International Journal Of Health Medicine and Current Research
E - ISSN : 2528 - 3189
P - ISSN : 2528 - 4398

International Journal of Health Medicine and Current Research
Vol. 2, Issue 01, pp.286-294, March, 2017

DOI:
10.22301/IJHMCR.2528-3189.286

Article can be accessed online on:
http://www.ijhmcr.com

ORIGINAL ARTICLE

INTERNATIONAL JOURNAL OF HEALTH MEDICINE AND CURRENT RESEARCH

MEDICATION BEFORE ASSISTED REPRODUCTIVE TECHNOLOGY

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ARTICLE INFO

Article History:
Received 25th January, 2017
Received in revised form
27th February, 2017
Accepted 28th March, 2017
Published online 30th March, 2017

Key words:
Assisted Reproductive, Infertility Treatment.

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ABSTRACT

Conversely, fecundability is the ability to conceive, and data from large population studies show that a monthly probability of conceiving is 20 to 25 percent. In those attempting con- ception, approximately 50 percent of women will be pregnant at 3 months, 75 percent will be pregnant at 6 months, and more than 85 percent will be pregnant by 1 year. Infertility affecting 10 to 15 percent of reproductive-aged couples. Even without treatment, approximately half of women will conceive in the second year of attempting. Most couples are more correctly considered to be subfertile, rather than infertile. However, there are obvious exceptions, such as the woman with bilaterally obstructed fallopian tubes or the azoospermic male.

Infertility evaluation should be considered in any couple that has failed to conceive in 1 year. Furthermore, fecundability is highly age related, thus evaluation at 6 months should be performed in women older than 40 years who desire conception, and according to some experts, in women older than 35.

Infertility treatment is a complex process influenced by numerous factors. Important considerations include duration of infertility, a couple's age (especially the female's), and diagnosed cause. The first step involves identification of a primary cause and contributing factors, and treatment is aimed at their direct correction. Most couples are treated with conventional therapies such as medication or surgery. Lastly, infertility treatment can be a financial burden, a significant source of emotional stress, or both.

Citation: Hermanus Suhartono, 2017 "Medication Before Assisted Reproductive Technology", *International Journal of Health Medicine and Current Research*, 2, (01), 288-294.

INTRODUCTION

Infertility is generally defined as one year of unprotected intercourse without conception[1]. Some prefer the term subfertility to describe women or couples who are not sterile but exhibit decreased reproductive efficiency. Studies suggest that after 1 year of having unprotected sex, 15% of couples are unable to conceive, and after 2 years, 10% of couples still have not had a successful pregnancy[2,3]. In couples younger than age 30 who are generally healthy, 20% to 37% are able to conceive in the first 3 months[4]. However, aging of the female partner affects fertility. After age 30, a woman's chances of getting pregnant decrease rapidly every year[5]. Infertility therefore affects approximately 10–15% of couples and is an important part of the practice of many clinicians. Cycle fecundability is the probability that a cycle will result in pregnancy and fecundity is the probability that a cycle will result in a live birth[1].

Cause of Infertility

Before any formal investigation begins, the major causes of infertility and the basic com- ponents of the infertility evaluation should be outlined for the couple. *The major causes of infertility include ovulatory dysfunction (20–40%), tubal and peritoneal pathology (30–40%), and male factors (30–40%); uterine pathology is relatively uncommon, and the remainder is largely unexplained.* To some extent, the prevalence of each cause of infertility varies with age. Ovulatory dysfunction is more common in younger than in older couples, tubal and peritoneal factors have a similar prevalence, and male factors and unexplained infertility are observed somewhat more often in older couples. The distribution of causes also varies with the duration of infertility and the level of care[1].1

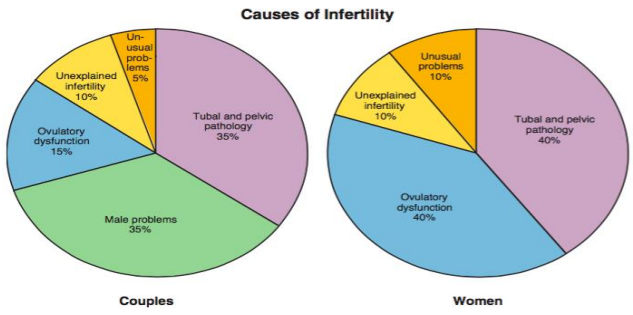

Figure 1. Causes of Infertility[1]

