Advance Research Journal of medical and clinical science
Received 3 May 2021 | Revised 28 May 2021 | Accepted 5 June 2021 | Published Online 9 June 2021

DOI: https://doi.org/10.15520/arjmcs.v7i05.3 19
ARJMCS 07 (06), 571–581 (2021)

ISSN (O) 2455-3549 IF:1.6

REVIEW ARTICLE

Assisted Conception: Preparing the Ovaries for Eggs Collection and Determination of the Outcome in Frozen Embryos Transfer (FET) During Natural Cycle IVF

Mustafa Zakaria [1*] | Marcuse F. Steven [2*] | Noureddine Louanjli [3] | Wassym R. Senhaji [4] | Abdelhafid Natiq [5] | Mohammed Zarqaoui [6]

[1]MD. Senior Clinical Embryology and Assisted Conception , Consultant in IRIFIV Fertility Center , IVF laboratoy, Casablanca ,Morocco

[2]Chairman of the Board of Directors of the Royal Center of Obstetrics and Gynecology, Fertility Expert and Research Supervisor, Association for Scientific Research of the IRIFIV-AISRG Group - England

[3]Chairman of the LABOMAC Laboratory, and IRIFIV Fertility Center, AFC Fertility Center, Association for Scientific Research of the IRIFIV-AISRG Group Casablanca, Morocco

[4]Chairman of the Les Iris Clinc - Obstetrics and Gynecology and Member of the Association for Scientific Research of the IRIFIV-AISRG Group Casablanca, Morocco

[5]Genopath, Faculty of Medicine and Pharmacy, Mohammed V University Rabat Morocco, Team of Genomics and Molecular Epidemiology of Genetic Diseases (G2MG), Genomic Center of Human Pathologies (GENOPATH). Faculty of Medicine and Pharmacy. Mohammed V University in Rabat, Researcher in the Association for Scientific Research of the IRIFIV-AISRG Group. Rabat, Morocco.

[6]Chairman of the IRIFIV Center Fertilit y- Obstetrics and Gynecology and Association for Scientific Research of the IRIFIV-AISRG Group Casablanca, Morocco

Abstract

The degree of pituitary suppression during treatment with the GnRHa triptorelin (Decadently) is dose dependent. 0.05 mg triptorelin causes pituitary desensitization comparable to that of a dose of 0.1 mg. Reduction of the triptorelin dose to 0.025 mg forms a state of pituitary desensitization that is less profound than the higher doses used. Restoration of the spontaneous and stimulated LH release is slow and also dose dependent, while restoration of FSH stimulated release is more rapid, and independent of the triptorelin dose used. Long Protocol - Disadvantages of the GnRHa long protocol *Long treatment period until suppression is achieved.* Higher doses and longer duration of gonadotropin therapy which subsequently increase the total cost of the treatment.*Increased risk of ovarian hyperstimulation syndrome (OHSS).- Advantages of the GnRHa long protoco * Prevents a premature LH surge during exogenous gonadotropin stimulation.*Higher pregnancy rate in the long protocol, as compared to a short or ultrashort protocol. * Synchronization of recruited follicles. Pituitary gonadotropin secretions are blocked upon desensitization when a continuous GnRH stimulus is provided by means of an agonist or when the pituitary receptors are occupied with a competitive antagonist. GnRH antagonists were not available originally; therefore, prolonged daily injections of agonist with its desensitizing effect were used.

Keywords: GnRH Agonists Protocol, GnRH Antagonist Protocol, Natural Cycle IVF, Frozen Embryos Transfer (FET).

1 | INTRODUCTION

GnRH agonists (GnRHa) were first introduced in the late 1980's. Before their use about 20% of IVF cycles were canceled due to spontaneous premature ovulation. Apart from suppressing the native LH surge, GnRH agonists use also improved egg yield and pregnancy rates and enabled scheduling flexibility. the GnRHa long protocol was considered, until recently, the standard ovarian stimulation regimen in an IVF cycle. Administration of multiple doses of GnRHa causes a reversible blockade of pituitary function after an initial stimulatory phase-the so-called "flare-up" effect. GnRHa suppresses pituitary GnRH receptors and causes inhibition of post-receptor events. Both follicular and luteal phase initiation of GnRHa are equally efficacious. When GnRHa is administered during the mid-luteal phase, down-regulation seems to be achieved more rapidly, is more profound and there is lower rate of ovarian cyst development (due to the additive central inhibition of high progesterone level). On the other hand, luteal initiation does not exclude the possibility of an already established spontaneous pregnancy. To date, no teratogenic effect was found after exposure to GnRHa. Pre-treatment with oral contraceptive pills is effective in the prevention of ovarian cyst formation and in shortening the period to ovarian suppression. GnRH antagonists (e.g. Cetrotide, Orgalutran) were first available for clinical use only in 1999 (20 year after the introduction og GnRHa). The delay in their availability for use was mostly due to anaphylactic reactions in the earlier generations of the drugs. In contrast to GnRHa, suppression attained by GnRH antagonists is immediate (there is no flare-up effect). There is no downregulation of GnRH receptors and thus constant supply of antagonists is required to achive effective pituitary suppression. Consequently, compared to GnRHa, a higher dose of GnRH antagonists is required.

