Clomiphene Citrate [1]

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Clomiphene citrate, more commonly known by its brand names Clomid [4] and Serophene, is a medication prescribed to women to stimulate ovulation [5] in order to treat infertility [6]. It stimulates ovulation [5] in women who do not ovulate or ovulate irregularly. This drug was created by Frank Palopoli [7] in 1956 while he worked for Merrell Company. It first successfully induced ovulation [5] in women in 1961 and was approved by the Food and Drug Administration [8] (FDA) in 1967. This medication can be used to help women conceive naturally, to time ovulation [5] for intrauterine insemination, or to stimulate the maturation of eggs to be extracted and used in procedures such as *in vitro* [9] fertilization [10] (IVF), gamete intrafallopian transfer (GIFT), and zygote intrafallopian transfer [11] (ZIFT).

Women with higher than normal levels of malehormones [12], known as hyperandrogenism [13], are good candidates for clomiphene therapy as are women with normal estrogen [14] levels but who do not ovulate, a condition called anovulation [15]. Certain conditions such as low estrogen [14] levels may limit the benefit of clomiphene therapy, especially when not used in conjunction with other assisted reproductive technologies (ART). Women with lower than normal estrogen [14] levels may still conceive by undergoing higher dosages of clomiphene therapy, but they will more likely benefit from menotropin therapy [16], another type of hormone [17] treatment. Also, women seeking clomiphene therapy must not have a history of liver disease (the liver metabolizes clomiphene resulting in further damage to the liver), no abnormal uterine bleeding, and no ovarian cysts (clomiphene may enlarge the cysts).

Physicians usually administer clomiphene between the third and fifth day of menstruation [18] (the first day being the day that menstruation [18] begins) and start with 50 mg per day for a five-day regimen (days five through nine of the menstrual cycle). Ovulation should occur five to ten days after the last dose of clomiphene is administered. If the 50 mg dose is not enough to stimulate ovulation [5], the physician will increase the dosage by 50 mg each trial until the minimum effective dosage that induces ovulation [5] is reached. Once that minimum effective dosage is determined, physicians typically recommend the patient undergo four to six treatment cycles at that level until the patient successfully becomes pregnant. The maximum dosage of clomiphene should not exceed 200–250 mg. These dosages have been found effective based on multiple clinical trials. Various methods that determine the exact timing of ovulation [5] are blood tests for luteinizing hormone [19] (LH) levels, urinary tests for LH levels, and ultrasounds to observe the condition of the pelvis. During ovulation [5], the physician instructs patients to have intercourse every other day for one week beginning on the fifth day following the last dose.

If the patient is unable to ovulate at the maximum daily dosage of 200–250 mg, the physician may combine clomiphene with other medications such as human chorionic gonadotropin [20] (hCG) or dexamethasone [21]. The addition of hCG to clomiphene therapy may benefit women who respond to clomiphene therapy with rising LH, follicle stimulating hormone [22] (FSH), and estrogen [14] levels but still fail to ovulate. Dexamethasone as an adjunct to clomiphene therapy benefits women with dehydroepiandrosterone sulfate (DHEAS) levels above the normal threshold. DHEAS is a precursor molecule to male and female sex hormones [23] that can increase androgens [24] (male hormones [12]) in the body and result ininfertility [6] problems.

Clomiphene citrate causes ovulation [5] by stimulating the pituitary gland [25] to secrete more FSH and LH while stimulating the ovaries to secrete estrogen [14]. After a five-day treatment with clomiphene, LH and FSH levels initially decline but estradiol [26] continues to increase resulting in a preovulatory peak and LH and FSH levels increasing once again.

Certain risk factors are associated with clomiphene therapy. One possible risk is luteal phase defect [27]. The luteal phase is the period beginning immediately after the end of ovulation [5] and continuing to the first day ofmenstruation [18]. During this period, a woman's body normally prepares the endometrium [28] (lining of the uterine wall) for afertilized egg [29] to implant. However, if there is a defect during this phase the endometrium [28] is not prepared for implantation [30]. Another risk is that clomiphene will affect the cervical mucus, preventing sperm [31] from entering the uterus [32] and fertilizing the egg [33].

Most women who undergo fertility treatments first try hormones [12] such as clomiphene before undergoing more expensive procedures such as IVF, which can exceed $10,000. However, clomiphene therapy does not treat male infertility [6] or female cervical mucus defects, in which case techniques such as IVF are recommended. Unlike most other assisted reproductive technologies, fertility medications such as clomiphene citrate [34] are considered an acceptable fertility treatment by the Catholic Church making them the preferred option for some patients.

Sources

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