Most couples seeking evaluation have been trying to conceive for 2 or more years, so few will be normally fertile. Those with longer durations of infertility generally have more severe or multiple problems and tend to congregate in tertiary care centers. The average duration of infertility for couples seen in tertiary care centers (42 months) is twice that for couples seen in the primary care setting (21 months).Predictably, the proportion of couples with easily treatable ovulatory dysfunction decreases from primary to tertiary care, and that with more severe tubal/peritoneal or male factors increases[1].

Causes of Female Infertility

Female infertility has many possible causes. More than one problem contributes to infertility in 25% of couples[6].

1. Problems with the menstrual cycle

   The process that prepares the female body for pregnancy, can lead to infertility. The menstrual cycle includes several phases, and problems at any one of the stages can lead to difficulty getting pregnant or to infertility.

2. Diseases and Conditions

   Many different health issues can affect a woman's ability to get pregnant. Some of the more common problems are listed below

Endometriosis

Research has found a link between infertility and endometriosis. Studies show that between 25% and 50% of infertile woman have endometriosis and between 30% and 40% of women with endometriosis are infertile[7-9]. Some current theories on how endometriosis causes infertility include the following[9]:

- Changes in the structure of the female reproductive organs may occur and affect the release of the egg after ovulation or interrupt the egg's movement through the fallopian tube.
- The peritoneum may go through changes that affect its function:
  - In women with endometriosis, the amount of fluid inside the peritoneum often increases.
  - The fluid in the peritoneum contains substances that can negatively affect the functions of the egg, sperm, and fallopian tubes.
- Chemical changes in the lining of the uterus that occur as a result of endometriosis may affect an embryo's ability to implant properly and make it difficult for a woman to stay pregnant after conception

Polycystic Ovary Syndrome (PCOS)

PCOS is one of the most common causes of female infertility[10]. It is a condition in which a woman's

ovaries, and in some cases the adrenal glands, produce more androgens than normal. High levels of these hormones interfere with the development of ovarian follicles and release of eggs during ovulation. Researchers estimate that 5% to 10% of women in the United States have PCOS[10]. The exact cause of PCOS is unknown, but current research suggests that a combination of genetic and environmental factors leads to the disease.

Primary Ovary Insufficiency (POI)

POI is a condition in which a woman's ovaries stop producing hormones and producing eggs at a young age. Women with POI do not ovulate regularly, or sometimes not at all, and may have abnormal levels of hormones due to problems with their ovaries. However, pregnancy is still possible. About 5% to 10% of women with POI get pregnant without medical treatment[11].

Uterine Fibroids

Fibroids can contribute to infertility and are found in 5% to 10% of infertile women. Submucous uterine fibroids or those that are larger than 6 centimeters in diameter are more likely to have a negative effect on fertility. Fibroids are more likely to affect a woman's fertility if they[12]:

- Change the position of the cervix, which can reduce the number of sperm that enter the uterus
- Change the shape of the uterus, which can interfere with the movement of sperm or implantation
- Block the fallopian tubes, which prevents sperm from reaching the egg and keeps a fertilized egg from moving to the uterus
- Interfere with blood flow to the uterus, which can prevent the embryo from implanting.

General Causes of Infertility

General causes of infertility include:

1. Failure to ovulate

The most common overall cause of infertility is the failure to ovulate, which occurs in 40% of women with infertility issues. Not ovulating can result from:

- POI
- PCOS
- Aging
- Diminished ovarian reserve. This refers to a low number of eggs remaining in a woman's ovaries due to normal aging. This situation may result in hormone levels that can affect ovulation.
- Endocrine disorders.
- Tobacco use. Smoking or other use of tobacco can also affect ovulation and can cause complications with pregnancy[13].

