BEST STRATEGIES FOR EGG DONOR PREPARATION: A RETROSPECTIVE ANALYSIS OF A SINGLE-CENTER COHORT

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ABSTRACT

Egg donation is a critical component of assisted reproductive technology, but its success hinges on optimal donor selection and stimulation protocols. This article summarizes a retrospective analysis of egg donor preparation strategies at a single fertility center. The study evaluated donor selection criteria, oocyte quantity and quality, the role of preimplantation genetic testing for aneuploidy (PGT-A), and the comparative efficacy and safety of different follitropin preparations. Key findings indicate that while age is a significant factor, anti-Müllerian hormone (AMH) is a more crucial marker for ovarian reserve. A substantial proportion of cycles experienced "unmet expectations", highlighting the physiological variability of AMH and the importance of considering antral follicle count (AFC) in cases of discordance. The data suggest no statistically significant difference in oocyte quantity or quality in younger donor age groups (≤30 years). Furthermore, PGT-A did not improve live birth rates in this donor oocyte population, though it did prevent transfers in cycles with no euploid embryos. The use of follitropin delta demonstrated a higher safety profile in terms of ovarian hyperstimulation syndrome (OHSS) risk. These findings underscore the need for a personalized approach to donor stimulation, with AMH as the primary guide for selection and dose determination, while also acknowledging the value of other markers and protocols.

Keywords: egg donation; IVF; ovarian stimulation; AMH; FSH; follitropin delta; oocyte quality; PGT-A

Introduction

Egg donation (ED) has become an indispensable treatment for infertility, offering hope to patients with diminished ovarian reserve, late reproductive age, genetic disorders, or other conditions precluding the use of their oocytes. The success of an ED program is fundamentally dependent on the quality and quantity of donated oocytes, which in turn are determined by meticulous donor selection and the effectiveness of the ovarian stimulation protocol.

For decades, the primary criteria for selecting egg donors have focused on age and ovarian reserve markers. The ESHRE register data from 2016 and subsequent clinical guidelines have

established a framework, typically recommending donors aged 21 to 31 with a body mass index (BMI) up to 30kg/m2 and an AMH level of at least 3ng/ml.[1] However, despite these guidelines, challenges persist. One of the main hurdles is the unpredictability of ovarian response, leading to "unmet expectations" where the number of retrieved oocytes falls short of the expected yield.[2] This unpredictability can be attributed to several factors, including the physiological variability of ovarian reserve markers, limitations of current laboratory assays, and the individualized response to gonadotropin stimulation.[3]

The choice of gonadotropin and the starting dose are also critical decisions in controlled ovarian stimulation (COS).[4,5] The development of recombinant follicle-stimulating hormone (r-FSH) has allowed for more precise dosing, but the optimal dose remains a subject of debate. Furthermore, the introduction of novel gonadotropins, such as follitropin delta, with different pharmacological profiles, necessitates a re-evaluation of current practices.[6,7]

This article aims to address these challenges by presenting a retrospective analysis of our center's experience with egg donor preparation. We will explore the relationships between donor age, AMH, and oocyte quality; the impact of AMH and antral follicle count (AFC) discordance; the clinical utility of PGT-A in donor oocyte cycles; and the efficacy and safety of different follitropin types. The ultimate goal is to provide a comprehensive overview of best practices to optimize egg donor preparation, maximize oocyte yield and quality, and improve the safety and efficiency of ED programs.

Materials and Methods

This retrospective study analyzed data from 184 egg donor cycles performed at the IVMED Fertility Center between October 2020 and March 2021.

Study Population and Inclusion Criteria

All egg donors were selected based on criteria consistent with the Ministry of Health Order № 787 and international standards. These criteria included:

- Age between 21 and 31 years old.
- AMH level ≥3.0ng/ml.
- BMI up to 30kg/m2.
- Absence of bad habits, hereditary pathology, and severe somatic diseases.
- No more than six previous donation attempts.
- Sufficient compliance and awareness to understand and fulfill the requirements of the program.

Ovarian Stimulation Protocols

The standard stimulation protocol for egg donors was a short GnRH antagonist protocol. The starting dose of r-FSH was typically in the range of 200-250 IU or corypholitropin alpha at 150 IU. The primary objective of the stimulation was to obtain 20-30 follicles. In some cases, follitropin delta was used. The dosage of follitropin delta was determined according to the manufacturer's recommendations based on the donor's AMH level and body weight.[6,8,9,10]

Data Collection and Parameters

Data were collected on donor demographics (age, BMI), oocyte yield, and quality. Oocyte quality was assessed by the number of metaphase II (MII) oocytes and the proportion of grade 1 (Q1) eggs. Embryological parameters, including the number of MII oocytes, were analyzed

concerning donor age. The study also examined the correlation between AMH and AFC, physiological AMH variability, and the incidence of "unmet expectations" (cycles with fewer than 12 oocytes retrieved).