Natural cycle IVF (in vitro fertilization) is very similar to standard in vitro fertilization, but just without the use of medications to stimulate the ovary to make multiples eggs (sometimes a small amount of medication is used to prevent ovulation).

In **natural cycle IVF** (NC-IVF) **no drugs** are administered. Patients are monitored in a natural cycle

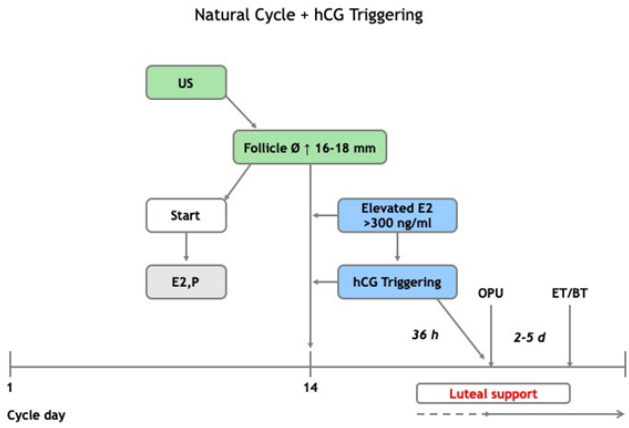

FIGURE 1:

with US to track the growth of the dominant follicle and serum hormonal level (E2, P) + LH every 6 h. An egg retrieval is then performed when the dominant follicle is determined to be an appropriate size + 36 h from double elevation of LH level from the time that the follicle reach 16 mm in diameter.

In **natural cycle IVF** (NC-IVF) + **hCG** triggering patients are monitored in a natural cycle with US to track the growth of the dominant follicle and serum hormonal level (E2, P). Ovulation triggering with hCG administration is given when the follicle size is 16-18 mm and serum estradiol rises >300 ng/ml.

An egg retrieval is then performed 36 h after hCG triggering

Supplementary information The online version of this article (https://doi.org/10.15520/arjmcs.v7i05.319) contains supplementary material, which is available to authorized users.

Corresponding Author: *Mustafa Zakaria*
The Association for Scientific Research of the IRIFIV-AISRG Group
MD. Senior Clinical Embryology and Assisted Conception , Deputy Executive Director and Administrative Coordinator of the Association for Scientific Research of the IRIFIV-AISRG Group, Consultant in IRIFIV Fertility Center , IVF laboratoy, Casablanca ,Morocco

Email: dr.zakaria@irifiv-aisrg.com

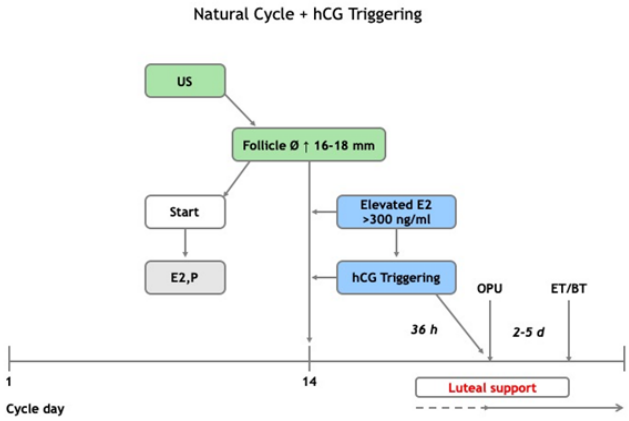

FIGURE 2:

In the case of a LH surge, either cancellation or advancement of oocyte retrieval occurs The egg that is retrieved is then fertilized in the laboratory in the same way as traditional IVF. If an embryo is produced and continues to develop, it is transferred back to the uterus, again in the same manner as conventional IVF.

2 | LONG PROTOCOL

2.1 | Advantages of the GnRHa long protocol

1. Prevents a premature LH surge during exogenous gonadotropin stimulation.
2. Higher pregnancy rate in the long protocol, as compared to a short or ultrashort protocol.
3. Synchronization of recruited follicles.

2.2 | Disadvantages of the GnRHa long protocol

1. Long treatment period until suppression is achieved.
2. Higher doses and longer duration of gonadotropin therapy which subsequently increase the total cost of the treatment.
3. Increased risk of ovarian hyperstimulation syndrome (OHSS).

2.3 | Side effects

1. Since GnRHa causes chemical hypogonadotropic-hypogonadism, it can result with hot flashes, headaches and vaginal dryness.
2. Other potential side effects are bleeding and ovarian cyst development.

2.4 | Which route of administration is the best?

1. **IM injection:** the duration of action is prolonged and rather unpredictable. Following IM injection of 3.75 mg Deca-peptyl, normal menstruation is restored after 120 days. This route requires increased gonadotropin doses and longer stimulation period. This route is mostly used in patients with endometriosis or for fertility preservation in patients with an oncologic disease.
2. **Intranasal route:** The absorption of GnRHa (Synarel, Buserelin) fluctuates which cause an unpredictable desensitization level. Nevertheless, this is mostly sufficient to prevent the premature LH surge.
3. **Subcutaneous daily injections:** this route is preferable because of a more stable effect (Decapeptyl).