2. Structural problems of the reproductive system

Structural problems usually involve the presence of abnormal tissue in the fallopian tubes or uterus. If the fallopian tubes are blocked, eggs are not able to move from the ovaries to the uterus and sperm is not able to reach the egg for fertilization. Blockage of the fallopian tubes can be associated with:

- Endometriosis
- Uterine fibroids
- Pelvic inflammatory disease, an infection of the female reproductive structures that is often caused by bacteria resulting from a common sexually transmitted infection (STI), such as gonorrhea or chlamydia[14]
- Tubal ligation, a surgical procedure that closes a woman's fallopian tubes permanently[15].
- Scarring in the uterus from previous injuries or surgery. Scarring may increase the risk of miscarriage and infertility.
- An unusually shaped uterus, which can affect a woman's ability to remain pregnant after conception.

3. Infections

Chlamydia is one of the most common sexually transmitted infections that affect female fertility. Chronic infections in the cervix can also reduce the amount or quality of cervical mucus, the sticky or slippery substance that collects on the cervix and in the vagina. Reduced amount or quality of cervical mucus can make it difficult for women to get pregnant[13].

4. Failure of an Egg to Mature Properly

For some women, the egg does not mature properly, resulting in fertilization failure. This can be caused by[16]:

- Hormonal problems, ranging from PCOS to problems with the hypothalamus or the pituitary gland.
- Lack of proteins called cyclin-dependent kinases. New studies suggest this protein may be involved in the process of egg maturation.[12]

- Injury to the ovaries. Scarred ovaries from multiple surgeries or repeated ovarian cysts can prevent the egg from maturing.
- POI

5. Implantation Failure

Implantation failure is a common cause of infertility among couples trying to conceive with assisted reproductive techniques (ART). Causes of implantation failure include[16]:

- Genetic defects
- Thin endometrium
- Embryonic defects, such as problems with male or female or sperm defects
- Endometriosis

6. Autoimmune Disorders

Autoimmune disorders, such as lupus or rheumatoid arthritis, may cause a woman's immune system to reject the egg and prevent it from implanting or cut off the blood supply to an implanted embryo[11]. Autoimmune disorders may also attack sperm or the reproductive organs

Lifestyle Factors

Lifestyle factors that influence fertility include weight problems and smoking. The American Society for Reproductive Medicine reports that 12% of infertility cases are the result of women weighing either too much or too little[17]. Smoking can also reduce fertility by affecting ovulation and reducing the amount or quality of cervical mucus.

Age-Related Factors

It is currently believed that women are born with between 1 and 2 million eggs, with the number decreasing throughout life. A gradual decline in fertility begins around age 32 and continues to decrease rapidly after age 37 because of the reduction in the number and quality of eggs in the ovaries[18]. The lower number of eggs leads to changes in hormone levels, which further reduces a woman's fertility.

New research suggests that eggs can be made from stem cells in the ovaries[19]. This finding challenges the belief that women are born with a certain number of eggs, and the discovery could help women undergoing early menopause or preserve fertility for women undergoing cancer treatment.

In addition, women with a history of ovarian surgery, chemotherapy, radiation therapy, severe endometriosis, smoking, or pelvic infections may have premature reduction in the number of eggs in the ovaries and a simultaneous reduction in fertility. As a woman ages, the risk increases for miscarriage and for having an embryo with abnormal chromosomes, which can lead to problems with development and loss of the pregnancy.

Unexplained Infertility

Health care providers diagnose a woman with unexplained infertility when the infertility examination shows that ovulation is occurring with no obvious abnormality, the fallopian tubes are unobstructed, and there are adequate numbers of motile sperm. About 30% of cases of infertility in women cannot be explained[20]. More advanced testing may determine the cause of infertility, but knowing the exact cause may not be necessary. When a specific cause is not determined for women and when male infertility has also been ruled out, the health care provider may begin treatment to improve the chances of conception and then progress to more complex fertility treatments.

What are the causes of male infertility?

Men can also contribute to infertility in a couple. In fact, men are found to be the only cause or a contributing cause of infertility problems in couples in 30% to 40% of cases[21]. The most common issues that lead to infertility in men are problems that affect how the testicles work. Other problems are hormone imbalances or blockages in the male reproductive organs. In about 50% of cases, the cause of male infertility cannot be determined[13].A complete lack of sperm is the cause of infertility in about 10% to 15% of men who are infertile[22].

