



# A REVIEW ON CURRENT DRUG THERAPY USED IN FEMALE INFERTILITY

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**Abstract-** Infertility is a multidimensional problem with social, economic and cultural implications affecting approximately 8-10% of couples. In the present study a total of 635 infertile females from three infertile centers who are taking medical counseling were screened. A validated questionnaire has been administered to collect the data pertaining to the causes of infertility, period of infertility, education, occupation and life styles besides anthropometric measurements.. Both overweight (41.3%) and obesity (36%) has shown positive association with infertility in 5-9 yrs and >15yrs groups. Our results show a strong association of infertility with body mass index. A majority of educated and higher income groups sought medical counseling to resolve the infertility related problems. When the infertility cases were rated based on the issues around 30% females needed medical aid, 65% were normal and only 5% are refractory in nature. In conclusion it is stated that female infertility can be treated and managed with medication, minor surgical operations, laparoscopic procedures, hormonal therapy and prevention of preconception failure and maintenance of healthy life style

**Key Words:-** clomiphene citrate (CC) , Letrozole , Clomiphene , Gonadotrophin

**Introduction** :- Infertility is the inability of a couple to achieve pregnancy within 12 months of unprotected intercourse (Devroey et al.,2009)<sup>(1)</sup> .Or Infertility is the inability of a couple to achieve pregnancy over an average period of one year (in a woman under 35 years of age) or 6 months (in a woman above 35 years of age) despite adequate, regular (3-4 times per week), unprotected sexual intercourse<sup>(2)</sup>

## \*RISK FACTORS AND CAUSES :

1)Infertility may be caused by an underlying medical condition that may damage the fallopian tubes, interferes with ovulation, or causes hormonal complications.

2)These medical conditions include pelvic inflammator disease, endometriosis, polycystic ovarian syndrome, premature ovarian failure, uterine fibroids and environmental factors.

3) Other causes of infertility in females include ovulation problems, tubal blockage, age-related factors, uterine problems, previous tubal ligation and hormone imbalance while the main cause of male infertility is poor semen quality<sup>(3)</sup>.

4) Environmental factors and infertility The etiological importance of environmental factors in infertility has been stressed<sup>(4)</sup>.

5) Toxins such as glues, volatile organic solvents or silicones, physical agents, chemical dusts, and pesticides are implicated in infertility<sup>(5)</sup>.

6) Other potentially harmful occupational environmental exposures such as chlorinated hydrocarbons and fumigants have also been discovered to be associated with the increased link of spontaneous miscarriage in women<sup>(6)</sup>.

### **Treatment Modalities :-** Fertility Drugs :

Fertility drugs are often used alone as initial treatment to induce ovulation. If they fail as sole therapy, they may be used with assisted reproductive procedures, such as in vitro fertilization, to produce multiple eggs, a process called superovulation. According to the American Society for Reproductive Medicine, fertility drugs can be divided into three main categories:

- Medications for Ovarian Stimulation. Clomiphene (Clomid, Serophene); letrozole (Femara), follicle stimulating hormone (FSH) [Follistim, Gonal-F, Bravelle]; human menopausal gonadotrophin (HMG) [Humegon, Repronex, Menopur]; luteinizing hormone (LH) [Luvetris]
- Medications for Oocyte Maturation. Human chorionic gonadotropin (hCG) [Profasi, APL, Pregnyl, Nova90el, Ovidrel]
- Medications to Prevent Premature Ovulation. GnRh agonists (Lupron and Synarel); Gn RH antagonists (Antagon, Cetrotide)<sup>(26)(27)</sup>.

