International Science and Technology Journal
المجلة الدولية للعلوم والتقنية
Volume 38 العدد
Part 2 المجلد
المجلة الدولية للعلوم والتقنية
International Science and Technology Journal
ISTJ

http://www.doi.org/10.62341/istj-vol38-2-md20

Received	**2026/04/25**	**تم استلام الورقة العلمية في**
Accepted	**2026/05/16**	**تم قبول الورقة العلمية في**
Published	**2026/05/17**	**تم نشر الورقة العلمية في**

FSH Therapy for Improving Ovarian Response in Poor Responders with Low Ovarian Reserve: A Retrospective Study of 100 Cases

Mohamed Omar Abdulhamid

Department of Pharmacology and Toxicology, Faculty of Pharmacy, Omar Al-Mukhtar University, Al Bayda, Libya

mohammed.abdalhafid@omu.edu.ly

Abstract

Background: Poor ovarian response (POR) affects 9–24% of women undergoing ovarian stimulation. The optimal Follicle-Stimulating Hormone (FSH) dose for improving ovarian response in POR patients with low ovarian reserve remains controversial.

Objective: To compare the effect of high dose (300–450 IU/day) versus low dose (150–225 IU/day) FSH on ovarian response improvement and to identify predictors of normal response.

Methods: A retrospective study was conducted on 100 POR women (mean age 37.5 ± 1.7 years; 50 low dose, 50 high dose) at the Al Bayda – Al Jabal Al Akhdar National Educational Center for Diagnosis and Treatment of Infertility. All patients had documented poor response before treatment. After FSH stimulation, response was classified as Poor (follicles < 3 AND Estradiol (E_2) < 500 pg/mL) or Normal (follicles ≥ 3 OR E_2 ≥ 500 pg/mL). Chi-square, independent t-tests, Pearson correlation, and logistic regression were used.

Results: The improvement rate was 26% (13/50) in the low dose group and 38% (19/50) in the high dose group, with no significant difference ($\chi^2 = 1.654$, df = 1, p = 0.198). No significant differences were observed in follicle count (2.04 ± 0.70 vs. 2.26 ± 0.92, p = 0.182) or peak E_2 (445.8 ± 104.7 vs. 467.4 ± 140.9 pg/mL, p =

FSH Therapy for Improving Ovarian Response in Poor Responders with Low Ovarian Reserve: A Retrospective Study of 100 Cases

http://www.doi.org/10.62341/istj-vol38-2-md20

0.386). Anti-Müllerian Hormone (AMH) was strongly correlated with follicle count ($r = 0.772$, $p < 0.001$).

Conclusion: High dose FSH did not significantly improve ovarian response compared to low dose FSH in poor responders with low ovarian reserve. A low dose protocol (150–225 IU/day) is a reasonable first-line strategy.

Keywords: Poor ovarian response, FSH dose, ovarian reserve, AMH, retrospective study, improvement rate.

علاج FSH لتحسين استجابة المبيض لدى ضعيفات الاستجابة مع الاحتياطي المنخفض للمبيض: دراسة استرجاعية على 100 حالة

محمد عمر عبد الحميد

قسم الأدوية والسموم، كلية الصيدلة، جامعة عمر المختار، البيضاء، ليبيا

البريد الإلكتروني للمراسلة: mohammed.abdalhafid@omu.edu.ly

الملخص

تؤثر استجابة المبيض الضعيفة على 9–24% من النساء الخاضعات لتحفيز المبيض. تهدف هذه الدراسة الاسترجاعية إلى مقارنة تأثير الجرعة العالية (300–450 وحدة دولية/يوم) مقابل الجرعة المنخفضة (150 – 225 وحدة دولية/يوم) من الهرمون المنبه للجريب (FSH) على تحسين استجابة المبيض لدى 100 مريضة. أُجريت الدراسة في المركز الوطني التعليمي للبيضاء – الجبل الأخضر لتشخيص وعلاج العقم. وجد معدل التحسن 26% في مجموعة الجرعة المنخفضة و38% في مجموعة الجرعة العالية دون فرق إحصائي معنوي ($p = 0.198$). ارتبط AMH بقوة بعدد الجريبات ($r = 0.772$, $p < 0.001$). توصي الدراسة باعتبار الجرعة المنخفضة خياراً أولياً معقولاً لتقليل الأعباء الدوائية والتكاليف.

