ISSN: 2457-0400

Impact Factor: 7.675

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

www.wjahr.com

Volume: 10, Issue: 3

Page N. 20-23

Year: 2026

Original Article

Coden USA: WJAMA3

THE EFFECTIVENESS AND DISADVANTAGES OF SOME PROTOCOLS USED FOR OVULATION INDUCTION AND IN VITRO INFERTILITY TREATMENT

Maya Ahmad Najm[1]*, Zeina Mohammad blaidi[2], Rana makhous[3], Ammar alsawa[4], Bashar Mahmoud[5]

[1,2]Faculty of Pharmacy, Al sham Private University, Latakia, Syria.
[3]Professor in the Department of Pharmacology, Faculty of Pharmacy, AL sham Private University and latakia University, Latakia, Syria.
[4]Doctor in Gynecologist, Latakia, Syria.
[5]Doctor in Gynecologist, In Vitro Fertilization Specialist, Latakia, Syria.

Article Received: 24 January 2026 **Article Revised:** 13 February 2026 **Article Published:** 01 March 2026

***Corresponding Author: Maya Ahmad Najm**

Faculty of Pharmacy, Al sham Private University, Latakia, Syria.

DOI: https://doi.org/10.5281/zenodo.18814801

How to cite this Article: Maya Ahmad Najm1*, Zeina Mohammad blaidi2, Rana makhous3, Ammar alsawa4, Bashar Mahmoud5. (2026). The Effectiveness And Disadvantages of Some Protocols Used For Ovulation Induction and In Vitro Infertility Treatment. World Journal of Advance Healthcare Research, 10(3), 20–23.

ABSTRACT

Recent decades have witnessed significant development advances in In Vitro Fertilization (IVF) and Intracytoplasmic Sperm Injection (ICSI), core Assisted Reproductive Technologies (ART). These techniques are considered a revolution in infertility treatment for couples facing challenges. They depend on inducing ovulation (Controlled Ovarian Stimulation (COS)) Using multiple hormonal protocols to boost mature eggs for better fertilization. IVF being the most common ART for conception, it is used in managing cases of patients who have difficulty achieving pregnancy. GnRH (Gonadotropin-Releasing Hormone) protocols are widely used in IVF for ovulation induction, divided into: **Agonist protocol** (gradual LH suppression, longer) and **Antagonist protocol** (immediate LH suppression, faster). Recent studies have showed differences in rates of live birth, OHSS (Ovarian Hyperstimulation Syndrome) risk, and maternal/fetal safety when comparing these two protocols. Systematic reviews and meta-analyses show that the GnRH-antagonist protocol has equivalent effectiveness in clinical pregnancy and live birth rates comparing to the GnRH-agonist protocol, but with better safety, lower (OHSS) risk. Based on global studies, there was controversy about the effectiveness of the second (antagonistic) protocol, which prompted us to conduct this study to compare the effectiveness and safety of these two protocols. This study was conducted to compare protocols used for ovulation induction among patients attending fertility clinics in Syria. The study included two groups of patients: the first group (350 participants) used Triptorelin as a GnRH agonist (agonist group), and the second group (110 participants) used Cetrorelix as a GnRH antagonist (antagonist group).The results of this study showed that the protocol based on the use of the GnRH agonist is the most used in Syria. When comparing between these two protocols, we found that the rate of ovarian hyperstimulation was similar between the two groups and negligible, as both drugs achieved a hyperstimulation rate of 0%. On the other hand, the antagonist group achieved a higher fertilization rate than the agonist group by 10-15%. Also, the quality of the eggs was better in the antagonist group, but the rates of collecting fertilizable eggs were lower than the agonist group.

KEYWORDS: In Vitro Fertilization, Gonadotropin-Releasing Hormone, Ovarian Hyperstimulation Syndrome, Cetrorelix, Infertility, Individualized Controlled Ovarian Stimulation, Decapeptyl.

