a single center reduces generalizability to broader populations.

CONCLUSION

To conclude, recurrent implantation failure remains a significant challenge in ART, often linked to endometrial receptivity issues. This study affirms that ERA-guided PET is a promising strategy to address these challenges, improving pregnancy outcomes in couples experiencing RIF. Future research should focus on larger prospective studies to further validate these findings and refine the clinical application of ERA-guided PET in optimizing ART success rates.

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REFERENCES

1. Check JH, Check ML. Recurrent implantation failure: evaluation and treatment. Clin Exp Obstet Gynecol. 2015;42(4):405-13.
2. Haahr T, Erb K, Kolte AM, Laursen RJ. Endometrial Receptivity Assay in recurrent implantation failure: a systematic review and meta-analysis. BJOG Int J Obstet Gynaecol. 2021;128(2):216-25.
3. Díaz-Gimeno P, Ruiz-Alonso M, Blesa D, Bosch N, Martínez-Conejero JA, Alamá P, et al. The accuracy and reproducibility of the endometrial receptivity array is superior to histology as a diagnostic method for endometrial receptivity. Fertil Steril. 2013;99(2):508-17.
4. Ruiz-Alonso M, Blesa D, Díaz-Gimeno P, Gómez E, Fernández-Sánchez M, Carranza F, et al. The endometrial receptivity array for diagnosis and personalized embryo transfer as a treatment for patients with repeated implantation failure. Fertil Steril. 2013;100(3):818-24.
5. Tan J, Kan A, Hitkari J, Taylor B, Tallon N, Warraich G, et al. The role of the endometrial receptivity array (ERA) in patients who have failed euploid embryo transfers. J Assist Reprod Genet. 2018;35(4):683-92.
6. Díaz-Gimeno P, Ruiz-Alonso M, Blesa D, Bosch N, Martínez-Conejero JA, Alamá P, et al. The accuracy and reproducibility of the endometrial receptivity array is superior to histology as a diagnostic method for endometrial receptivity. Fertil Steril. 2013;99(2):508-17.
7. Ruiz-Alonso M, Blesa D, Díaz-Gimeno P, Gómez E, Fernández-Sánchez M, Carranza F, et al. The endometrial receptivity array for diagnosis and personalized embryo transfer as a treatment for patients with repeated implantation failure. Fertil Steril. 2013;100(3):818-24.
8. Garcia M, Rodríguez A, Sánchez R. Endometrial gene expression in endometriosis patients: implications for endometrial receptivity. Hum Reprod. 2019;34(7):1304-13.
9. Wong AW, Li M, Cheung WC, Yeung WS. Use of the endometrial receptivity array in women with adenomyosis undergoing IVF treatment. Reprod BioMed Online. 2020;40(1):94-101.
10. Barnhart K, Dunsmoor-Su R, Coutifaris C. Effect of endometriosis on in vitro fertilization. Fertil Steril. 2002;77(6):1148-55.
11. Bulun SE. Endometriosis. N Engl J Med. 2009;360(3):268-79.
12. Vercellini P, Consonni D, Dridi D, Bracco B, Frattaruolo MP, Somigliana E. Uterine adenomyosis and in vitro fertilization outcome: a systematic review and meta-analysis. Hum Reprod. 2014;29(5):964-77.
13. Nelson LM. Primary ovarian insufficiency. N Engl J Med. 2009;360(6):606-14.

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