#### **1) CLOMIPHENE :-**

The first-line medication for infertility of unknown origin and the medication most providers use is clomiphene citrate (CC). Clomiphene is a selective estrogen receptor modulator (SERM) with estrogen antagonist and agonist effects that ultimately increase gonadotropin release from the anterior pituitary. Clomiphene effectively treats WHO class 2 anovulation but ineffective in WHO class 1 and class 3 anovulation. Clomiphene is dosed starting at 50mg starting on cycle day 2, 3, 4, or 5 for 5 sequential days. The couple is encouraged to have intercourse every other day for one week, beginning 5 days after the last pill. However, the odds for pregnancy may be increased when clomiphene is combined with intrauterine insemination (IUI). There is little difference in the results of ovulation, pregnancy, or live birth regarding which day the medication is started, between cycle days 2 to 5.<sup>(28)</sup>

### **MECHANISM OF ACTION :-**

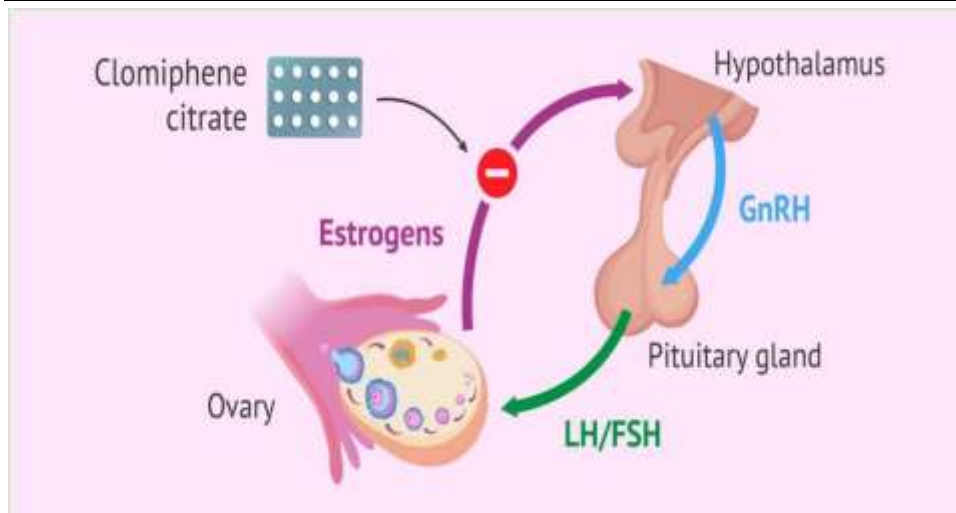


Fig 1: mechanism of action of clomiphene

**Adverse effect :-**

- flushing
- upset stomach
- vomiting
- breast discomfort
- headache
- abnormal vaginal bleeding

**contraindication**

- in pregnancy
- Hepatic disease
- Abnormal uterine bleeding
- Uncontrolled adrenal dysfunction □ Non –PCOS related ovarian cyst

**2) GONADOTROPHIN :-**

If clomiphene does not work or is not an appropriate choice, gonadotropin drugs are a second option. Gonadotropins include several different types of drugs that contain either a combination of follicle-stimulating hormone (FSH) and luteinizing hormone (LH), or only FSH. Whereas clomiphene works indirectly by stimulating the pituitary gland to secrete FSH, (which prompts follicle production), gonadotropin hormones directly stimulate the ovaries to produce multiple follicles. Gonadotropins are given by injection. Gonadotropins include:

- Human Menopausal Gonadotropins (hMG), also called menotropins
- Human Chorionic Gonadotropins (hCG)
- Follicle Stimulating Hormone (FSH)
- Gonadotropin-releasing hormone (GnRH) analogs, which include GnRH agonist and GnRH antagonists.

This action helps prevent the premature release of the eggs before they can be harvested for assisted reproductive technologies. (regarding which day the medication is started, between cycle days 2 to 5.<sup>(28)</sup> regarding which day the medication is started, between cycle days 2 to 5.<sup>(28)</sup> <sup>(29)</sup> GnRH agonists include leuprolide (Lupron), nafarelin (Synarel), and goserelin (Zoladex).