INTRODUCTION

Infertility is defined as no pregnancy after 12 months (under age 35) or 6 months (over age 35) of unprotected sex. Recent decades have witnessed significant development advances in In Vitro Fertilization (IVF) and Intracytoplasmic Sperm Injection (ICSI), core Assisted Reproductive Technologies (ART). These techniques are considered a revolution in infertility

treatment for couples facing challenges. They depend on inducing ovulation (Controlled Ovarian Stimulation (COS)) Using multiple hormonal protocols to boost mature eggs for better fertilization.[1,2]

If the female partner is suffering from oligomenorrhea, infrequent periods, endometriosis, or if there are known male problems, early assessment is recommended.

The assessment plan for couples experiencing infertility includes the following: assessment of ovulation, estimating ovarian reserve, fallopian tube patency, and semen analysis.

IVF being the most common ART for conception, it is used in managing cases of patients who have difficulty achieving pregnancy.[1,2]

GnRH (Gonadotropin-Releasing Hormone) protocols are widely used in IVF for ovulation induction, there are two main protocols[3]:

- Agonist protocol (gradual LH suppression, longer)
- Antagonist protocol (immediate LH suppression, faster).[3]

Recent studies have showed differences in live birth rates, OHSS risk, and maternal/fetal safety when comparing the previous two protocols. Systematic reviews and meta-analyses show that the GnRH-antagonist protocol has equivalent effectiveness in clinical pregnancy and live birth rates in comparison with the GnRH-agonist protocol, but with better safety, lower Ovarian Hyperstimulation Syndrome (OHSS) risk, making it ideal for fertility preservation (like egg freezing for cancer patients or age-related decline) and for addressing infertility (e.g., blocked tubes, male infertility) by bypassing tubal damage. IVF is resorted to by women wishing to preserve their fertility, Women with cancer or other conditions requiring gonadotoxic treatments, such as chemotherapy or radiation, can freeze their eggs or embryos before starting treatment for later use. Oocyte cryopreservation is also a practical option for women who wish to delay childbearing.[3,4,5]

Female fertility is known to decline significantly in the fourth decade of life due to a decrease in egg quantity and quality, so women not planning pregnancy soon can freeze their eggs for future use.

It is also used in cases of male infertility if drug or surgical treatments fail, used with or without Intracytoplasmic Sperm Injection (ICSI).[3,4]

It is also used in women with salpingitis (fallopian tube inflammation), peritonitis, blocked fallopian tubes, or per tubal adhesions, where intrauterine fertilization is unlikely, as IVF surpasses this tubal damage by transferring embryos directly into the uterus.

The IVF process involves several stages, starting with ovarian stimulation using multiple protocols. The ovaries are stimulated in the majority of IVF cycles to obtain about 10 to 20 eggs.[4,6] Long GnRH agonist (GnRH a) protocol begins with administration of GnRHa starting on day 21 of the previous menstrual cycle, (to suppress the pituitary gland during ovarian stimulation) and GnRHa continuing until the hCG injection. Stimulating hormones are injected in doses ranging from 75 to 450 IU daily starting on the second day of the cycle, with doses adjusted according to follicle growth and estradiol levels. An hCG injection is given when at least three follicles reach a size of 18 mm.

The GnRHant protocol begins with daily administration of ovulation-stimulating hormones (OSHs) at doses of 75–450 IU starting on day 2 or 3 of the cycle. GnRHant is initiated to suppress the natural LH surge when the follicle reaches a diameter of 14 mm or on day 6 of ovarian stimulation. An hCG injection is then administered when at least three follicles reach a diameter of 18 mm. Mature eggs are then retrieved 34 to 36 hours after the hCG injection.[2,4,6]

The procedure involves ultrasound-guided transvaginal aspiration for egg retrieval under intravenous sedation, where a vaginal probe displaysovaries, and a needle guide helps aspirate eggs and follicular fluid from follicles, followed by fertilization (IVF/ICSI), and then embryo transfer at the cleavage or blastocyst stage, guided by transabdominal ultrasound through the cervix into the uterus.[2,4,6]

Ovaries are visualized using a vaginal ultrasound probe, and a needle guide helps the physician direct a needle into each follicle to aspirate the egg and follicular fluid.