FSH Therapy for Improving Ovarian Response in Poor Responders with Low Ovarian Reserve: A Retrospective Study of 100 Cases

http://www.doi.org/10.62341/istj-vol38-2-md20

الكلمات المفتاحية: ضـعف اسـتجابة المبيض، جرعة هرمون FSH، مخزون المبيض، هرمون AMH، دراسة استرجاعية، معدل التحسن

Introduction

Poor ovarian response (POR) is one of the most challenging conditions in reproductive medicine, occurring in 9–24% of women undergoing controlled ovarian stimulation (Ferraretti et al., 2011). POR is associated with reduced oocyte yield, increased cycle cancellation rates, and lower pregnancy rates. The Bologna criteria define POR as the presence of at least two of the following: advanced maternal age (≥ 40 years), a previous POR (≤ 3 oocytes with a conventional stimulation), or an abnormal ovarian reserve test (AMH < 1.0 ng/mL or AFC < 5 – 7) (Ferraretti et al., 2011).

Despite frequent use of high FSH doses (300 – 450 IU/day) to overcome POR, evidence of their superiority over standard doses (150–225 IU/day) is conflicting. A recent randomized controlled trial found that in poor ovarian reserve women, FSH 300 IU/day did not improve cumulative live birth rates compared to 150 IU/day (Yan et al., 2024). Another large RCT demonstrated that an increased FSH dose (225/450 IU/day) does not improve cumulative live birth rates in predicted poor responders (Lensen et al., 2017). A Cochrane review concluded that individualized FSH dosing based on ovarian reserve tests yields similar pregnancy outcomes to conventional dosing (Ngwenya et al., 2024).

AMH has been established as the strongest predictor of ovarian response. A meta-analysis confirmed that AMH and AFC accurately predict ovarian response, with AMH being particularly valuable for individualizing FSH dose (Broer et al., 2011; Maged et al., 2024). However, most studies focus on post-treatment response rather than on improvement from a pre-treatment poor status.

This retrospective study therefore aimed to:

- To compare the effect of high dose (300 – 450 IU/day) versus low dose (150 – 225 IU/day) FSH on ovarian response improvement and to identify predictors of normal response.

http://www.doi.org/10.62341/istj-vol38-2-md20

Methods

Study Design

This was a retrospective chart review conducted at the Al Bayda – Al Jabal Al Akhdar National Educational Center for Diagnosis and Treatment of Infertility (Libya). The study was approved by the institutional research ethics committee. All data were extracted from the center's electronic medical records; no direct contact with patients was made. A waiver of informed consent was granted because the study involved only anonymized, pre-existing data.

Participants

Inclusion criteria:

- Age 35 – 40 years.
- Diagnosis of poor ovarian response based on a previous cycle with ≤ 3 oocytes or cycle cancellation, and/or low ovarian reserve (AMH < 2.0 ng/mL).
- Complete medical records.

Exclusion criteria:

- Polycystic ovary syndrome (PCOS).
- Endometriosis grade III/IV.
- Untreated endocrinopathy (hyperprolactinemia, thyroid dysfunction).
- Male factor infertility.

FSH Therapy and Dose Groups

All patients received recombinant FSH (Gonal F® or Puregon®) starting on day 2–3 of the menstrual cycle. The daily dose was either low dose (150 – 225 IU/day, n = 50) or high dose (300 – 450 IU/day, n = 50) according to the treating physician's judgement. Stimulation continued until at least one follicle reached ≥ 17 mm, at which point Human Chorionic Gonadotropin (hCG) was administered (except for cycles cancelled due to extremely poor response).