Additionally, data on PGT-A cycles were reviewed to compare live birth rates, pregnancy rates, and aneuploidy rates between cycles with and without PGT-A. Finally, the safety and efficacy of follitropin delta were compared to follitropin alpha/beta, with a specific focus on the risk of OHSS and the number of oocytes and blastocysts obtained.

Results

A total of 184 donor oocyte retrievals were performed, resulting in 24,890 eggs. The average number of eggs per retrieval was 28, and the average number of MII oocytes was 24.6. The donor population had an average age of 28 years, with the majority (68.6%) between 26 and 30 years old.

Donor Age and Oocyte Quality

Data comparing oocyte quality across different age groups revealed no statistically significant differences in the number and quality of eggs in young age groups (≤25, 26-30, and ≥31 years). Approximately 60-70% of MII oocytes were classified as Q1 across all age groups. This finding suggests that within the donor age range, oocyte quality is more of an individual characteristic than a function of age (Table 1).

Table 1. Oocyte Yield and Quality by Donor Age Group (IVMED Data, 2021)

Parameter	≤25 years old	26-30 years old	≥31 years old
Follicles number	31.5	27.7	25.9
Oocytes number	30.0	25.8	24.0
MII oocytes	24.6	21.3	18.9
Q1 oocytes (%)	57.9	73.2	69.8
Non-usable oocytes (%)	12.5	14.2	11.9

AMH and AFC as Markers

While AMH is a primary selection criterion, the study noted a significant rate of "unmet expectations", with 27.7% of cycles yielding less than 20 oocytes despite high AMH levels. This can be partially explained by physiological AMH variability, which was found to be up to 28% within a single cycle. A discordance between AMH and AFC was also observed in up to 20% of cases, with this mismatch being more pronounced in women over 35 years of age. In cases of discordance, the best outcomes were observed in women with normal AFC and low AMH. The data support the conclusion that AMH is the most critical single marker for egg donor selection, but in cases of discordance, both AMH and AFC should be considered.

PGT-A Outcomes

A study on the use of PGT-A in donor oocyte recipients showed that while the median aneuploidy rate per recipient was 25%, the use of PGT-A did not significantly improve the likelihood of a live birth (53.8% with PGT-A vs. 55.8% without; P=0.44). However, PGT-A did help to avoid embryo transfers in cycles with no euploid embryos. The literature supports this thesis.[11]

Follitropin Comparison

A systematic review and meta-analysis comparing follitropin delta to follitropin alpha/beta demonstrated a higher safety profile for follitropin delta, with a lower risk of OHSS.[10-12] The study also noted that on average, 150IU of follitropin alpha corresponded to 10.3µg of follitropin delta in all patients, and 9.5µg in patients with normal or high ovarian reserve. This non-linear relationship highlights the different biological activities and dosing profiles of the two drugs.

Discussion

The findings of this retrospective analysis reinforce several key principles of modern egg donor preparation while also highlighting areas for improvement. The central role of AMH as a marker of ovarian reserve is confirmed. Yet, the high rate of "unmet expectations" and the observed physiological variability of AMH underscore the limitations of relying solely on a single baseline measurement. The data suggest that a more dynamic approach, possibly incorporating AFC and repeated AMH measurements in ambiguous cases, is warranted.

The comparison of oocyte quality across different age groups within the donor range is particularly insightful. The lack of a significant difference in oocyte quantity and quality in younger age groups (≤30 years) suggests that once a donor meets the initial screening criteria, other individual characteristics become more predictive of a cycle's success. This supports the notion that "proven fertility does not exclude the possibility of receiving eggs with poor quality" and that the "quality of eggs is mostly a 'personal' characteristic of the egg donor."

The PGT-A data present a compelling argument for careful patient counseling. While PGT-A can provide valuable information about aneuploidy, it did not translate to a higher live birth rate in this population of recipients of young, healthy donor oocytes. This suggests that the cost and potential for unnecessary cycle delays or cancellations due to PGT-A may not be justified in this context.

Finally, the data on follitropin delta vs. follitropin alpha/beta offer a practical path toward improving the safety of ovarian stimulation. The ability of follitropin delta to be dosed based on AMH and weight, combined with its reduced risk of OHSS, makes it an attractive option, particularly for high responders, which is a typical profile among egg donors. The understanding of FSH isoform variability further supports the move toward personalized medicine in COS, where the type and dose of gonadotropin are tailored to the individual's specific physiological state.

In conclusion, the optimal preparation of egg donors requires a multifaceted strategy. AMH should be the primary selection marker, but with careful consideration of AFC in discordant cases. The starting FSH dose should be individualized, with a keen awareness of the different pharmacological profiles of available gonadotropins. While age is a factor, oocyte quality appears to be a more individual characteristic. This holistic approach, guided by continuous data analysis and a commitment to personalized medicine, is essential for maximizing the success and safety of egg donation programs.

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