

## Original article

# Comparison of GnRH Agonist Long Protocol and Stop GnRH-agonist Protocol in IVF/ICSI Patients at Misurata National Infertility and Diagnostic Center

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Corresponding Email. [Manajla73@gmail.com](mailto:Manajla73@gmail.com)**Abstract**

In clinical practice, the main stimulation protocol is frequently employed: the long GnRH agonist protocol. The long protocol involves continuous GnRHa administration starting in the luteal phase, whereas the “stop” protocol entails early discontinuation of GnRHa to enhance ovarian response, particularly in poor responders. This study compared the outcome of GnRH Agonist Long Protocol and Stop GnRH-agonist Protocol in women undergoing IVF/ICSI treatment at Misurata National Infertility and Diagnostic Center. 129 infertile women were recruited, and they were assigned to the long protocol (n=72) and Stop protocol (n=57) groups. Baselines were comparable except for advanced age, AMH level, and AFC, which were lower in the Stop protocol group. Both protocols were adequate in suppressing LH, E2, and AFC. The Long protocol group showed higher E2 activation and AFC after stimulation. Ovarian stimulation parameters like total gonadotropin consumption and days of stimulation were equal; however, the Long protocol group required more recombinant LH and higher E2 levels on hCG day. Embryological outcomes, e.g., obtained oocytes, MII oocytes, fertilization, and pregnancy rates, were comparable between groups, with greater Day 3 transfer in the Long protocol group. The Stop protocol is an appropriate alternative for women with diminished ovarian reserve, offering shorter treatment, diminished estrogen exposure, and comparable clinical outcomes.

**Keywords:** IVF, ICSI, GnRH agonist, Long Protocol, Stop Protocol, Ovarian Stimulation.**Introduction**

Infertility affects approximately 10–15% of couples worldwide and is defined as the inability to achieve a clinical pregnancy after 12 months of regular, unprotected sexual intercourse or due to reduced reproductive capacity in either partner [1]. Assisted reproductive technology (ART) has become an essential therapeutic option for couples experiencing difficulty conceiving [2]. Among ART techniques, in vitro fertilization (IVF) remains the most widely applied worldwide and has significantly improved pregnancy outcomes over the past decades [3]. Gonadotropin-releasing hormone (GnRH) agonist protocols are commonly used in IVF/ICSI cycles to prevent premature luteinizing hormone (LH) surges through pituitary downregulation [4].

Controlled ovarian stimulation (COS) is a crucial step in IVF, as it promotes the recruitment of multiple follicles, thereby increasing the likelihood of successful fertilization and embryo transfer [5]. In clinical practice, the main stimulation protocol is frequently employed: the long GnRH agonist protocol [6]. The long protocol involves continuous GnRHa administration starting in the luteal phase [4], whereas the “stop” protocol entails early discontinuation of GnRHa to enhance ovarian response, particularly in poor responders [7]. This study aimed to compare the clinical, hormonal, and embryological outcomes of the Long and Stop GnRHa protocols in patients undergoing IVF/ICSI at Misurata National Infertility and Diagnostic Center.

**Methods**

A retrospective comparative study was conducted between January and June 2025. A total of 129 infertile women aged 24–43 years were included. Patients with PCOS or uterine pathology were included. The population was divided into GnRH Agonist Long Protocol (n=72) and Stop GnRH-agonist Protocol (n=57) groups based on the stimulation protocol used.

**Stimulation regimens**

**Long Protocol:** Decapeptyl® 0.1 mg daily starting on cycle day 17–20, with recombinant FSH (150–300 IU) initiated on cycle day 2–3. hCG trigger was administered when  $\geq 2$  follicles reached 16–22 mm, followed by oocyte retrieval 34–36 hours later.

**Stop Protocol:** Decapeptyl® was started in the luteal phase and discontinued at menstruation onset, followed by high-dose gonadotropin stimulation.

**Laboratory procedures**

Oocyte retrieval, ICSI or conventional IVF, embryo grading, and Day 3 or Day 5 embryo transfer were performed per standard protocols.

**Ethical approval**

Ethical approval was obtained from the Misurata University Ethics Committee. Patient consent followed the Helsinki Declaration.

### Statistical analysis

Data were analyzed using SPSS 26.0. Continuous variables were expressed as mean  $\pm$  SD and compared using independent t-tests. Categorical variables were presented as percentages and analyzed using chi-square tests.  $P < 0.05$  was considered statistically significant.