3 | WHAT IS THE OPTIMAL DOSE?

The degree of pituitary suppression during treatment with the GnRHa triptorelin (Decapeptyl) is dose dependent. 0.05 mg triptorelin causes pituitary desensitization comparable to that of a dose of 0.1 mg. Reduction of the triptorelin dose to 0.025 mg forms a state of pituitary desensitization that is less profound than the higher doses used. Restoration of the spontaneous and stimulated LH release is slow and also dose dependent, while restoration of FSH stimulated release is more rapid, and independent of the triptorelin dose used.

TABLE 1: AllGnRHa seem effective and the differences can be explained by dosageincompatibility

Compound						Position 6				Position 10
Amino acid no.	1	2	3	4	5	6	7	8	9	10
Native GnrH	Glu	His	Trp	Ser	Tyr	Gly	Leu	Arg	Pro	Gly-NH2
Nonapeptides										
Leuprolide (Lupron, Lucrin)						Leu				N-Et-NH2
Buserelin (Suprefact)						Ser (O'Bu)				N-Et-NH2
Goserelin (Zoladex)						Ser (O'Bu)				AzaGly-NH2
Histrelin (Supprelin)						D-His (Bzl)				AzaGly-NH2
Deslorelin (Ovuplant)						D-Trp				N-Et-NH2
Decapeptides										
Nafarelin (Synarel)						2Nal				Gly-NH2
Triptorelin (Decapeptyl)						Trp				Gly-NH2

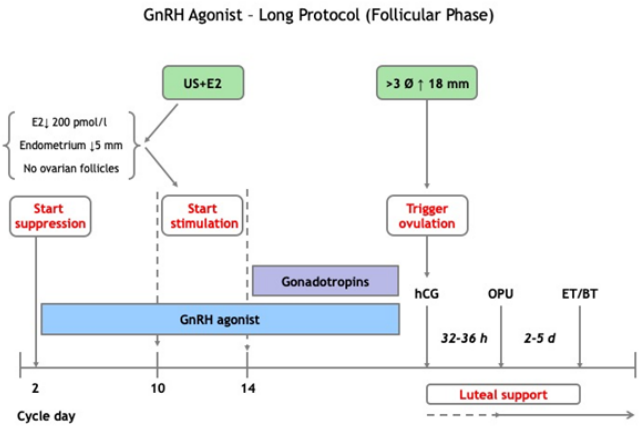

FIGURE 3:

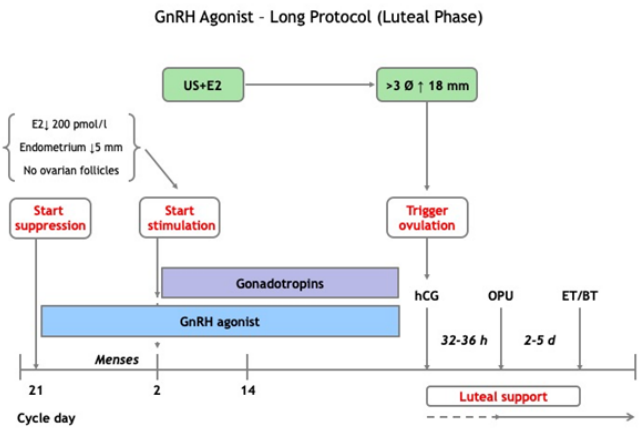

FIGURE 4:

3.1 | Start suppression

GnRHa in follicular phase (day 2 of the menstrual cycle) or in luteal phase (7 days post ovulation-usually day 21 of the menstrual cycle). Schedule a visit 10-14 days after the beginning of treatment to evaluate the efficacy of suppression.

Monitoring:

- US (endometrial thickness + number and diameter of follicles)
- E2 level

Start stimulation if:

- Endometrial thickness less than 5 mm
- E2 level less than 100 pmol/L
- No follicles >10 mm

4 | EXOGENOUS GONADOTROPINS

Follicular development requires FSH stimulation. In most cases the endogenous LH is sufficient for follicular growth (this is not true in patients with hypogonadotropic hypogonadism and possibly in poor responders). FSH can be administered in the form of urinary FSH (uFSH), recombinant FSH (rFSH- e.g.

Puregon & Gonal-F) orurinary menotropins (hMG-e.g. Menopur & Menogon) and the dose must be tailored to the needs of the individual woman. All FSH products are administered subcutaneously and are given on a daily basis, apart from Corifollitropin alpha (Elonva) which is a recombinant chimeric FSH with a longer half-life that causes sustained FSH levels for 1 week. There is a slightly higher live birth rate (LBR) in women stimulated by hMG. However, human products raise concerns of purity and contamination with other unwanted substances (such as prions).