Embryos are transferred at the cleavage stage (Day 3 post-fertilization) or the blastocyst stage (Day 5 post-fertilization). Blastocyst transfer offers a higher live birth rate per cycle with fewer embryos, reducing multiple pregnancies.Transabdominal ultrasound guides a catheter through the cervix into the uterus. Embryos are placed 1-2 cm from the uterine fundus (top). After that, The catheter is checked under a microscope post-transfer to ensure no embryos are retained.[2,4,6]

To improve implantation and pregnancy continuation, Progesterone replacement therapy is started on the day of egg retrieval or transfer. Good quality surplus embryos are frozen for future use.[2,4,6]

MATERIALS AND METHODS

Pharmaceutical and Chemical Materials

Triptorelin (trade name: Decapeptyl) 0.1 mg was used as a GnRH agonist.

Cetrorelix (trade name: Cetrotide) 0.25 mg was used as a GnRH Antagonist.

These drugs were administered according to approved protocols as previously mentioned and under the supervision of specialist physicians.

Study Participants

This study was conducted on 460 patients from fertility clinics in Syria, divided as follows:

Group 1: 350 patients underwent testing for the use of a GnRH agonist, specifically Triptorelin.

Group 2: 110 patients underwent testing for the use of a GnRH antagonist, specifically Cetrorelix.

STUDY DESIGN

Protocol for Group 1

Triptorelin was administered daily at a dose of 0.1 mg starting on day 20-22 of the menstrual cycle until menstruation. Estradiol and LH levels were measured 9-11 days after starting the medication and compared to their levels at the beginning of treatment to determine if pituitary suppression had occurred. If pituitary suppression was confirmed, it was monitored by administering a stimulator starting on day 2 of the cycle. The stimulation dose was evaluated based on ovarian reserve, hormone levels, and the patient's age.

The protocol followed in the second group

Estradiol and LH levels were measured before starting this protocol. LH levels should be less than 5 IU and estradiol levels less than 47 ng/ml.

Induction is initiated until follicles measuring 10-12 mm are reached on day 6 of induction. Induction begins on day 2 of the menstrual cycle and is given for 5 days. On day 6, monitoring is performed. If the follicles are between 10-12 mm, Cetrorelix is started at a dose of 0.25 mg daily until follicular maturation. Then, a GnRH agonist or hCG is given to further mature the follicles.

RESULTS

- **Rates of retrieval fertilizable eggs**

The rate of retrieval fertilizable eggs in the patients of the agonist group was 75% of the number of mature follicles, while the number of retrievable eggs in the patients of the antagonist group was less than the agonist group (and less than expected from the assessment of initiation in terms of ovarian reserve)

- **Egg quality and fertilization rate**

80% of the fertilizable eggs were fertilized under the microscope in the agonist group, while the fertilization rate was 10-15% higher in the antagonist group.

- **First-grade embryo percentage**

The agonist group achieved a first-grade embryo percentage of 60% when using recombinant FSH (Follitropin alpha) and 45-90% when using hMG or a mixture of FSH and LH. However, the first-grade embryo percentage in the antagonist group was only 5% higher.

- **Ovarian hyperstimulation rates**

The incidence of ovarian hyperstimulation in groups 1 and 2 was negligible (0%).

DISCUSSION

Recent scientific evidence suggests that gonadotropin-releasing hormone (GnRH-ant) protocols offer better control in the stimulation process, with a significant reduction in the likelihood of ovarian hyperstimulation syndrome (OHSS), making them a safe and effective option, particularly in high-risk cases or in patients with a hyperresponsive ovarian response. In contrast, the GnRH-agonist protocol remains relevant in some cases with a low response or when the need for high fertilization rates outweighs the potential risks.[7]

Accordingly, choosing the appropriate Ovarian Stimulation Protocol for each patient is one of the most important factors determining the success of In Vitro Fertilization (IVF) and Intracytoplasmic Sperm Injection (ICSI) programs.[7]

Recently, the use of assisted reproductive technologies (ART), such as in vitro fertilization (IVF) or artificial insemination, has increased in Syria, representing a significant advancement in the treatment of infertility for couples facing difficulties conceiving for various reason.[7,8]

Gonadotropin-releasing hormone (GnRH) protocols are among the most commonly used methods for ovulation induction within IVF programs in Syria. The two most frequently used protocols are **Agonist protocols,** which gradually suppress luteinizing hormone (LH) secretion.