Ovarian Response Assessment

On the day of hCG (or the last stimulation day), the following were recorded:

http://www.doi.org/10.62341/istj-vol38-2-md20

- Number of follicles ≥ 14 mm by transvaginal ultrasound.
- Peak serum estradiol (E_2) level (pg/mL).

Response was classified as:

- Normal: ≥ 3 follicles OR E_2 ≥ 500 pg/mL.
- Poor: < 3 follicles AND E_2 < 500 pg/mL.

Improvement was defined as a change from pre-treatment Poor (documented in medical history) to post-treatment Normal.

Statistical Analysis

Statistical analysis was performed using SPSS version 23. Continuous variables are presented as mean ± standard deviation and were compared between dose groups using independent t-tests. Categorical variables were compared using chi-square tests (or Fisher's exact when appropriate). Pearson correlation coefficient was used to assess the association between AMH and follicle count. Binary logistic regression was performed to identify independent predictors of normal response. A p-value < 0.05 was considered statistically significant.

Results

Baseline Characteristics

A total of 100 patients (50 low dose, 50 high dose) were analyzed. The baseline characteristics are shown in Table 1. All 100 patients had documented Poor response before treatment.

TABLE 1. Baseline characteristics of the study population (N = 100).

Variable	Mean ± SD	Min	Max
Age (years)	37.46 ± 1.71	35	40
BMI (kg/m²)	29.70 ± 1.18	27.5	31.8
AMH (ng/mL)	1.20 ± 0.38	0.50	1.90
Basal FSH (IU/L)	9.85 ± 1.63	7.0	13.6

http://www.doi.org/10.62341/istj-vol38-2-md20

Primary Outcome: Improvement Rates

After FSH therapy, the overall improvement rate was 32% (32/100). The improvement rate was 26% (13/50) in the low dose group and 38% (19/50) in the high dose group. This difference was not statistically significant ($\chi^2 = 1.654$, df = 1, p = 0.198).

Secondary Outcomes: Comparison of Continuous Parameters

Comparison of post-treatment parameters between the two dose groups is presented in Table 2.

TABLE 2. Comparison of post-treatment outcomes between low dose and high dose groups.

Parameter	Low dose (n=50)	High dose (n=50)	Mean diff.	95% CI	p value
Follicles ≥14 mm	2.04 ± 0.70	2.26 ± 0.92	-0.22	-0.545 to 0.105	0.182
Peak E_2 (pg/mL)	445.8 ± 104.7	467.4 ± 140.9	-21.6	-70.87 to 27.67	0.386
AMH (ng/mL)	1.228 ± 0.373	1.168 ± 0.394	0.060	-0.092 to 0.212	0.436
Basal FSH (IU/L)	9.628 ± 1.478	10.072 ± 1.750	-0.444	-1.087 to 0.199	0.174

No significant differences were found in follicle count or peak E_2 between the two dose groups.

FSH Therapy for Improving Ovarian Response in Poor Responders with Low Ovarian Reserve: A Retrospective Study of 100 Cases