The starting dose of FSH depends on the patient's age and ovarian reserve and the response observed in previous cycles. There are two main strategies of stimulation: "Step-up" - beginning with a low dose of FSH (usually 150IU) and increasing, as necessary, according to the response noted. "Step-down" - beginning with a higher dose of FSH (usually 300-450IU) and decreasing, as necessary, according to the response noted. Response to stimulation is monitored with serial measurements of serum estradiol levels and assessing follicular growth by US. First follow-up visit is scheduled after 3-5 days of stimulation to determine whether the chosen dose of gonadotropins requires adjustment. Monitoring US+E2 is done every 1-3 days, based on the quality of response.

4.1 | Trigger ovulation if

>3 follicles with diameter 17-18 mm. E2 concentration reflects the overall size and maturity of the follicles cohort. In the natural ovulatory cycle E2 levels peak between 700 and 1400 pmol/L just before the LH surge. Thus appropriate response should be evaluated according to the number of preovulatory follicles. An approximate doubling of E2 level every 48 hours is considered as a promising sign of good follicle development. The endometrial thickness is also measured every visit. A thin endometrium (<6-7mm) with homogenous echogenicity was correlated, in some studies, with poor implantation rates.

4.2 | Endometrium 8-9 mm,"trilaminar"

hCG (Ovitrelle) is administrated to stimulate the final stage of oocyte maturation (mimics the endogenous LH surge). 32-36 hours after its administration ovarian pickup (OPU) is performed and the oocytes are fertilized with sperm (or cryoprecipitate in cases of fertility preservation).

FIGURE 5:

4.3 | Luteal phase support

GnRHa use causes sustained suppression of LH secretion even 10 days after its discontinuation. Thus, abnormally low levels of LH during the luteal phase may be insufficient to stimulate and maintain the level of luteal function required to promote timely endometrial maturation in preparation for implantation or to support an early pregnancy once estab-

lished. This suppression causes the need for artificial luteal phase support. Progesterone supplementation is the most widely used and is generally begun on the day of oocyte retrieval, or at the time of embryo transfer. It can be administered orally, vaginally or by the intramuscular route. The optimal duration of treatment has not been established and varies between the first positive pregnancy test and 12 weeks of pregnancy. hCG can also be administered for luteal support, but it increases the risk of OHSS with no apparent positive effect on LBR. In some studies supplemental estrogen was found to increase the clinical pregnancy rate (CPR).

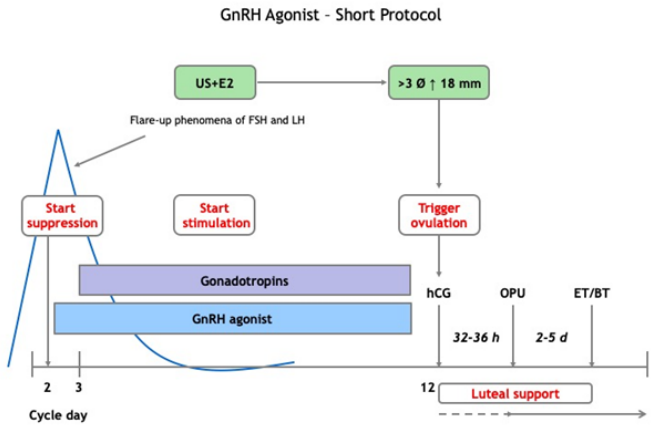

FIGURE 6:

5 | SHORT PROTOCOL

The Short protocol is an alternative stimulation regimen. It is also called the ”flare” protocol because it uses the initial flare-up effect of GnRHa administration to assist in follicular recruitment.

5.1 | Advantages of the GnRHa short protocol

1. Shorter stimulation time
2. Lower amount of GnRHa used
3. Lower dose and duration of gonadotropins used
4. Lower total cycle’s cost
5. Possibly more effective in poor responders

5.2 | Disadvantages of the GnRHa short protocol

1. Less schedule flexibility
2. Lower LBR in most patients (except for poor responders)
3. Higher androgen and progesterone levels due to late corpus luteum rescue, which can adversely affect oocyte quality and pregnancy rates

GnRHa is administered on cycle day 2 (with similar doses of those used in the long protocol) followed by gonadotropin treatment started on cycle day 3. Pituitary desensitization will occur several days later while the patients are still treated with gonadotropins. Monitoring with US and E2 levels is done every 1-3 days, based on the quality of response. Preliminary use of oral contraceptive pills for 14-21 days can be done in order to induce menses (and thus restore schedule flexibility) and to reduce androgen levels.

5.3 | GnRHa Ultra-Short protocol

GnRHa is begun on cycle day 2 and given for only three days with the flare up phenomena. This protocol is based on the assumption that suppression of the endogenous LH surge may be obtained through a very short course of GnRHa administration. This protocol might help retrieve more oocytes with minimal risk of premature LH surge and is sometimes used in poor responders.