Evaluation Before Having an Assisted Reproductive Technology

Before starting ART, each patient is evaluated to help maximize her chances for success and a healthy pregnancy. Good preconception health is essential to achieving pregnancy with IVF. Chronic medical conditions such as diabetes, hypertension and asthma should be well controlled before attempting to conceive. In addition, women planning an IVF cycle should optimize their weight. Obesity has been associated with infertility, a reduced chance of success with IVF, and an increase in the risk of miscarriage and preterm birth. Your physician can help you determine your ideal weight and refer you to appropriate resources for weight management.

General Blood Tests

Prior to starting IVF, the woman's blood type should be verified, and she should be screened for conditions that could affect the health of a pregnancy. Documentation of immunity to rubella (German measles) and varicella (chicken pox) may also require a blood test. The patient and her partner will also be tested for hepatitis B and C, HIV and syphilis. Other genetic tests may be requested depending on the patient's genetic background, such as cystic fibrosis and sickle cell trait [1, 23].

Ovarian Reserve Testing

As women age they have a decreased ability to conceive and an increased risk of miscarriage. Ovarian reserve testing tries to measure egg quality, quantity and reproductive potential. The following tests may be used to measure ovarian reserve[23]:

1. **Day 3 Levels of FSH, LH, and Estradiol.** Women with elevated levels of FSH and/or estradiol measurements may have reduced pregnancy rates with IVF or may require more medications during IVF.
2. **Clomiphene Citrate Challenge Test.** This test requires patient to take 100 mg of clomiphene citrate on menstrual cycle days 5-9. Blood levels of FSH are measured on cycle day 3 and again on cycle day 10. Elevated blood levels of FSH on cycle day 3 or cycle day 10 are associated with reduced pregnancy rates.
3. **Anti-Mullerian Hormone Test (AMH).** Anti-Mullerian hormone levels are thought to reflect the remaining number of eggs/ ovarian reserve. This test can be performed on any day of the cycle

Semen Quality

Semen quality should be assessed not long before the treatment cycle is scheduled to start, to ensure there has been no appreciable change that might affect the choice between conventional fertilization and intracytoplasmic sperm injection (ICSI). Evaluation of sperm morphology, as judged by "strict" criteria (WHO III standard), also may help to determine whether ICSI should be planned.

Imaging of the uterine cavity

Imaging of the uterine cavity can identifies submucosal myomas or endometrial polyps that may interfere with implantation or have an adverse effect on pregnancy outcome. An HSG performed earlier during the diagnostic evaluation may suffice if entirely normal and relatively recent (within approximately 6 months), but sonohysterography and hysteroscopy are the more sensitive and preferred methods. Routine office hysteroscopy before IVF can be expected to identify potentially significant abnormalities such as polyps, myomas, adhesions, or septa in 10–20% of patients without symptoms[1].

Reproductive aged women have an estimated 20–150 growing follicles in the ovaries at any one time, although only a few are large enough to be imaged (≥2 mm) by transvaginal ultrasonography. Histologic studies have revealed that the number of small antral follicles in the ovaries is proportional to the number of primordial follicles remaining. Therefore, as the supply of primordial follicles decreases, the number of visible small antral follicles also *declines.* The antral follicle count (AFC; total number of antral follicles measuring 2–10 mm in both ovaries) thus provides an indirect but useful measure of ovarian reserve[1].

Fertility Treatments for Females

Once a woman is diagnosed with infertility, the overall likelihood for successful treatment is 50%.[1] Whether a treatment is successful depends on the:

- Underlying cause of the problem
- Woman's age
- History of previous pregnancies
- How long she has had infertility issues

Fertility treatments are most likely to benefit women whose infertility is due to problems with ovulation. Treatment is least likely to benefit infertility caused by damage to the fallopian tubes or severe endometriosis[13]. Fertility treatments for women fall into the following categories:

- Medication Treatments for Female Infertility
- Surgical Treatments for Female Infertility
- Assisted Reproductive Technology (ART)

Medication Treatments for Female Infertility

The most common medications used to treat infertility help stimulate ovulation. Examples of these types of medications include[24]:

- Clomiphene or Clomiphene Citrate
- Gonadotropins or human chorionic gonadotropin (hCG)
- Bromocriptine or cabergoline

Clomiphene or Clomiphene Citrate

Clomiphene causes the body to make more of the hormones that cause the eggs to mature in the ovaries. Patients take clomiphene on days 3 to 5 of the menstrual cycle. It causes ovulation to occur in 80% of

women treated. About half of those who ovulate are able to achieve a pregnancy or live birth. Use of clomiphene increases the risk of having a multiple pregnancy. There is a 10% chance of twins, but having triplets or more is rare—less than 1% of cases [24].