## Results

### Demographic Characteristics

Most demographic characteristics were comparable between groups. Advanced age and HRT usage were higher in the Stop protocol group ( $p = 0.04$  and  $0.000$ , respectively) (Table 1).

### Baseline Hormonal Profile

Basal FSH, LH, and E2 were similar between groups. AMH and basal AFC were significantly lower in the Stop protocol group ( $p = 0.003$  and  $0.031$ , respectively) (Table 2), indicating diminished ovarian reserve.

### Pre-treatment Decapeptyl® dosage.

The mean number of Decapeptyl® doses was similar between the groups ( $12.0 \pm 2.5$  vs.  $12.6 \pm 1.7$ , N/S). Most patients received injections on day 17, with more in the Stop protocol group ( $30/57$  vs.  $18/72$ ,  $p < 0.001$ ). Other injection days showed no significant differences (Table 3).

### Suppression effect of Decapeptyl®

Both protocols effectively suppressed LH, E2, and AFC. Mean bLH suppression was  $6.3 \pm 3.7$  vs.  $6.2 \pm 4.4$  IU/L, bE2 suppression  $41.7 \pm 23.1$  vs.  $37.7 \pm 28.2$  pg/ml, and bAFC suppression  $5.3 \pm 8.3$  vs.  $4.7 \pm 5.3$ , with no significant differences between groups (Table 4).

### Activation Effects of Decapeptyl®

Both protocols effectively suppressed LH, E2, and AFC. The Long protocol group demonstrated higher E2 and AFC activation post-stimulation ( $p = 0.02$  and  $0.001$ , respectively) (Table 5).

### Ovarian Stimulation Parameters

Total gonadotropin consumption, stimulation duration, endometrial thickness, and AFC on hCG day were comparable. The Long protocol group required more recombinant LH and had higher E2 on hCG day (Table 6).

### IVF/ICSI Outcomes

The number of retrieved oocytes, MII oocytes, fertilized embryos, transferred embryos, and pregnancy rates were similar between groups. Day 3 embryo transfers were more frequent in the Long protocol group ( $p = 0.007$ ) (Table 7).

**Table 1: Demographic Characteristics of Patients in the Stop and Long Protocol Groups**

| Parameter                                           | Stop Protocol (n=57) | Long Protocol (n=72) | P-value |
|-----------------------------------------------------|----------------------|----------------------|---------|
| Mean age (years) $\pm$ SD                           | 36.2 $\pm$ 6.0       | 33.2 $\pm$ 6.0       | N/S     |
| Young age (%)                                       | 21/57 (36.8%)        | 50/72 (69.4%)        | N/S     |
| Advanced age (%)                                    | 36/57 (63.2%)        | 22/72 (30.6%)        | 0.04    |
| Mean infertility period (years) $\pm$ SD            | 4.2 $\pm$ 3.2        | 7.0 $\pm$ 5.0        | N/S     |
| History of parity: P0 (%)                           | 39/57 (68.4%)        | 50/72 (69.4%)        | N/S     |
| P1 (%)                                              | 18/57 (31.6%)        | 6/72 (8.3%)          | N/S     |
| Multi-P (%)                                         | 0/57 (0%)            | 2/72 (2.8%)          | N/S     |
| History of miscarriages: A0 (%)                     | 42/57 (73.7%)        | 16/72 (22.2%)        | N/S     |
| A1 (%)                                              | 12/57 (21.1%)        | 6/72 (8.3%)          | N/S     |
| Rec. A (%)                                          | 3/57 (5.3%)          | 1/72 (1.4%)          | N/S     |
| Structural gynecological disease: Endometriosis (%) | 3/57 (5.3%)          | 2/72 (2.8%)          | N/S     |
| Uterine polyp (%)                                   | 3/57 (5.3%)          | 2/72 (2.8%)          | N/S     |
| Ovarian cyst (%)                                    | 12/57 (21.1%)        | 5/72 (6.9%)          | N/S     |
| BMI (kg/m <sup>2</sup> ) $\pm$ SD                   | 27.9 $\pm$ 3.9       | 27.7 $\pm$ 4.7       | N/S     |
| PCOS patients (%)                                   | 15/57 (26.3%)        | 13/72 (18.1%)        | N/S     |
| Patients treated with HRT (%)                       | 33/57 (57.9%)        | 15/72 (20.8%)        | 0.000   |