6 | TREATMENT PROTOCOL

6.1 | Advantages

- Shorter duration of suppression
- No estrogen deficiency related side effects
- The total dose and duration of gonadotropin treatment is reduced
- Substantially lower risk for OHSS

TABLE2: *Summary ofadvantages and disadvantages of the different GnRH agonist protocols*

GnRH agonist protocol	Route of ad-ministration	Administration days of cycle (CD)	Duration of administration	Advantages	Disadvantages
Ultrashort protocol	In / sc	CD 2,3–4,5	3 days	Patient's comfort	Low PR
Short protocol	In / sc	CD 2,3 until day of hCG	8-12 days	Patient's comfort	No programming
Long follicular	In / sc	CD 2 until day of hCG	28-35 days	Program-ming, good PR	Long duration of administration
Long luteal	In /sc	CD 21 until day of hCG	21-28 days	Program-ming, good PR	Long duration of administration
Menstrual early cessation	In / sc	CD 21 until menses	7-12 days	Inconclu-sive	Low estradiol levels
Follicular early cessation	In / sc	CD 21 until stim. day 6,7	13-20 days	Inconclu-sive	Low estradiol levels
Long follicular (depot)	Depot	CD 2	Once	Patient's comfort	(Too) long duration of action
Long luteal (depot)	Depot	CD 21	Once	Patient's comfort	(Too) long duration of action
Ultralong	In / sc / depot	CD 2 or 21	8–12 weeks, depot 2 or 3 times	Only for special cases	Side effects due to estrogen deficiency

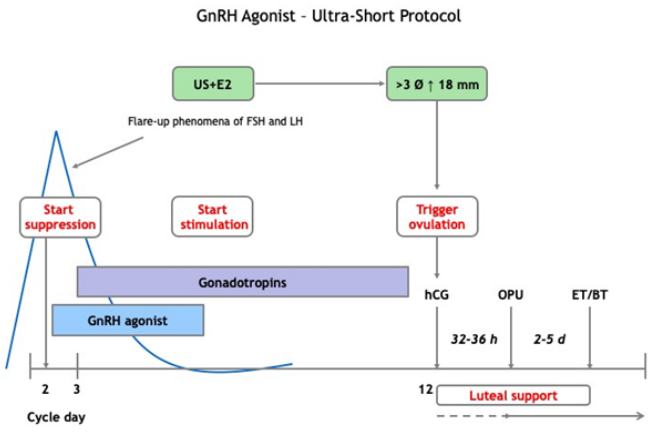

FIGURE 7:

- Lower total cycle cost

Because all of these advantages described and mainly because they nearly eliminated the potentially life threatening iatrogenic OHSS, GnRH antagonists currently became the protocol of choice in most IVF patients. GnRH antagonists are given subcutaneously and can be administrated in a daily (0.25 mg) or a single (3 mg) dose regimen. The single dose regimen provides suppression for 4 days and if further suppression is needed the drug is continued with the daily dose. There is no difference in clinical pregnancy rates between the single- and the daily-dose regimens. The majority of GnRH-antagonist cycles given today follow the daily-dose scheme. Stimulation with gonadotropins resembles that of the GnRHa short protocol (standard starting dose of 150IU). It is mostly initiated on day 2 of the cycle and the patient is usually invited for a follow-up visit 5 days later to undergo blood tests and US. A later

initiation of gonadotropin stimulation, on day 5, is also possible in the so-called "mild stimulation protocol". GnRH antagonist treatment can be initiated either in a fixed or in a flexible way. In the fixed protocol GnRH antagonist is started after a fixed days of stimulation (5 days). This protocol is simple and requires less monitoring as compared to the flexible one. In the flexible protocol GnRH antagonist is administered only after certain endocrine and/or sonographic criteria are met (at least 1 follicle . These criteria reflect a higher risk for LH surge. The flexible protocol might avoid unnecessary GnRH antagonist administration in patients in whom an LH surge is unlikely to occur on day 5 of the stimulation (due to absence of follicular development). No significant differences in the clinical pregnancy rate were noted between the fixed and the flexible protocols. The timing of trigger for ovulation and the rest of the protocol including luteal phase support is similar to that in the GnRHa protocols. The use of antagonists, rather than agonists, provides the opportunity to use an agonist instead of hCG to induce final oocyte maturation, thereby nearly eliminating the risk of OHSS. Whereas a single bolus injection of an agonist (triptorelin 0.2 mg) triggers a physiologic LH surge that lasts less than 24 hours, hCG levels remain elevated for several days and stimulate markedly higher estradiol and progesterone concentrations. The main possible disadvantage of GnRH antagonists is the slightly lower pregnancy rates as compared with the use of agonists.

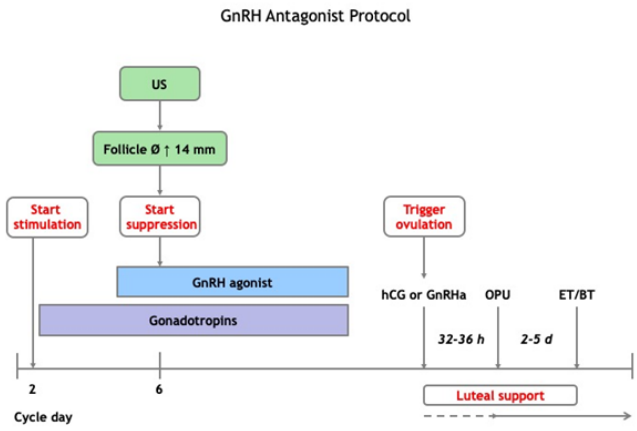

FIGURE 8:

TABLE 3:

