TO CHANGE OR NOT TO CHANGE? THE BENEFIT OF IVF PROTOCOL MODIFICATION IN A SUBSEQUENT CYCLE

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Background

Optimization of ovarian stimulation protocols is an important strategy for improving outcomes in in vitro fertilization (IVF). Following a suboptimal first IVF cycle, clinicians commonly modify stimulation medications or dosages to improve ovarian response and embryo development. However, there is limited real-world evidence evaluating the effectiveness of these individualized protocol changes.

Understanding whether protocol modification improves subsequent IVF outcomes may help optimize treatment strategies and improve patient care.

Objective and Study Methods

To evaluate whether individualized stimulation protocol modification between a patient's first and second IVF cycle improves ovarian response and embryologic outcomes.

Study Design: Retrospective longitudinal cohort study
Patients Analyzed: 213 paired IVF cycles with protocol modification and 46 paired IVF cycles without protocol modification
Time Frame: January 1, 2020 – December 31, 2025
Protocol Modification: Change in stimulation medication type and/or dosage between the first and second IVF cycle.

The primary outcomes evaluated were the number of oocytes retrieved, fertilization rate, blastocyst yield, and blastocyst utilization rate (BUR). Descriptive statistics were reported as mean ± standard deviation, and first- and second-cycle outcomes were compared using paired t-tests, with statistical significance defined as $p < 0.05$.

Results and Interpretation

A total of 213 paired IVF cycles with protocol modification and 46 paired IVF cycles without protocol modification were analyzed. Mean patient age was similar between the first and second cycles in the protocol modification cohort (35.86 ± 3.76 vs. 36.16 ± 5.92 years), indicating comparable baseline characteristics.

Following stimulation protocol modification, the mean number of oocytes retrieved increased significantly from 9.45 ± 5.94 to 11.19 ± 6.71 ($p=0.005$), while blastocyst yield increased significantly from 1.92 ± 1.90 to 2.89 ± 2.77 ($p<0.001$) (Figure 1). Blastocyst utilization rate (BUR) also improved significantly, increasing from 34.0% to 41.2% ($p=0.012$). Although fertilization rate increased from 53.2% to 56.8%, this difference was not statistically significant ($p=0.134$) (Figure 2). In contrast, among patients who underwent repeat IVF cycles without protocol modification (n = 46), no significant improvements were observed in oocyte yield, fertilization rate, blastocyst yield, or blastocyst utilization rate between cycles.

Overall, protocol modification was associated with significant improvements in ovarian response and embryo development, whereas repeat cycles without protocol modification demonstrated no measurable improvement.

Figure 1. Ovarian Response Following Protocol Modification

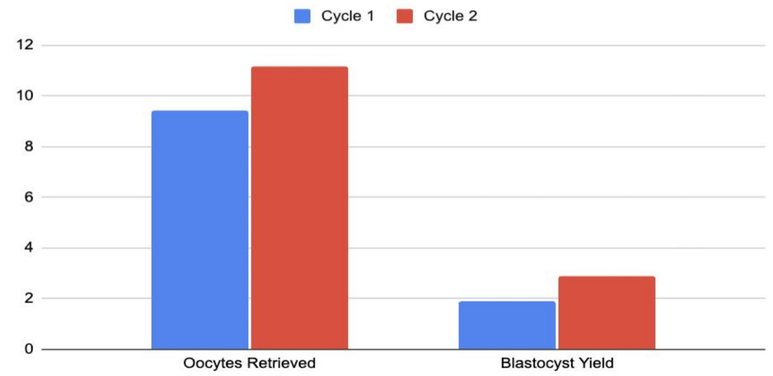

Figure 1. Oocytes retrieved and blastocyst yield increased significantly following stimulation protocol modification.

Figure 2. Embryologic Outcomes Following Protocol Modification

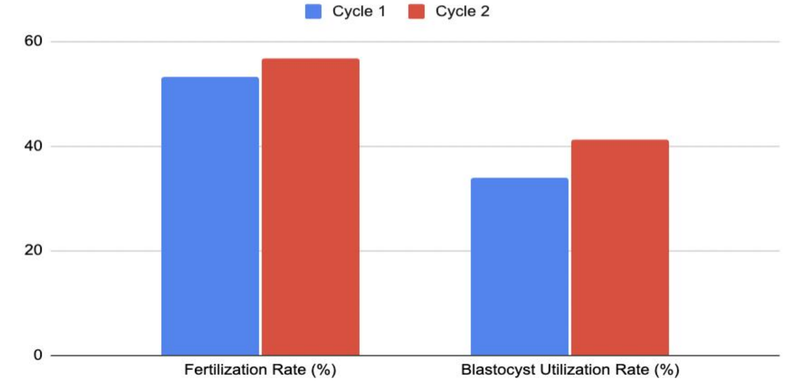

Figure 2. Blastocyst utilization rate increased significantly, while fertilization rate remained unchanged.

Conclusion

Individualized stimulation protocol modification between consecutive IVF cycles was associated with significant improvements in ovarian stimulation and embryo development outcomes, whereas repeat IVF cycles without protocol modification showed no significant improvement. Patients undergoing revised stimulation protocols produced more oocytes, greater blastocyst yield, and higher blastocyst utilization rates than during their initial cycle. These findings support reassessing and personalizing stimulation strategies following an initial IVF response to optimize subsequent cycle outcomes and improve treatment efficiency.

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References

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