Data are presented as a number (n), mean  $\pm$  SD for continuous variables, and percentage (%) for categorical variables. Statistical %n: Number of patients in each group, SD: Standard Deviation, N/S: Not Significant, BMI: Body Mass Index, P: Parity (number of previous births), P0: Nulliparous (zero previous births), P1: Primiparous (one previous birth), Multi-P: Multiparous (multiple previous births),

A: Abortion or Miscarriage (number of previous miscarriages), A0: Zero previous miscarriages, A1: one abortion, Rec. A: Recurrent Abortion, PCOS: Polycystic Ovary Syndrome, HRT: Hormone Replacement Therapy

**Table 2: Basal Demographic Characteristics of Patients in the Stop and Long Protocol Groups.**

| Parameter                                        | Stop Protocol (n=57) | Long Protocol (n=72) | P-value |
|--------------------------------------------------|----------------------|----------------------|---------|
| Mean Basal FSH (bFSH) (IU/L) $\pm$ SD            | 9.4 $\pm$ 3.9        | 7.9 $\pm$ 1.9        | N/S     |
| Mean Basal LH (bLH) (IU/L) $\pm$ SD              | 8.9 $\pm$ 3.8        | 9.7 $\pm$ 4.0        | N/S     |
| Mean Basal E2 (bE2) (pg/ml) $\pm$ SD             | 78.6 $\pm$ 76.4      | 58.9 $\pm$ 26.8      | N/S     |
| Mean Basal Antral Follicle Count (bAFC) $\pm$ SD | 9.7 $\pm$ 7.0        | 10.5 $\pm$ 6.3       | 0.031   |
| Mean AMH (ng/ml) $\pm$ SD                        | 7.9 $\pm$ 1.9        | 9.7 $\pm$ 4.0        | 0.003   |

Data are presented as a number (n), mean  $\pm$  SD for continuous variables, and percentage (%) for categorical variables. Statistical significance is at  $P < 0.05$ . n: Number of patients in each group, SD: Standard Deviation, N/S: Not Significant, FSH: Follicle-Stimulating Hormone, bFSH: Basal Follicle-Stimulating Hormone, LH: Luteinizing Hormone, bLH: Basal Luteinizing Hormone, E2: Estradiol, bE2: Basal Estradiol, AMH: Anti-Müllerian Hormone, AFC: Antral Follicle Count, bAFC: Basal Antral Follicle Count, IU/L: International Units per Liter (Unit for FSH and LH), pg/ml: Picograms per Milliliter (Unit for E2), ng/ml: Nanograms per Milliliter (Unit for AMH).

**Table 3. Pre-treatment Decapeptyl® 0.1mg injectable medication dosage.**

| Parameter                    | Stop Protocol (n=57) | Long Protocol (n=72) | P-value |
|------------------------------|----------------------|----------------------|---------|
| Day 17 (%)                   | 30/57                | 18/72                | 0.000   |
| Day 18 (%)                   | 15/57                | 4/72                 | N/S     |
| Day 19 (%)                   | 9/57                 | 2/72                 | N/S     |
| Day 20 (%)                   | 3/57                 | 2/72                 | N/S     |
| Mean No. of dosages $\pm$ SD | 12.0 $\pm$ 2.5       | 12.6 $\pm$ 1.7       | N/S     |

Data are presented as a number (n), mean  $\pm$  SD for continuous variables, and percentage (%) for categorical variables. Statistical significance is at  $P < 0.05$ . n: Number of patients in each group, SD: Standard Deviation, N/S: Not Significant

**Table 4. Suppression effect of Decapeptyl® 0.1mg on baseline characteristics of patients in the stop and long protocol groups.**

| Parameter                             | Stop Protocol (n=57) | Long Protocol (n=72) | P-value |
|---------------------------------------|----------------------|----------------------|---------|
| bLH Suppression (IU/L) Mean $\pm$ SD  | 6.3 $\pm$ 3.7        | 6.2 $\pm$ 4.4        | N/S     |
| No. of patients (%)                   | 48/57 (84.2%)        | 62/72 (86.1%)        | N/S     |
| bE2 Suppression (pg/ml) Mean $\pm$ SD | 41.7 $\pm$ 23.1      | 37.7 $\pm$ 28.2      | N/S     |
| No. of patients (%)                   | 45/57 (78.9%)        | 61/72 (84.7%)        | N/S     |
| bAFC Suppression Mean $\pm$ SD        | 5.3 $\pm$ 8.3        | 4.7 $\pm$ 5.3        | N/S     |
| No. of patients (%)                   | 48/57 (84.2%)        | 56/72 (77.8%)        | N/S     |

