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Research Article

Assisted Hatching of Early Blastocysts Improves Pregnancy Outcomes in Fresh Embryo Transfers

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Abstract

Objective: Assisted hatching (AH) is the disruption of the zona pellucida; a technique used to improve implantation and communication between blastocyst and endometrium. AH is widely utilized in poor prognosis patients or when pre-implantation genetic testing is planned. Our retrospective cohort study aims to determine if AH of early blastocysts improves pregnancy outcomes specifically in the setting of delayed embryo development at fresh embryo transfers.

Design: Retrospective cohort study was conducted at an academic IVF center. A total of 71 fresh Day 5 early blastocyst transfers were analyzed from the year 2014 to 2021. Among with or without AH group, pregnancy outcome and implantation rate were compared.

Results: The result showed that AH significantly improved implantation rate (AH 36.5% vs control 9.4%, p = 0.0005), clinical pregnancy rate (AH 54.3% vs control 16.7%, p = 0.0012), and even live birth rate (AH 40.0% vs control 13.9%, p = 0.0166).

Conclusion: Our study supports that AH enhances the implantation potential as well as live birth outcomes of Day 5 fresh embryo transfers and should be considered, especially in patients with delayed blastocyst development. AH in early blastocysts can improve pregnancy outcomes for fresh cycle transfers likely by enhancing the interaction between herniated trophectoderm via AH and endometrial epithelium within the window of implantation.

Keywords: *Assisted Hatching; Fresh Embryo Transfer; In-Vitro Fertilization; Pregnancy Outcomes*

Introduction

Assisted hatching (AH) was first described in 1990 where the mechanical opening of the zona pellucida was shown to increase implantation rates [1]. Initiation of implantation depends on the interaction between blastocyst and maternal uterine luminal epithelium for apposition and adhesion. Many programs now utilize AH, commonly performed with a laser for full thickness hatching on the day of

embryo transfer or for preimplantation genetic testing [2]. Potential complications include damage to the embryo and an increased risk of monozygotic twinning [3]. However, the practice of AH has produced mixed results in pregnancy outcomes. Studies show improved live birth, while others demonstrate no significant difference between AH and no AH [4,5]. Currently, ASRM recommend that AH not be routinely performed, and mainly utilized in poor prognosis patients [2].

Objective of the Study

Our objective is to investigate whether assisted hatching of early blastocysts during fresh transfers affect pregnancy outcomes. By understanding whether this intervention is beneficial to patients with delayed embryo development may help improve their treatment outcomes.

Materials and Methods

Approval for this study was granted by the University Hospitals Institutional Review Board (STUDY20200244). All day 5 fresh embryo transfers of early blastocysts from 2014 to 2021 at a single academic-based fertility center were included. Cohort analysis was performed to evaluate the pregnancy outcomes between assisted hatching (AH) versus no AH (control) of the early blastocysts. Early blastocysts were defined as all blastocysts leading up to the pre-expanding stage (e.g. expansion grade 1 by Gardner's grading system, Figure 1A). We compared participants' demographics, embryo and cycle characteristics. Primary outcomes included implantation rate (IR), pregnancy rate per transfer (PR), clinical pregnancy rate per transfer (CPR) and live birth rate per transfer (LBR). A sub-analysis was also performed excluding early expanding blastocysts to reflect the outcomes of "true" early blastocysts (Figure 1B) that have developed blastocoel but have not differentiated inner cell mass (ICM) or trophectoderm (TE). Multiple linear and logistic regression analysis were performed to assess the impact of AH on pregnancy outcomes. P-value < 0.05 was statistically significant by using Fisher's Exact Test and T-test.

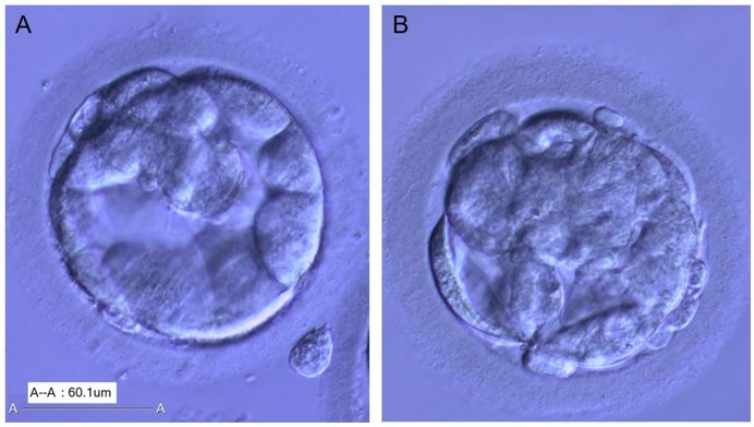

Figure 1: *A. Pre-expanding early blastocyst. B. "true" early blastocyst on day 5.*

Results and Discussion

A total of 71 fresh embryo transfers of early blastocysts were analyzed (AH N = 35 vs control N = 36). The average number of embryos transferred between both cohorts were significantly different (AH 1.5 embryos vs control 1.8 embryos, p = 0.02). Although the control group had a higher number of embryos transferred, regression analysis showed that AH significantly improved IR (AH 36.5% vs. control 9.4%, p = 0.0005), CPR (AH 54.3% vs control 16.7%, p = 0.0012) and even LBR (AH 40.0% vs control 13.9%, p = 0.0166) in early blastocyst transfers.