Gonadotropins and Human Chorionic Gonadotropin (hCG)

Gonadotropins is a hormone similar to leutenizing hormone that can be used to trigger release of the egg after the follicles have developed. It will directly stimulate eggs to grow in the ovaries, leading to ovulation. Health care providers normally prescribe gonadotropins when a woman does not respond to clomiphene or to stimulate follicle growth for ART.

Gonadotropins are injected starting on day 2 or day 3 of the menstrual cycle for 7 to 12 days. While a woman is treated with gonadotropins, a health care provider uses transvaginal ultrasound to monitor the size of the developing follicles. They also draw blood frequently to check the ovarian production of estrogen. The chance of a multiple birth is higher with gonadotropins than with clomiphene, and 30% of women who conceive a pregnancy with this medication have multiple births[24]. About two-thirds of multiple births are twins. Triplets or larger multiple births account for the remaining third.

Bromocriptine or Cabergoline

Bromocriptine and cabergoline are pills taken orally to treat abnormally high levels of the hormone prolactin. Certain medications, kidney disease, and thyroid disease can cause high levels of prolactin. Both allow 90% of women to have normal prolactin levels. Once prolactin levels become normal, 85% of women using bromocriptine or cabergoline ovulate[13].

Surgical Treatments for Female Infertility

If disease of the fallopian tubes is the cause of infertility, surgery can repair the tubes or remove blockages in the tubes. Success rates of these types of surgery, however, are low. These surgeries involving the fallopian tubes also increase the risk of ectopic pregnancy. Ectopic pregnancies are also called "tubal pregnancies" because they most often occur in a fallopian tube[25].

Surgery to remove patches of endometriosis has been found to double the chances for pregnancy. Surgery can also remove uterine fibroids, polyps, or scarring, which can affect fertility.

Fertility Treatments for Males

Treatment with Medication

Medication can treat some issues that affect male fertility, including hormone imbalances and erectile dysfunction[13]. Some health provider give folic acid as antioxidant and chlamydial infection prophylaxis.

Treatment with Surgery

Surgery can be effective for repairing blockages in the tubes that transport sperm from the testicles to the penis. Surgery also can be used for repair of varicocele, or varicose veins, in the testicles. Current research suggests that surgical repair of varicocele can improve health of sperm, but it has not affected the chances for conception[13]. If surgery does not restore fertility, ART can be effective.

Ovarian Stimulation Regimens

The ideal ovarian stimulation regimen for IVF should have a low cancellation rate, minimize drug costs, risks and side effects, require limited monitoring for practical convenience, and maximize singleton pregnancy rates. Ovarian stimulation has been a basic element of IVF for more than 25 years, but concerns about multiple pregnancies and the costs of IVF have sparked renewed interest in natural cycle IVF and mild stimulation regimens[1].

Natural Cycle

The first birth resulting from IVF derived from a single oocyte collected in a natural ovulatory cycle. Compared to stimulated IVF cycles, natural cycle IVF offers a number of attractive advantages. Natural cycle IVF involves only monitoring the spontaneous cycle and retrieving a single oocyte before the midcycle LH surge occurs. It is physically less demanding, requires little or no medication, decreases costs by 75–80%, and all but eliminates risks for multiple pregnancy and ovarian hyperstimulation syndrome (OHSS). The chief disadvantages of natural cycle IVF are high cancellation rates due to premature LH surges and ovulation, and the comparatively low success rate, which is approximately 7%[1].

Clomiphene Citrate

Clomiphene (100 mg daily) usually is administered for 5–8 days, beginning on cycle day 3, and induces development of two or more follicles in most normally ovulating women, although egg yields (1–3) are only slightly greater than in unstimulated

cycles and substantially lower than in cycles stimulated with exogenous gonadotropins. Cycle cancellation rates are somewhat lower than in natural cycles and the numbers of oocytesAccessed, embryos transferred, and pregnancy rates are greater. As in natural cycles, exogenous hCG is administered when the lead follicle reaches mature size and a GnRH antagonist can be used to prevent a premature endogenous LH surge.