Data are presented as a number (n), mean  $\pm$  SD for continuous variables, and percentage (%) for categorical variables. Statistical significance is at  $P < 0.05$ . n: Number of patients in each group, SD: Standard Deviation, N/S: Not Significant, IU/L: International Units per Litre, pg/ml: Picograms per milliliter, bLH: Baseline Luteinizing Hormone, bE2: Baseline Estradiol, bAFC: Baseline Antral Follicle Count

**Table 5. Unexpected activation effect of Decapeptyl® 0.1mg on baseline characteristics of patients in the stop and long protocol groups**

| Parameter                            | Stop protocol (n=57) | Long protocol (n=72) | P-value |
|--------------------------------------|----------------------|----------------------|---------|
| bLH (IU/L) Mean activation $\pm$ SD  | 3.0 $\pm$ 2.3        | 4.1 $\pm$ 3.7        | N/A     |
| No. of patients (%)                  | 9/57 (15.8%)         | 11/72 (15.3%)        |         |
| bE2 (pg/ml) Mean activation $\pm$ SD | 17.7 $\pm$ 9.4       | 34.7 $\pm$ 47.5      | 0.02    |
| No. of patients (%)                  | 12/57 (21.1%)        | 18/72 (25.0%)        |         |
| bAFC Mean activation $\pm$ SD        | 2.7 $\pm$ 1.5        | 17.7 $\pm$ 9.4       | 0.001   |
| No. of patients (%)                  | 9/57 (15.8%)         | 17/72 (23.6%)        |         |

Data are presented as a number (n), mean  $\pm$  SD for continuous variables, and percentage (%) for categorical variables. Statistical significance is at  $P < 0.05$ . n: Number of patients in each group, SD: Standard Deviation, N/S: Not Significant, IU/L: International Units per Litre, pg/ml: Picograms per milliliter, bLH: Baseline Luteinizing Hormone, bE2: Baseline Estradiol, bAFC: Baseline Antral Follicle Count

**Table 6. Comparison of ovulation induction parameters in the stop and long protocol groups.**

| Parameter                                      | Stop Protocol (n=57) | Long Protocol (n=72) | P-value |
|------------------------------------------------|----------------------|----------------------|---------|
| Mean dosage of rFSH (IU) $\pm$ SD              | 260 $\pm$ 54.7       | 240 $\pm$ 43.3       | N/S     |
| Patients needing rLH (%)                       | 6/57 (10.5%)         | 14/72 (19.4%)        | 0.000   |
| Mean total of Gonadotrophins (IU) $\pm$ SD     | 2883 $\pm$ 831       | 2655 $\pm$ 576       | N/S     |
| Mean days of ovarian stimulation $\pm$ SD      | 10.9 $\pm$ 1.8       | 10.7 $\pm$ 1.5       | N/S     |
| Mean endometrial thickness on hCG day $\pm$ SD | 10.4 $\pm$ 1.5       | 10.5 $\pm$ 3.3       | N/S     |
| Mean AFC on hCG day $\pm$ SD                   | 9.4 $\pm$ 6.9        | 10.5 $\pm$ 6.3       | N/S     |
| Mean E2 on hCG day (pg/ml) $\pm$ SD            | 1820 $\pm$ 1297      | 2946 $\pm$ 1450      | 0.014   |

Data are presented as a number (n), mean  $\pm$  SD for continuous variables, and percentage (%) for categorical variables. Statistical significance is at  $P < 0.05$ . n: Number of patients in each group, SD: Standard Deviation, N/S: Not Significant, IU: International Units, pg/ml: Picograms per milliliter, rFSH: Recombinant Follicle-Stimulating Hormone, LH: Recombinant Luteinizing Hormone, hCG: Human Chorionic Gonadotropin.