http://www.doi.org/10.62341/istj-vol38-2-md20

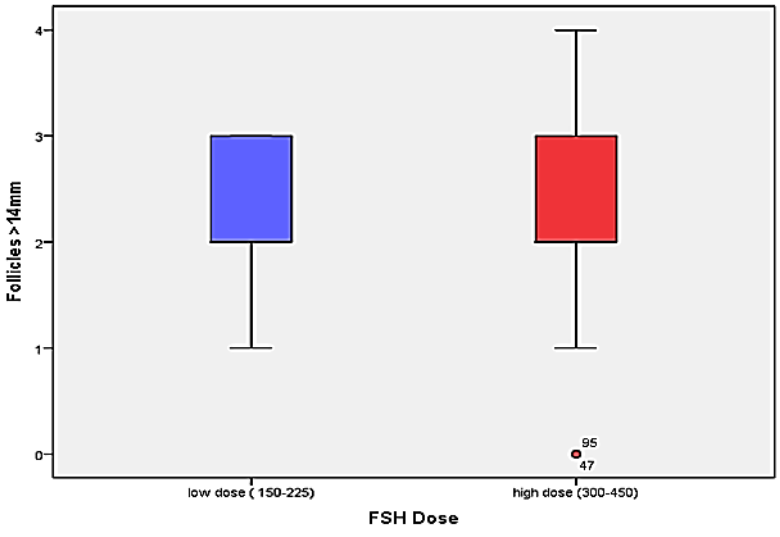

Figure 1. Boxplot of follicle count (≥14 mm) by dose group

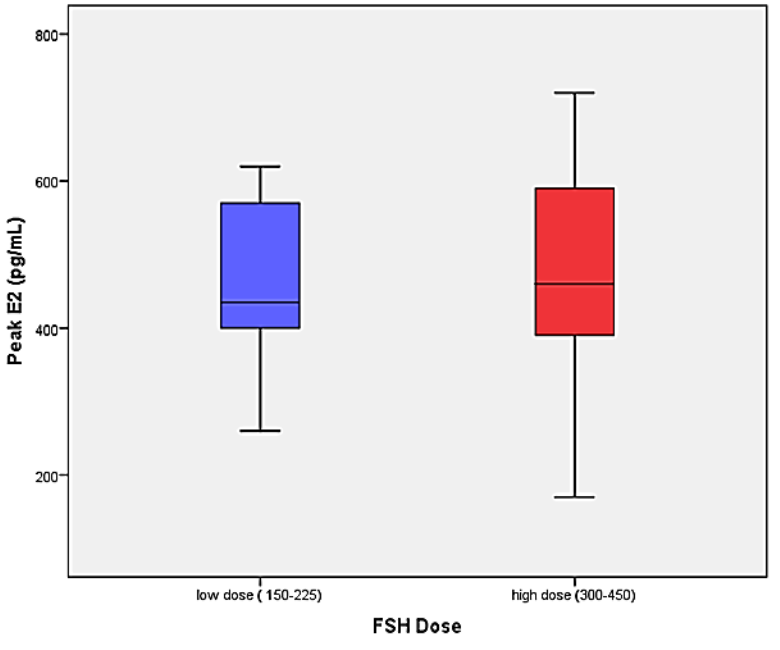

Figure 2. Boxplot of peak E_2 (pg/mL) by dose group.

FSH Therapy for Improving Ovarian Response in Poor Responders with Low Ovarian Reserve: A Retrospective Study of 100 Cases

http://www.doi.org/10.62341/istj-vol38-2-md20

Correlation between AMH and Follicle Count

There was a strong positive correlation between pre-treatment AMH and post-treatment follicle count (Pearson $r = 0.772$, $p < 0.001$), indicating that baseline ovarian reserve is the dominant determinant of response.