Antagonist protocols, which immediately and rapidly inhibit LH secretion.

Based on global studies, there was controversy about the effectiveness and safety of these protocols, which prompted us to conduct this study to compare the effectiveness and safety of these two protocols.

In this study when comparing the two protocols used in Syria, we found that the rate of ovarian hyperstimulation was similar between the two groups and negligible, as both drugs achieved a hyperstimulation rate of 0%. On the other hand, the antagonist group achieved a higher fertilization rate than the agonist group by 10-15%. Also, the quality of the eggs was better in the second group, but the rates of collecting fertilizable eggs were lower in the antagonist group.

Returning to the results of the reference studies, the review conducted by *Chenhong Liu*[9] and colleagues in 2023 in China addressed a similar comparison to our study between these two protocols by conducting a systematic review of 52 previous studies (4757 participants in the agonist protocol and 5193 participants in the antagonist protocol). In this study, the live birth

rates between the two protocols were evaluated, and there was no difference between the two protocols in this result, while the protocol based on the use of the antagonist was less likely to cause ovarian hyperstimulation. This differs from the results of our study, which showed better efficacy for the antagonist protocol in terms of fertilization rates and egg quality, and lower in terms of the rates of collecting fertilizable eggs, and there was no difference in the rates of causing ovarian hyperstimulation. The reason for the difference is mainly attributed to the difference in sample size.[9]

CONCLUSION

Ovulation induction is the cornerstone of successful IVF/ICSI programs, as it is essential for achieving successful fertilization and the development of high-quality embryos capable of implantation. Comparative studies of the protocols used have shown that the balance between therapeutic efficacy and clinical safety is the decisive factor in selecting the optimal regimen for each patient. According to our study results, the safety of the two protocols was similar, while efficacy varied depending on the criterion studied.

Finally, it is important to emphasize the recommendations of the recent study regarding the importance of tailoring the stimulation plan to the individual patient's characteristics (Individualized Controlled Ovarian Stimulation – iCOS), which is the optimal approach for achieving a balance between therapeutic efficacy and clinical safety.

REFERENCES

1. SINGH, Kadambari; DEWANI, Deepika. Recent advancements in in vitro fertilisation. *Cureus*, 2022; 14.10.
2. BOCZAR, Agata, et al. A comparison of the effectiveness of different assisted reproductive techniques (ART) in couples with unexplained infertility. *Journal of Education, Health and Sport*, 2024; 71: 56073-56073.
3. SURREY, Eric S. GnRH agonists in the treatment of symptomatic endometriosis: a review. F&S Reports, 2023; 4.2: 40-45.
4. KADOURA, Sally; ALHALABI, Marwan; NATTOUF, Abdul Hakim. Conventional GnRH antagonist protocols versus long GnRH agonist protocol in IVF/ICSI cycles of polycystic ovary syndrome women: a systematic review and meta-analysis. *Scientific reports*, 2022; 12.1: 4456.
5. YANG, Rui, et al. Comparison of the long-acting GnRH agonist follicular protocol with the GnRH antagonist protocol in women undergoing in vitro fertilization: a systematic review and meta-analysis. Advances in Therapy, 2021; 38.5: 2027-203.
6. CHOE, Jennifer; SHANKS, Anthony L. In vitro fertilization, 2020.
7. DAFOPOULOS, Konstantinos; TARLATZIS, Basil C. Ovarian stimulation protocols. In: Management of Infertility. Academic Press, 2023; 199-204.
8. ESHRE GUIDELINE GROUP ON OVARIAN STIMULATION, et al. ESHRE guideline: ovarian stimulation for IVF/ICSI. Human reproduction open, 2020; 2020. 2: hoaa009.
9. LIU, Chenhong, et al. Live birth rate of gonadotropin-releasing hormone antagonist versus luteal phase gonadotropin-releasing hormone agonist protocol in IVF/ICSI: a systematic review and meta-analysis. *Expert Reviews in Molecular Medicine*, 2024; 26: e2.