Sequential treatment with clomiphene (100 mg daily for 5 days) and modest doses of exog- enous gonadotropins (150–225 IU daily beginning on the last day of clomiphene treatment or the day after) stimulates multifollicular development more effectively than treatment with clomiphene alone. Drug costs and monitoring requirements are moderately higher, but still substantially less than in standard stimulation regimens involving higher dose gonadotropin treatment after down-regulation with a long-acting GnRH agonist[1].

GnRH Agonist Down-Regulation Gonadotropin Stimulation—The "Long" Protocol

In the typical cycle, GnRH agonist treatment begins during the midluteal phase, approximately 1 week after ovulation, at a time when endogenous gonadotropin levels are at or near their nadir and the acute release of stored pituitary gonadotropins in response to the agonist, known as the "flare" effect.

GnRH agonist treatment can be scheduled to begin on cycle day 21 (assuming a normal cycle of 28 days duration), but most prefer to first con- firm that ovulation has occurred by measuring the serum progesterone concentration. In women who do not cycle predictably, oral contraceptives (OC) can be used to control the onset of menses, starting GnRH agonist treatment 1 week before their discontinuation.

For leuprolide, the usual treatment regimen begins with 1.0 mg daily for approximately 10 days or until onset of menses or gonadotropin stimulation, decreasing to 0.5 mg daily thereafter until hCG is administered.

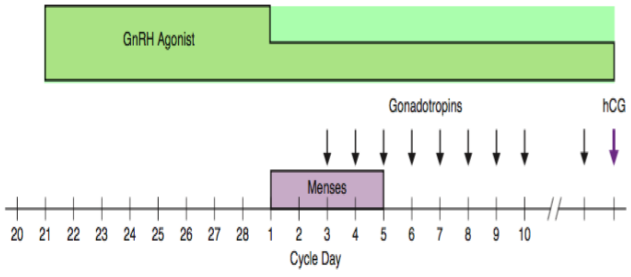

Figure 2. The GnRH Agonist Down-Regulation Gonadotropin Stimulation - Long Protocol.

Gonadotropin stimulation begins after confirming that effective pituitary down-regulation has been achieved (serum estradiol level <30–40 pg/mL, no follicles >10 mm in diameter). Typical starting doses range between 150 and 300 IU of urinary FSH (uFSH), recombinant FSH (rFSH), or urinary menotropins (hMG) daily, depending on age, the results of ovarian reserve testing, and the response observed in any previous stimulation cycles.

The response to stimulation is monitored with serial measurements of serum estradiol and transvaginal ultrasonography. The first estradiol level usually is obtained after 3–5 days of stimulation to determine whether the chosen dose of gonadotropins requires adjustment. Thereafter, serum estradiol concentrations and sonography are obtained every 1–3 days, based on the quality of the response and the need to evaluate the impact of any further adjustments in the dose of gonadotropin treatment.

In general, stimulation continues until at least two follicles measure 17–18 mm in mean diameter, and the serum estradiol concentration reflects the overall size and maturity of the cohort. Most women require a total of 7–12 days of stimulation.

The endometrium is monitored during stimulation by measuring the endometrial thickness or "stripe" (the sum thickness of the two layers, measured in the mid-sagittal plane). Many have suggested that results are best when endometrial thickness measures 8–9 mm or greater or appears "trilaminar," and poor when the endometrium is less than 6–7 mm in thickness or appears homogeneous on the day of hCG administration[1].

GnRH Agonist "Flare" Gonadotropin Stimulation Protocol

In a typical standard short protocol, leuprolide acetate 1.0 mg daily is administered on cycle days 2–4, continuing thereafter at 0.5 mg daily, and gonadotropin stimulation 225–450 IU daily begins on cycle day 3.

The "OC microdose GnRH agonist flare" stimulation regimen is a variation of the standard short protocol involving 14–21 days of preliminary ovarian suppression with an OC (one pill daily), followed by microdose leuprolide treatment (40 μg twice daily) beginning 3 days after discontinuation of OC treatment, and high-dose gonadotropin stimulation (300–450 IU daily) starting on day 3 of leuprolide therapy.