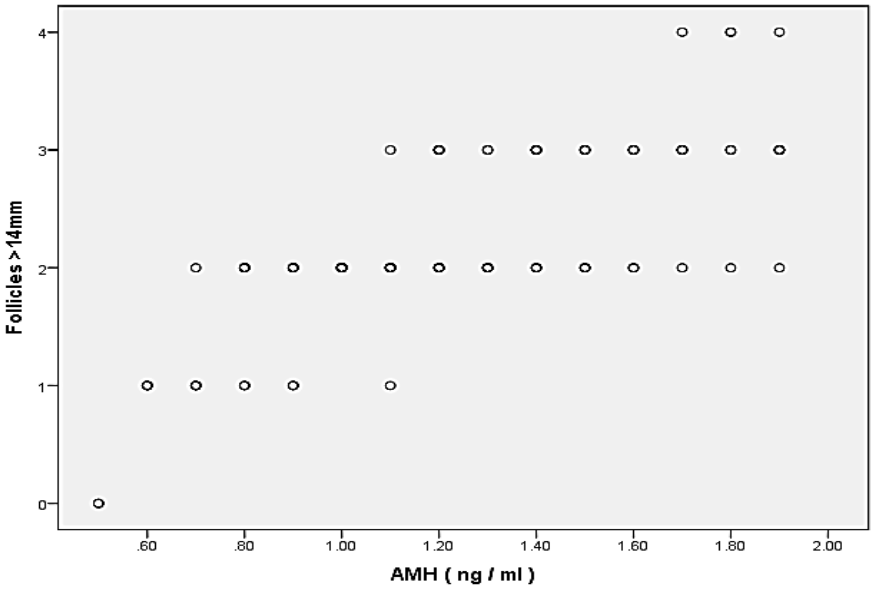

Figure 3. Scatter plot of AMH vs. follicles with regression line ($r = 0.772$, $p < 0.001$).

Comparison between Improved and Non-Improved Patients

Patients who improved ($n = 32$) had significantly higher AMH (1.55 ± 0.26 vs. 1.03 ± 0.32 ng/mL, $p < 0.001$), more follicles (3.13 ± 0.34 vs. 1.69 ± 0.53, $p < 0.001$), and higher peak E_2 (604.7 ± 43.6 vs. 386.9 ± 80.2 pg/mL, $p < 0.001$) compared to non-improved patients.

Cycle Cancellation

Cycle cancellation occurred in 11 low dose patients (22.0%) and 8 high dose patients (16.0%), with no significant difference ($\chi^2 = 0.585$, $df = 1$, $p = 0.444$).

http://www.doi.org/10.62341/istj-vol38-2-md20

Logistic Regression Analysis

Due to the small number of normal responders (n = 32), the full logistic regression model (including age, BMI, AMH, basal FSH, total dose, and dose group) showed wide confidence intervals. AMH was the only variable that approached significance, but the wide CI indicates instability. The chi-square test remains the most reliable for the primary comparison.

Discussion

This retrospective study found that high dose FSH (300–450 IU/day) did not significantly improve ovarian response compared to low dose FSH (150–225 IU/day) in poor responders with low ovarian reserve. The improvement rate was numerically higher in the high dose group (38% vs. 26%), but the difference was not statistically significant ($p = 0.198$). Furthermore, post-treatment follicle numbers and peak E_2 levels were similar between the two dose groups.

Our findings align with recent randomised controlled trials. Yan et al. (2024) reported no improvement in cumulative live birth rates with 300 IU/day FSH in poor ovarian reserve women. Lensen et al. (2017) found that an increased FSH dose (225/450 IU/day) does not improve cumulative live birth rates in predicted poor responders. The 2024 Cochrane review (Ngwenya et al., 2024) concluded that individualized FSH dosing based on ovarian reserve tests yields similar pregnancy outcomes to conventional dosing. Leijdekkers et al. (2020) in a systematic review and meta-analysis showed that increasing FSH dose above 150 IU/day does not improve live birth rates in poor responders.

The strong correlation between AMH and follicle count ($r = 0.772$, $p < 0.001$) confirms that baseline ovarian reserve is the dominant determinant of response, not the FSH dose itself. This is consistent with Broer et al. (2011) and the recent meta-analysis by Maged et al. (2024), who demonstrated that AMH is the best single predictor of ovarian response.

http://www.doi.org/10.62341/istj-vol38-2-md20

Strengths and Limitations

Strengths**:**

- Use of pre-treatment documentation to define improvement.
- Balanced dose groups (50/50).
- Standardized response criteria based on follicles and E_2.
- Comprehensive statistical analysis.
- No direct contact with patients; all data were obtained from routine clinical records, eliminating recall bias.

Limitations:

- Retrospective design with potential selection bias.
- Small number of normal responders (n = 32) limiting logistic regression stability.
- Single center data.
- No pregnancy or live birth data.
- Lack of blinding in dose assignment.