When early expanding blastocysts were excluded, there were a total of 40 "true" early blastocyst transfers (AH N = 17 vs control N = 23). Participant, embryo, and cycle characteristics were not different, including age and numbers of embryos transferred. In this sub-analysis, AH also showed a significant improvement in IR (AH 28.6% vs. control 7.3%, p = 0.0405) and CPR (AH 47.1% vs. control 13.0%, p = 0.0305). LBR was also improved but was not statistically significant (AH 29.4% vs. control 13.0%, p = 0.25).

Conclusion

Currently, in the United States, AH is predominately utilized for patients who are ≥ 38 years old and have failed ≥ 2 IVF cycles. There has been an increasing number of AH for day 5 embryo transfers, but studies have shown limited improvement in pregnancy outcomes [5]. Early blastocysts transferred on Day 5 could be delayed in their development and have poorer implantation rates due to dys-synchrony of the endometrium and the embryo (Figure 2). Our data demonstrate that AH in day 5 fresh embryo transfers improves pregnancy outcomes by enhancing the implantation of early blastocysts to the endometrium. For patients with slow blastocyst development or no supernumerary embryos to cryopreserve, AH in early blastocysts can improve rates of IR, CPR, and LBR for fresh cycle transfers likely by enhancing the interaction between herniated trophectoderm via AH and endometrial epithelium within the window of implantation. Although the data is promising, future larger studies are needed.

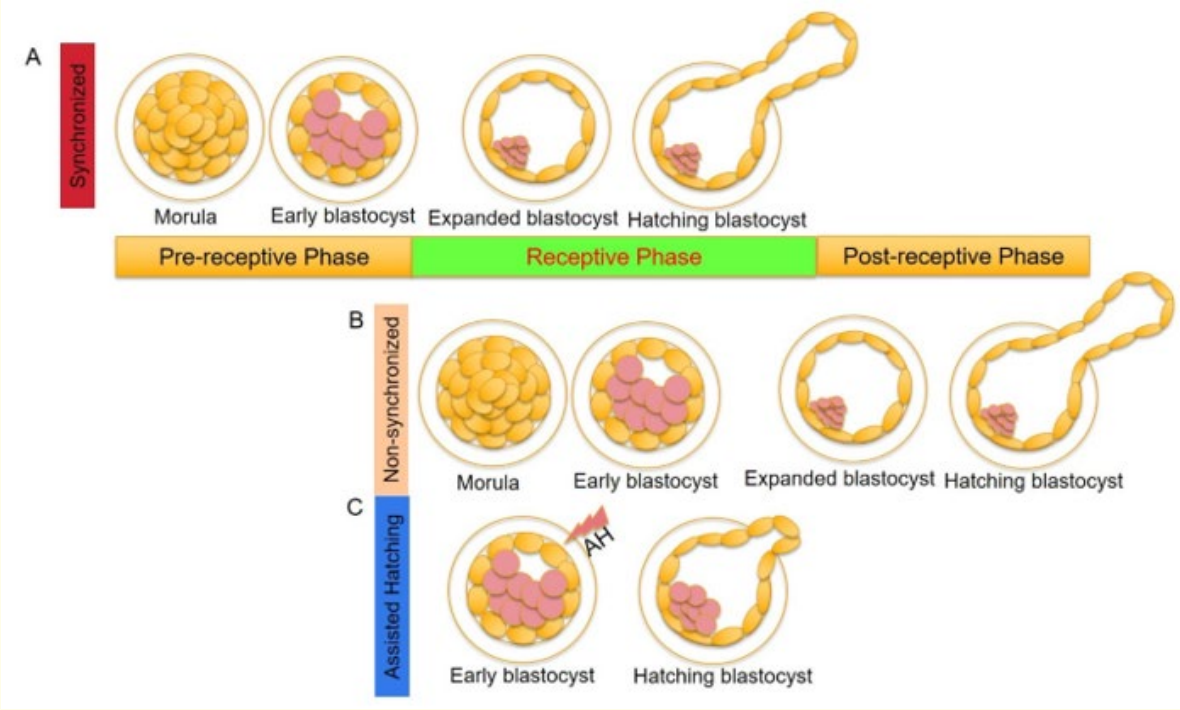

Figure 2: *Synchronization of blastocyst and endometrium. A. Normal blastocyst development. Trophectoderm of hatching blastocyst can communicate with receptive endometrium and successful implantation can be occurred. B. Delayed blastocyst development. Dys-synchrony between endometrium and the embryo can cause implantation failure when blastocyst hatches after the receptive phase of the endometrium. C. With delayed embryo development, AH of an early blastocyst may lead to synchronization.*

Conflict of Interest

Authors don't have any conflict of interest.

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