Reducing early discontinuation in IVF: the role of a multicycle treatment approach

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Introduction

Patient engagement is one of the key factors contributing to success in assisted reproductive technologies. Frequently, the decisionmaking process follows a conventional cycle-by-cycle approach, which delays treatment planning until after each failed attempt, often resulting in emotional distress and treatment discontinuation. However, growing evidence supports a multicycle approach that acknowledges the possibility of failure and highlights the benefits of planning multiple attempts in advance. This strategy aims to improve the cumulative Live Birth Rate (cLBR) and encourages patients to persist with treatment or, when appropriate, to consider oocyte donation. In this context, reducing the overall time spent in treatment—through strategies such as the use of unconventional stimulation protocols like DuoStim—plays a critical role in maintaining patient motivation and continuity throughout the IVF journey.

Objectives

This study aimed to identify factors associated with treatment discontinuation between the first and second IVF attempts. An observational study included 3542 IVF-naïve couples who underwent their first attempt between 2014–2020, with \geq 3 years of follow-up. Median maternal age was 38 years (IQR: 35–41), median AMH 1.2 ng/mL (IQR:0.8–2.4), and 18% had Severe Male Factor (SMF). DuoStim was performed in 328 patients. The cLBR after the first attempt was 35% (1241/3542); among those without live birth, 47% (1083/2301) discontinued treatment. Ninety-seven switched to oocyte donation after the first failure. Among second attempts, cLBR was 25% (275/1121); the conservative cLBR after two attempts was 43% (1516/3542). Another 207 patients opted for oocyte donation after a failed second attempt or DuoStim. All underwent conventional or DuoStim stimulation, ICSI, blastocyst culture, and single fresh or vitrified-warmed untested/euploid transfer. Endpoints included: cLBR per first attempt, time to complete first and two attempts, treatment discontinuation (primary outcome), time between attempts, and switch to oocyte donation. Regression analyses assessed associations between these outcomes and clinical/anamnestic variables, IVF features, and first-attempt results.

Results

Maternal age (adjusted-OR: 0.81), AMH (adjusted-OR: 1.03), and SMF (adjusted-OR:0.75) were independently associated with cLBR. The duration of the first attempt (median: 50 days, Q1:17;Q3:120) was inversely related to maternal age (-8 days), and positively influenced by AMH (+2 days), with an extension of 26-days per blastocyst formed. When comparing cycle outcomes, those resulting in live birth had a median duration of 95 days. In comparison, cycles with no mature (MII) oocytes were significantly shorter by 126 days, and those with no transferable blastocysts were 64 days shorter. Conversely, cycles ending in implantation failure lasted 8 days longer, while those ending in miscarriage extended the duration by 56 days. Treatment discontinuation was associated with increased maternal age (adjusted OR: 1.04), lower AMH (adjusted OR: 0.98), and poor first-attempt outcomes: 46% discontinued after no transferable blastocyst, while the odds of discontinuation decreased with no MII oocyte (adjusted OR: 0.63) and increased after implantation failure (adjusted OR: 1.5). Discontinuation rates declined over time, from 57% in 2014 to 33% in 2020, during which the use of DuoStim protocols rose from 0% to 17%. Time between attempts (median: 147 days, Q1:84; Q3:248) decreased with maternal age (-6 days), increased with AMH (+1.5 days), and extended 13 days per blastocyst. Compared to no blastocyst (median: 107 days), implantation failure/miscarriage added 49 days. Time to complete two attempts (median: 193 days, Q1:85; Q3:371) decreased with maternal age (-22 days) and DuoStim use (-79 days), and increased with AMH (+4 days). Switch to oocyte donation increased with maternal age (adjusted-OR: 1.11), year of first attempt (adjusted-OR:1.5), and DuoStim (adjusted-OR:2.2).

Conclusions

The progressive adoption of DuoStim and oocyte donation reduced treatment discontinuation and time in treatment, supporting multicycle counseling to personalize IVF journeys and better prepare couples to deal with potential failures.