Conclusions

In poor responders with low ovarian reserve, a high dose of FSH (300 – 450 IU/day) does not provide a statistically significant advantage over a low dose (150 – 225 IU/day) in improving ovarian response. The low dose regimen (150 – 225 IU/day) should be considered first-line to reduce medication burden, cost, and potential side effects. AMH remains the strongest predictor of ovarian response. Prospective randomized controlled trials are needed to confirm these findings.

References

Broer, S. L., Dolleman, M., Opmeer, B. C., Fauser, B. C., Mol, B. W., & Broekmans, F. J. (2011). AMH and AFC as predictors of excessive response in controlled ovarian hyperstimulation: a meta-analysis. Human Reproduction Update, 17(1), 46–54.

Ferraretti, A. P., La Marca, A., Fauser, B. C., Tarlatzis, B., Nargund, G., & Gianaroli, L. (2011). ESHRE consensus on the definition of ‘poor response’ to ovarian stimulation for in

http://www.doi.org/10.62341/istj-vol38-2-md20

vitro fertilization: the Bologna criteria. Human Reproduction, 26(7), 1616–1624.

Klinkert, E. R., Broekmans, F. J., Looman, C. W., & te Velde, E. R. (2005). The poor responder in IVF: is the prognosis always poor? A systematic review. Human Reproduction Update, 11(1), 23–34.

La Marca, A., & Sunkara, S. K. (2014). Individualization of controlled ovarian stimulation in IVF using ovarian reserve markers. Human Reproduction Update, 20(1), 124 – 140.

Leijdekkers, J. A., Eijkemans, M. J., van Tilborg, T. C., Oudshoorn, S. C., van Golde, R. J., Hoeijmakers, Y., & Broekmans, F. J. (2020). Individualized versus conventional FSH dosing in IVF: a systematic review and meta-analysis. Human Reproduction Update, 26(4), 506–528.

Lensen, S. F., Wilkinson, J., Mol, B. W., & Farquhar, C. (2017). Individualised gonadotropin dose selection using markers of ovarian reserve for women undergoing IVF/ICSI (Cochrane review). Cochrane Database of Systematic Reviews, 2017(12), CD012693.

Maged, A. M., Kamel, A. M., & Al-Inany, H. (2024). The best ovarian reserve marker to predict ovarian response following controlled ovarian hyperstimulation: a systematic review and meta-analysis. Systematic Reviews, 13, Article 303. https://doi.org/10.1186/s13643-024-02684-0

Ngwenya, O., Lensen, S. F., Vail, A., Mol, B. W. J., Broekmans, F. J. M., & Wilkinson, J. (2024). Individualised gonadotropin dose selection using markers of ovarian reserve for women undergoing in vitro fertilisation plus intracytoplasmic sperm injection (IVF/ICSI). Cochrane Database of Systematic Reviews, 2024(4), CD012693. https://doi.org/10.1002/14651858.CD012693.pub3

Polyzos, N. P., & Sunkara, S. K. (2018). Poor ovarian responders: an update. Reproductive BioMedicine Online, 37(6), 699–710.

http://www.doi.org/10.62341/istj-vol38-2-md20

van Tilborg, T. C., Eijkemans, M. J., Laven, J. S., Koks, C. A., de Bruin, J. P., Scheffer, G. J., & Broekmans, F. J. (2017). Individualized versus standard FSH dosing in women starting IVF/ICSI: an RCT. Part 1: The predicted poor responder. Human Reproduction, 32(12), 2496–2505.

Yan, Q., Li, X., Liu, L., Li, Z., Wu, X., Sun, Z., & Wang, Y. (2024). Comparison of the cumulative live birth rate of different doses of rFSH in poor ovarian reserve women undergoing GnRH antagonist ART treatment: a randomized controlled trial. Human Reproduction, 39(Suppl 1), dead093.357.

Younis, J. S., Izhaki, I., & Ben-Ami, M. (2015). The impact of high-dose FSH on the outcome of IVF cycles in poor responders. Gynecological Endocrinology, 31(8), 597–601.