GnRH agonists	GnRH antagonists
Initial flare up effect	Immediate suppression of gonadotropin levels
Slow recovery of pituitary function	Quick recovery of pituitary function
Avoidance of endogenous LH surge	Avoidance of endogenous LH surge
More programmable IVF procedures	Less programmable IVF but greater patients' convenience
More oocytes for IVF and cryopreservation	Fewer oocytes, but also less OHSS
Expensive protocols with long duration	Less expensive protocols with shorter duration

7 | NATURAL CYCLE IVF

7.1 | The advantages of natural cycle IVF are

1. Simplicity
2. Can be performed in a clinic
3. Less invasive
4. Less stressful
5. Can be repeated every month
6. No use of stimulation drugs and, therefore, no risk of ovarian hyper stimulation syndrome (OHSS)

7.2 | Selecting patients for such treatment

1. Patients <34 years old (pregnancy rate with older patients is very low
2. Low-responder patients in whom IVF failed and before offering them oocyte donation.
3. Day 2-3 follicle-stimulating hormone (FSH) <10, with regular menstrual cycles (range, 25 – 34 days). For couples with infertility due to male factor (low or poor quality sperm) avoid

TABLE 4: *Advantages anddisadvantages of GnRH agonist protocols and GnRH antagonist protocols*

	GnRH Agonist Long	GnRH Antagonist Fixed	GnRH Antagonist Flexible	GnRH Agonist Short & Ultra-short
Ad-van tage	A. Stable and low LH and P levels throughout the stimulation phase B. Suppression of endogenous FSH levels leading to a follicular cohort of small follicles at the initiation of FSH stimulation resulting in a synchronized follicular development	A. Immediate, reversible suppression of gonadotropin secretion which avoids effects related to the initial flare up and subsequent down-regulation B. Initial of the IVF treatment in a normal menstrual cycle C. Endogenous intra-cycle FSH rise rather than FSH suppression, resulting in a significant reduction in the effective dosage and shorter treatment than with GnRHa	A. Reduce dosage of the antagonist is needed B. The cohort of follicles have more time to develop thus leading to a higher number of follicles in mid-follicular phase	A. The ovarian suppression is not excessive B. The initial stimulation of the GnRH receptors and consequent secretion of endogenous gonadotropins enhance the effects of the exogenously administered gonadotropins
Dis-ad-van-tages	A. More time consuming and complex stimulation protocols B. Acute stimulation of gonadotropins and steroid hormones due to the flare up effects C. Profound hypoestrogenemia due to down-regulation D. Risk of complications (OHSS)	A. High inter-cycle endogenous FSH concentrations inducing secondary follicle recruitment and leading to an asynchronous follicular development	A. LH levels remain unsuppressed during the early follicular phase and enhance E2 production	A. Flare up effects in mid-follicular phase
Clin i-cal com mei	A. Increased number of oocytes collected B. Additional pregnancy changes from cryopreserved embryos C. Improvement in routine patient treatment schedule	A. More IVF cycles to be carried out in a given period B. Starting stimulation in patient scheduled for antineoplastic treatments (oocyte preparation)	A. At makes it feasible to tailor stimulation patients' needs	A. A micro dose GnRHa flare protocol is useful in poor responders B. Several micro doses of GnRHa in the flare up protocols have been tested to achieve gonadotropin release and avoid side effects of the classic flare up protocol

multiple pregnancies and unnecessary stimulation for an otherwise fertile female partner

4. More than 85% egg retrieval with >40% of embryo stop developing before blastocyst stage.
5. Implantation rate per blastocyst is 40-50%.

7.3 | Major disadvantages are

1. Low pregnancy rates after transfer of individual embryos (around 7% per cycle)
2. High cancellation rates (over 30%) due to numerous reasons, such as abnormal folliculargenesis, premature ovulation, unsuccessful oocyte retrieval, fertilization failure, poor embryo quality, or premature luteinizing hormone (LH) surge
3. The need for frequent and repeated blood tests to monitor the increase in LH surge (if human chorionic gonadotropin [hCG] is not administered), with around-the-clock/24-hour availability of the IVF team for egg retrieval

8 | MODIFIED NATURAL CYCLE IVF

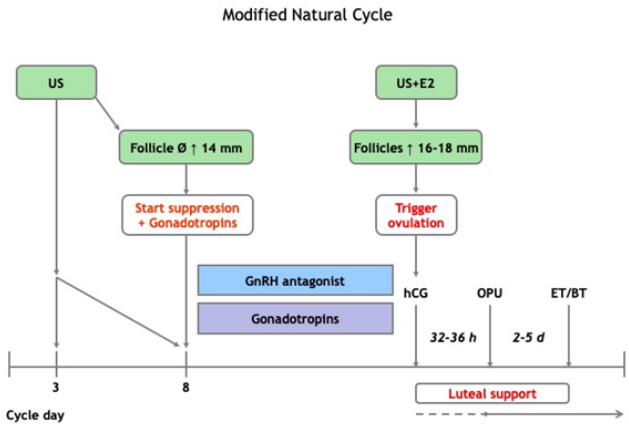

FIGURE 9:

Patients are monitored in a modified natural cycle from day 3 with US to track the growth of the follicle size. GnRH antagonist treatment was started when a follicle of 14 mm was present and hMG/rFSH were added daily during the antagonist treatment. Ovulation triggering with hCG administration is given when the follicle size is 16-18 mm. An egg retrieval is then performed 36 h after hCG triggering. Progesterone supplements are given to support implantation.