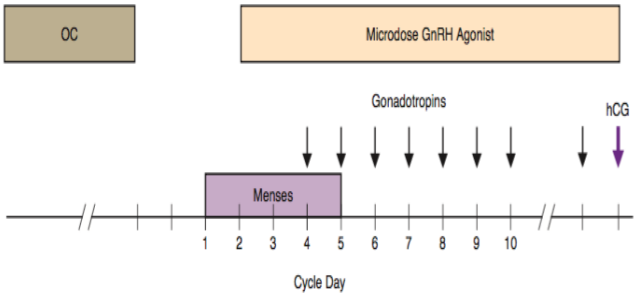

Figure 3. The GnRH Agonist Gonadotropin Stimulation Protocol - Short Protocol

GnRH Antagonist Gonadotropin Stimulation Protocol

GnRH antagonists offer several potential advantages over agonists.

1. First, the duration of treatment is substantially shorter than for an agonist. Since its only purpose is to prevent a premature endogenous LH surge and its effects are immediate, antagonist treatment can be postponed until later in follicular development (after 5–6 days of gonadotropin stimulation), after estradiol levels are already elevated, thereby eliminating the estrogen deficiency symptoms that may emerge in women treated with an agonist.
2. Second, because any suppressive effects that agonists may exert on the ovarian response to gonadotropin stimulation also are eliminated, the total dose and duration of gonadotropin stimulation required is decreased.For the same reason, GnRH antagonist stimulation protocols may benefit women who are poor responders when treated with a standard long protocol.
3. Third, by eliminating the flare effect of agonists, GnRH antagonists avoid the risk of stimulating development of a follicular cyst. Finally, the risk of severe OHSS associated with use of antagonists also appears lower than with agonists.

GnRH antagonists have some potential disadvantages. When administered in small daily doses, strict compliance with the prescribed treatment regimen is essential. Antagonists suppress endogenous gonadotropin secretion more completely than agonists.

The two GnRH antagonists available for clinical use, ganirelix and cetrorelix, are equally potent and effective. For both, the minimum effective dose to prevent a premature LH surge is 0.25 mg daily, administered subcutaneously. Either can be administered in a series of small daily doses (0.25 mg). The treatment protocol may be fixed and begin after 5–6 days of gonadotropin stimulation, or tailored to the response of the individual, starting treatment when the lead follicle reaches approximately 13–14 mm in diameter.

Alternatively, a single larger dose of cetrorelix (3.0 mg) will effectively prevent an LH surge for 96 hours. If given on day 6–7 of stimulation, the interval of effective suppression will encompass the day of hCG administration in most women (75–90%); the remainder may receive additional daily doses (0.25 mg) as needed, ending on the day of hCG treatment. The single dose antagonist treatment regimen also can be withheld until the lead follicle reaches 13–14 mm in diameter. A common variation of the antagonist stimulation regimen uses preliminary treatment with an OC to control the onset of menses, typically ending approximately 5 days before the scheduled start, which also may help to synchronize the follicular cohort before stimulation begins.

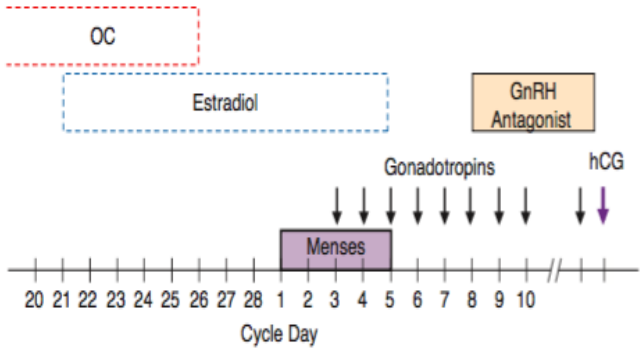

Figure 4. The GnRH Antagonist Stimulation Protocol

The antagonist treatment regimens currently in use have potential disadvantages for women with PCOS. Their tonically elevated LH levels will remain high until antagonist treatment begins. Consequently, LH levels may rise prematurely, particularly if antagonist treatment is withheld until the lead follicle reaches 14 mm or more[1].

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