**Table 7. Comparison of ICSI/IVF parameters in the stop and long protocol groups.**

| Parameter                                | Stop Protocol (n=57) | Long Protocol (n=72) | P-value |
|------------------------------------------|----------------------|----------------------|---------|
| Mean E2 per oocyte (pg/ml) $\pm$ SD      | 224.8 $\pm$ 220      | 212.9 $\pm$ 77       | N/S     |
| Mean retrieved oocytes $\pm$ SD          | 12.2 $\pm$ 9.3       | 15.2 $\pm$ 8.4       | N/S     |
| Mean No. of MII oocytes $\pm$ SD         | 8.7 $\pm$ 7.05       | 11.6 $\pm$ 7.5       | N/S     |
| Mean No. of Degenerated oocytes $\pm$ SD | 1.3 $\pm$ 1.8        | 2.5 $\pm$ 4.8        | N/S     |
| Mean No. of Fertilized embryos $\pm$ SD  | 5.6 $\pm$ 4.7        | 7.0 $\pm$ 5.8        | N/S     |
| Mean No. of Transferred embryos $\pm$ SD | 1.1 $\pm$ 1.1        | 1.3 $\pm$ 1.1        | N/S     |
| Embryo transfer on Day 3 (D3) (%)        | 33/57 (31.6%)        | 47/72 (65.3%)        | 0.007   |
| Embryo transfer on Day 5 (D5) (%)        | 27/57 (47.4%)        | 47/72 (65.3%)        | N/S     |
| Cycle cancellation (%)                   | 4/57 (7.0%)          | 0/72 (0%)            | N/S     |
| OHSS incidence (%)                       | 9/57 (15.8%)         | 17/72 (23.6%)        | N/S     |
| Pregnancy rate (%)                       | 27/57 (47.4%)        | 18/72 (25.0%)        | N/S     |

Data are presented as a number (n), mean  $\pm$  SD for continuous variables, and percentage (%) for categorical variables. Statistical significance is at  $P < 0.05$ . n: Number of patients in each group, SD: Standard Deviation, N/S: Not Significant, pg/ml: Picograms per milliliter, E2: Estradiol, MII: Metaphase II, OHSS: Ovarian Hyperstimulation Syndrome

## Discussion

This study contrasted the clinical, hormonal, and embryological outcomes of the Stop GnRH-agonist protocol with the Long GnRH-agonist protocol among infertile women undergoing IVF/ICSI treatment at the National Center. The findings indicated that both protocols had comparable demographic and baseline hormonal profiles, but the Stop protocol showed some advantages in some clinical parameters, particularly in patients with diminished ovarian response.

No significant differences were observed between baseline demographic factors such as age, BMI, length of infertility, and parity between both groups, as in the earlier research, concluding similar comparability between stimulation protocols. But more patients with high maternal age and HRT treatment were in the Stop group. These are typically markers of reduced ovarian reserve and poor reproductive outcomes [8], and this reflects that the Stop protocol is selectively selected by women with impaired ovarian reserve (DOR) or previous suboptimal response.

Current findings indicated lower AMH and basal AFC in the Stop protocol group compared with the Long protocol group ( $p < 0.05$ ), i.e., reduced ovarian reserve in the former. Findings are in line with ESHRE's poor response definition according to the Bologna criteria, which point out low AMH and AFC as significant predictors [9]. Despite these negative baseline markers, the Stop protocol group indicated the same level of stimulation compared to the Long protocol and illustrated improved efficiency in the management of poor responders. The study showed no significant differences in LH, E2, or AFC suppression between groups following the Decapeptyl® injection, demonstrating that both protocols resulted in pituitary gonadotropin secretion suppression. This is according to the GnRH agonist mechanism that causes an initial "flare-up" followed by downregulation of the receptors and suppression of endogenous LH and FSH [4].

Significantly, the Stop protocol was equally efficient in suppression, notwithstanding premature interruption of the agonist, confirming previous observations by Surrey and Schoolcraft [10] and Faber et al. [11] that brief downregulation is sufficient to allow for pituitary suppression.

Although both protocols had equivalent stimulation days and gonadotropin units, the Stop group showed fewer recombinant LH supplements and lower E2 on the day of hCG trigger. Lower estradiol levels may indicate a weaker ovarian response, which is likely to impart a reduced risk of ovarian hyperstimulation syndrome (OHSS) [12]. Furthermore, the Stop protocol had comparable endometrial thickness and antral follicle counts at trigger, in line with adequate follicular growth despite impaired hormonal exposure. These results are consistent with Faber et al. [11], who reported that discontinuation of GnRH agonist at the time of menstruation improves ovarian responsiveness without compromising synchronization. Similarly, Surrey and Schoolcraft [10] demonstrated that the Stop protocol gave good recruitment of follicles with minimal gonadotropin utilization.