8.1 | Advantages of Modified Natural Cycle IVF

1. This method has increased cumulative success rates of natural IVF as the risk of spontaneous ovulation is reduced.
2. Women with low AMH, previous poor response in conventional stimulated cycles can particularly benefit from this approach.
3. The treatment can be repeated in consecutive cycles and the total cost per cycle of treatment is significantly lower than conventional stimulated cycle.
4. More than one egg can be collected and two embryos could be available for transfer in many cycles.

9 | FROZEN EMBRYOS TRANSFER (FET)

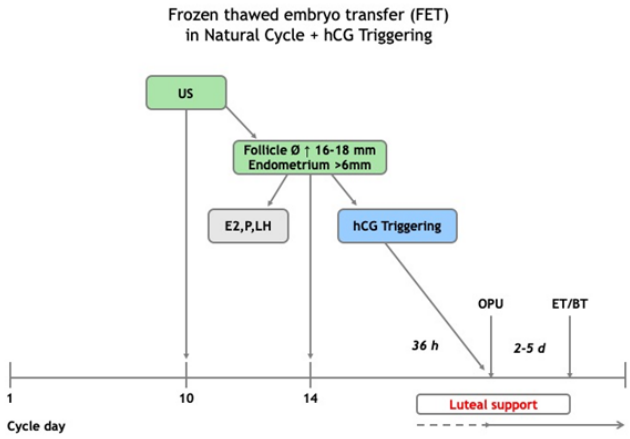

FIGURE 10: *Frozenembryos transfer (FET) during natural cycle*

If awoman hasregularovulatory menstrual cycles, a frozen embryo transfer can be performed without the use of hormone preparation. Several studies have shown that the pregnancy rates in natural FET cycles are equivalent to that of hormone prepared cycles. Patients monitoring in a FET natural cycle are starting on day 10, 11 or 12 of their cycle regular ultrasonic evaluation of the endometrium thickness and mean diameter of the dominant follicle is performed. When the endometrium is 6 mm or more and the diameter of the dominant follicle is 16-18 mm a blood sample is taken (for blinded analyses of progesterone, E2 and LH levels) and ovulation is induced using hCG injection. Progesterone supplements are given to support implantation.

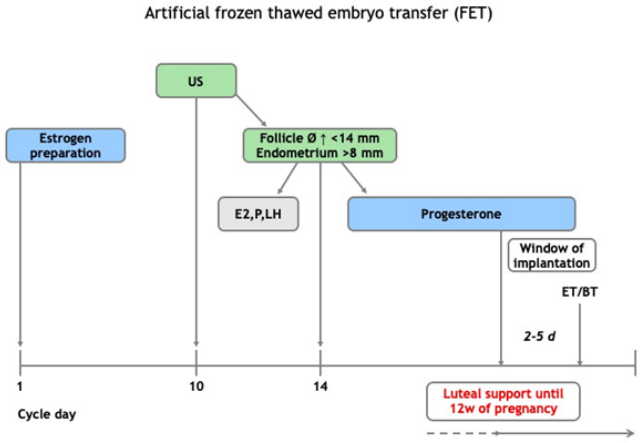

FIGURE 11: *Artificial cyclefrozen thawed embryo transfer (FET)*

From day one of the cycle oral estradiol (Progynova 2 mg) After 11, 12 or 13 days an ultrasound is performed. If no leading follicle is present and the endometrial thickness is $\geq$ 8 mm, micronized progesterone (utrogestan) is added to the regime and thawing and transferring is commenced 4 or 5 days later according to the stage of cryopreservation. Luteal support continues until week 12 of pregnancy because patient not given triggering by HCG and corpus luteum not developed.

Using hormones to prepare the uterus is the most common way in which a frozen embryo transfer is performed. The **first step** is to suppress the pituitary gland. This is necessary to reduce the chances of ovulation occurring unexpectedly. The **second step**

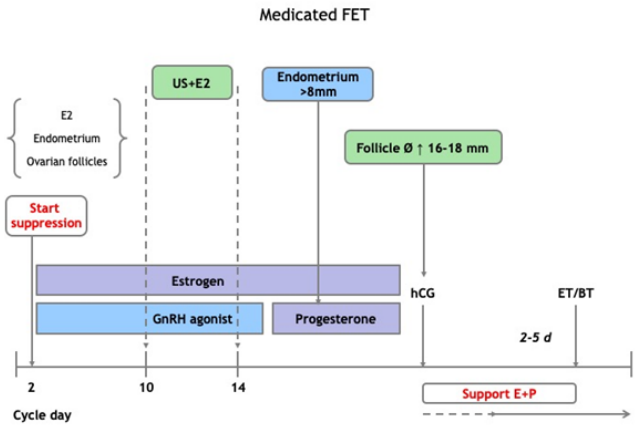

FIGURE 12: *Medicated cycle forfrozen embryos transfer (FET)*

in a frozen embryo transfer cycle is to use hormones to duplicate the changes that normally occur in the uterus during a regular menstrual cycle. This requires the use of two hormone medications: estrogen and progesterone.