**Adverse effect :-**

- Abnormal or stomach pain
- Bloating
- Decreased amount of urine
- Feeling of indigestion
- Nausea , vomiting or diarrhea
- Pelvic pain
- Shortness of breath
- Swelling of feet

**Contraindication :-**

- Cancer of the prostate gland
- Cancer of the testis
- A tumor of the pituitary gland
- Obstruction of blood vessel by a blood clot
- A tumor of the pituitary gland

**MECHANISM OF ACTION :-**

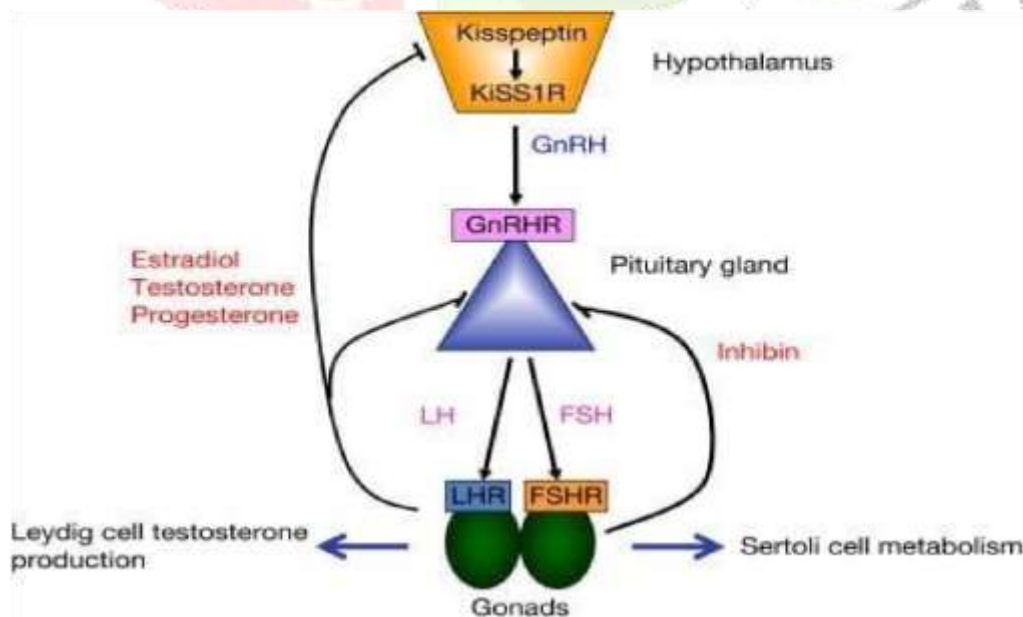


Fig 2: mechanism of action of Gonadotrophin

### 3) Letrozole :-

Another commonly used oral medication for ovulation induction is letrozole. Letrozole is an aromatase inhibitor that prevents estrogen production by preventing the conversion of androstenedione and testosterone to estrone and estradiol.<sup>(31)</sup>

#### MECHANISM OF ACTION :-

## Letrozole - Mechanism of Action

Letrozole blocks conversion of androgen to estrogen.

Temporary accumulation of intraovarian androgens

Increases follicular sensitivity to FSH.

Fig 3: mechanism of action of letrozole

#### Adverse effect :-

- Bone fracture
- Breast pain
- Chest pain
- Chills, fever
- Mental depression

#### Contraindication :-

- High cholesterol .
- Severe liver disease
- Osteoporosis
- High amount of bilirubin in blood
- Hardening of liver



**TABLE NO 1 :-**

| Drug Name                         | Brand name          | Dose             |
|-----------------------------------|---------------------|------------------|
| Clomiphene citrate tablet         | Clomitop-100        | 50 mg            |
| Chorionic gonadotrophin injection | Lupi-HCG HP 5000 IU | 10,000 USP units |
| Letrozole tablet                  | Letronol – 2.5      | 2.5 mg           |

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