Both protocols were equally good in terms of fertilization, cleavage, and embryo transfer parameters, including the number of retrieved oocytes, mature (MII) oocytes, and fertilized embryos, as well as overall pregnancy rates. The Stop protocol group exhibited fewer embryos and oocytes, but the difference was not statistically significant. Surprisingly, more Day 3 embryo transfers were seen in the long protocol group, which is not due to the effectiveness of treatment, but rather because of differences in embryo developmental patterns. The pregnancy rate was also greater in the Stop group (47.4%) compared to the long protocol (25%), though not statistically significant. This agrees with previous publications by García-Velasco et al. [13] and Tomás et al. [14], who stated similar or superior pregnancy rates with the Stop protocol in poor responders. The results suggest that the discontinuation of GnRH agonist prematurely can enhance endometrial receptivity by avoiding prolonged suppression and thus improve the implantation potential of the embryos.

The Stop GnRH-agonist protocol offers a few clinical advantages: Shorter treatment duration and lower medication costs. Less gonadotropin requirement. Less exposure to estradiol and conceivably less risk of OHSS. Equally good pregnancy rates as the conventional long protocol. These advantages make the Stop protocol particularly suitable for poor responders, older women, or those with decreased ovarian reserve. The findings substantiate previous evidence in studies by De Vos et al. [8], Surrey [10], and Faber et al. [11] that there are alternative protocols, like early agonist withdrawal, which can optimize stimulation and guarantee efficacy.

The updated European Society of Human Reproduction and Embryology (ESHRE) guideline continues to emphasize individualized ovarian stimulation and recognizes that protocol selection should account for ovarian reserve, safety, and patient characteristics. In the general IVF/ICSI population, GnRH-antagonist protocols are favored because they provide comparable efficacy with a more favorable safety profile; when a GnRH agonist is selected, the long agonist protocol remains the preferred agonist regimen. For predicted poor responders, however, the evidence does not establish a single superior pituitary-suppression strategy [15].

This interpretation is consistent with the recent systematic review and meta-analysis by Liu et al., which found no statistically significant difference in live birth between GnRH-antagonist and long GnRH-agonist protocols overall (RR 0.95, 95% CI 0.86–1.06). These data support the clinical relevance of the present finding that a stop GnRH-agonist approach can achieve comparable embryological and pregnancy outcomes in a selected population, while also underscoring that the present retrospective comparison cannot establish superiority or eliminate confounding by age, AMH, AFC, or treatment indication [16].

Protocol choice also has implications beyond laboratory and pregnancy outcomes. Although this study did not collect direct cost data, stopping triptorelin at menstruation may reduce the duration of GnRH-agonist exposure, the number of injections, clinic visits, and medication expenditure for selected patients. The observed lower recombinant-LH use and lower estradiol concentration on the hCG day in the Stop group are clinically relevant in this context, but they should not be interpreted as a demonstrated cost saving because gonadotropin consumption, monitoring, travel, laboratory, and cancellation costs were not formally evaluated. A prospective economic analysis should therefore report total cycle cost and cost per ongoing or live birth rather than medication price alone [17].

This issue is particularly important in resource-limited settings. A systematic review of ART costs in low- and middle-income countries reported that direct medical costs are frequently unaffordable relative to national income and may expose families to catastrophic expenditure [17]. A shorter or less medication-intensive protocol could improve affordability and reduce treatment interruptions, but only if clinical outcomes remain acceptable and the protocol is implemented with appropriate monitoring. Patient experience should also be considered: IVF commonly involves injection fatigue, physical side effects, anxiety, sadness, financial stress, and difficulty processing complex information. Clear counseling, shared decision-making, and practical support may therefore be as important as the choice of GnRH regimen itself [18]. The present study did not measure satisfaction, treatment-related distress, adherence, or out-of-pocket expenditure, and these outcomes should be included in future evaluations.

## Conclusion

The results of IVF/ICSI were comparable between the Long and Stop GnRHa protocols in this retrospective cohort. The Stop protocol may be a reasonable option for selected older women and patients with diminished ovarian reserve because it achieved effective pituitary suppression with shorter agonist exposure and lower estradiol levels, although its possible economic and patient-experience benefits were not directly measured in this study. These findings should be confirmed in adequately powered prospective randomized trials that include total treatment cost, medication burden, quality of life, satisfaction, and cumulative live birth as outcomes. Future research should also evaluate biomarker-guided protocol selection using AMH, AFC, age, prior response, and other clinically validated markers to improve personalization,

efficacy, and safety.

### Acknowledgments

The author thanks the Misurata National Infertility and Diagnostic Center staff for support and access to patient data.

### Conflicts of Interest

The authors declare no conflicts of interest.

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