10 | ESTROGEN PREPARATION FOR FET

During a normal menstrual cycle, estrogen is produced by the developing follicle. This estrogen acts on the uterus to thicken and mature the uterine lining. Estrogen is given in a FET cycle for the same reason. **Monitoring** — transvaginal ultrasound is performed to determine the thickness of the uterine lining and a blood test is performed to look at the level of estrogen in the blood

10.1 | Progesterone in an FET cycle

Once the uterine lining has been thickened sufficiently, progesterone is added. Once the progesterone is added, the GNRH agonist may be stopped. Progesterone matures the uterine lining and makes it receptive to an embryo to implant. Once the progesterone is begun, there is a certain "**window of implantation**" during which the embryo must be transferred. The stage of the embryo must match the stage of development of the uterus. Therefore, the only factor that locks the patient into performing the

transfer on a certain day is starting the progesterone. Once the progesterone is begun, if the embryo transfer is not performed on a certain day, the cycle must be cancelled and a new preparation with hormones must be begun after allowing a period to occur.

11 | ACKNOWLEDGEMENT

Objective of the Association for Scientific Research of the IRIFIV-AISRG Group (IRIFIV-AISRG), Research foundation in Casablanca, Maintaining consistent and reliably high success rates is a monthly challenge for in IVF labs, the IRIFIV Fertility Center in Casablanca – Morocco Department of Reproductive Medicine and Reproductive Biology and Embryology , advocacy of interdisciplinary Department of Reproductive Medicine and Reproductive Biology and Embryology study, encompassing the areas of research, collections and publishing Articles.

Abbreviations

Frozen embryos transfer **(FET)** , human chorionic gonadotropin **(HCG)**,luteinizing hormone **(LH)** , follicle-stimulating hormone **(FSH)** , Ovarian hyperstimulation syndrome **(OHSS),** Clinical Pregnancy Rate **(CPR)** , Embryo transfer **(ET)** , Ovarian pickup **(OPU)** , live birth rate **(LBR)** , in vitro fertilization **(IVF)** ,Intracytoplasmic sperm injection **(ICSI)** , Gonadotropin-releasing hormone **(GnRH).**

12 | REFERENCES

1. Gonadotrophin-releasing hormone agonist protocols for pituitary suppression in assisted reproduction. Maheshwari A, Gibreel A, Siristatidis CS, Bhattacharya S. Cochrane Database Syst Rev. 2011 Aug 10; (8)
2. GnRH agonist long protocol versus short protocol in women 40 years or more undergoing ICSI: Middle East Fertility Society Journal Vol. 13, No. 1, 2008.
3. Relationship between gonadotropin releasing hormone agonist dosage and in vitro fertilization outcome .Lorusso F1, Depalo R, Selvaggi. Gynecol Endocrinol. 2004 Feb; 18 (2): 69-73.
4. Short term pituitary desensitization: effects of different doses of the gonadotrophin- releasing hormone agonist triptorelin. Broekmans FJ, Hompes PG. Hum Reprod. 1996 Jan; 11 (1): 55-60.
5. GnRH agonist versus GnRH antagonist in in vitro fertilization and embryo transfer (IVF/ET) Raffaella Depalo, K Jayakrishan, Reproductive Biology and Endocrinology 2012, 10:26.
6. Textbook of Assisted reproductive techniques . Fourth edition. Garnder K., Shoham Z., Weissman A.
7. Modified Natural Cycle Using GnRH Antagonist Can Be an Optional Treatment in Poor Responders Undergoing IVF. Shai E. Elizur, Dilek Aslan, Adrian Shulman. J Assist Reprod Genet. Feb 2005; 22(2): 75–79
8. Cumulative pregnancy rates after sequential treatment with modified natural cycle IVF followed by IVF with controlled ovarian stimulation. M.J. Pelinck1,3, H.M. Knol1. Human Reproduction Vol.23, No.8 pp. 1808–1814, 2008.
9. Oocyte retrieval timing based on spontaneous luteinizing hormone surge during natural cycle in vitro fertilization treatment. Bodri D1, Kawachiya S2, Kondo M2, Kato R2, Matsumoto. Fertil Steril. 2014 Apr;101(4):1001-7.e2.
10. Natural cycle IVF for subfertile couples (Protocol) 2013, Issue 6.
11. Cryo-thawed embryo transfer: natural versus artificial. Eva R Groenewoud, BMC Women's Health 2012, 12:27

How to cite this article: M.Z., M.F.S., N.L., W.R.S., A.N., M.Z. Assisted Conception: Preparing the Ovaries for Eggs Collection and Determination of the Outcome in Frozen Embryos Transfer (FET) During Natural Cycle IVF. Advance Research Journal of medical and clinical science . 2021;571−581. https://doi.org/10.15520/arjmcs.v7i05.3 19