

Ovulation Inducing Agents

Mifepristone

Danazol

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Endocrine & Reproduction-II
Theme-5;Infertility and pregnancy
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Aims And Objectives

By end of this presentation you would be able to

Describe the mechanism of action, clinical use, and adverse effects of

- ▶ **Clomiphene**
- ▶ **Mifepristone**
- ▶ **Danazol**

Clomiphene Citrate

Clomiphene citrate, a partial estrogen agonist

- ▶ Nonsteroidal, Synthetic Compound, Triphenylethylene Derivative
- ▶ Structural Similarity To Estrogen
- ▶ Antiestrogenic Effect
- ▶ This Compound Is Well Absorbed When Taken Orally.
- ▶ It Has A Half-life Of 5–7 Days
- ▶ Excreted Primarily In The Urine.
- ▶ It Exhibits Significant Protein Binding And Enterohepatic Circulation
- ▶ Distributed To Adipose Tissues.

Mechanisms of Action

- ▶ Binds To Er Alpha, Er Beta
- ▶ Act As Pure Estrogen Antagonist In All Human Tissues
- ▶ Action At The Hypothalamic Level
- ▶ The Amount Of LH/FSH Released In Each Secretary Phase Is Increased

Clomiphene - MoA

Binds to hypothalamic and pituitary estrogen receptors



Blocks inhibitory feedback of estrogen



Increased release of GnRH



Increased FSH and LH



Ovulation occurs

Clomiphene
citrate



Hypothalamus

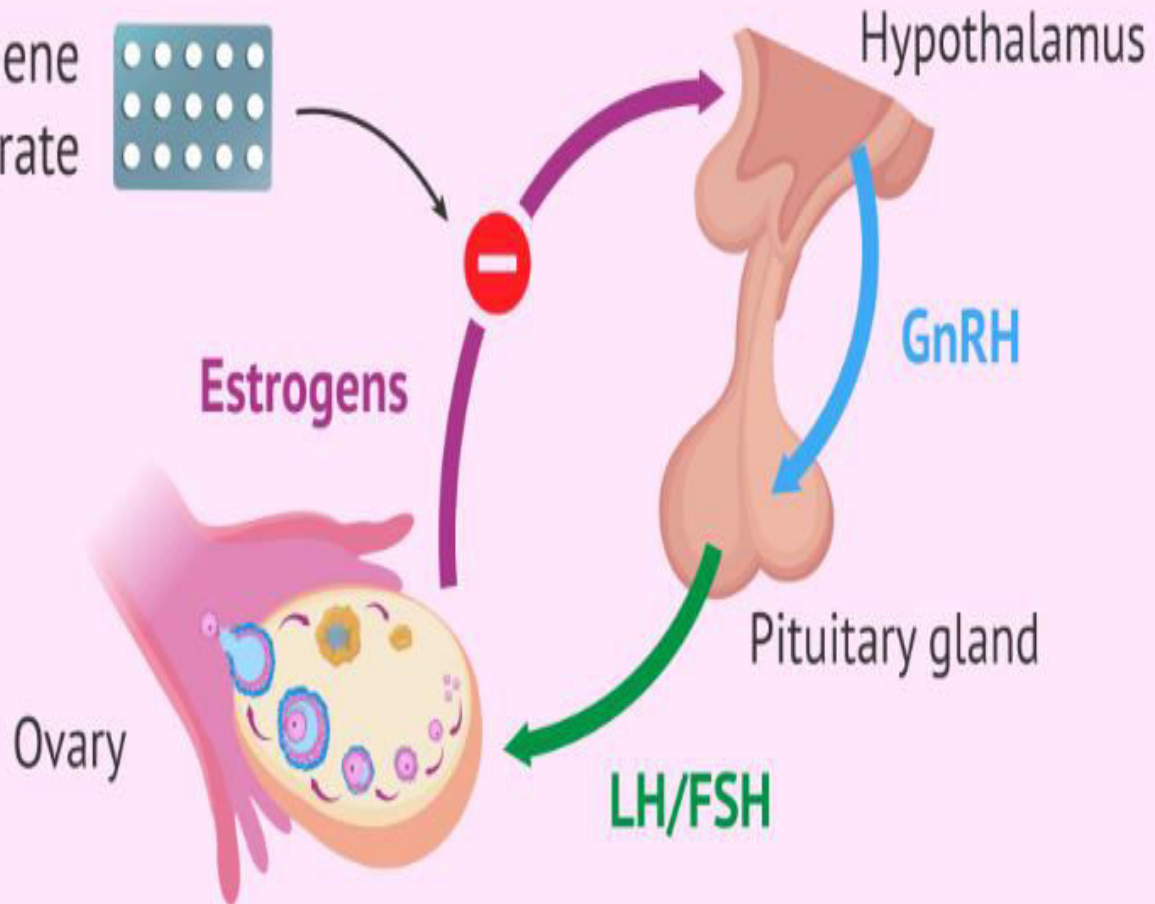
GnRH

Pituitary gland

LH/FSH

Estrogens

Ovary



Clinical uses



- ▶ Infertility due to anovulation.
 - ▶ 50-100mg per day od for 5 days
 - ▶ Starts on 3rd day of cycle
 - ▶ Cyclical therapy is recommended but not more than 6 cycle as increase chances of ovarian cancer.
- ▶ Male infertility for
 - ▶ oligospermia promote Spermatogenesis
 - ▶ Testosterone Secretion
- ▶ Assisted reproduction therapy (ART) and (GIFT)gametes intrafallopian transfer technique.

Clomiphene

- ▶ DOSE
 - ▶ 50mg/day starting from day 3-7 for 2 months
 - ▶ then double the dose 50mg BD for 3 months
 - ▶ maximum 200mg/day can be given
- ▶ Addition Of Hcg Injs On Day 13 Or 14 Improves Success Rate
- ▶ IN OLIGOSPERMIA DOSE IS
 - ▶ 25mg/day for 24 days in a month, 6 days rest up to 6 months

Adverse Effects

- ▶ Hot Flashes (Antagonism Of Peripheral Actions Of Estrogen)
- ▶ Gastric Upsets nausea vomiting
- ▶ Hyperstimulation syndrome. Polycystic Ovaries
- ▶ Multiple Pregnancy
- ▶ Ovarian cysts
- ▶ Allergic Dermatitis
- ▶ Risk Of Ovarion Tumours
- ▶ Weight gain breasts discomfort

Mifepristone

- ▶ Mifepristone is a “19-norsteroid”
- ▶ Binds strongly to the progesterone receptor
- ▶ Inhibits the activity of progesterone.
- ▶ Competitive antagonist of progesterone
- ▶ Has anti glucocorticoid anti androgenic activity
- ▶ The drug has luteolytic properties in 80% of women when given in the midluteal period.

Mifepristone

- ▶ Orally effective
- ▶ Long plasma half life
- ▶ Metabolized in liver
- ▶ Undergoes enterohepatic circulation

Mifepristone indications

- ▶ Contraceptive ; postcoital contraception causes shedding of decidua. A single dose of 600 mg is an effective emergency postcoital contraceptive.
- ▶ Termination of pregnancy early pregnancy single oral dose of mifepristone followed 48hrs later by prostaglandin(PGE1) raises success rate by 95%.
- ▶ For induction of labour incase of intrauterine death of fetus

Adverse effect Mifepristone

- ▶ Teratogenic
- ▶ Uterine bleeding
- ▶ Nausea vomiting

DANAZOL



- ▶ Weak progestational, androgenic, and glucocorticoid activities
- ▶ USED TO SUPPRESS OVARIAN FUNCTION
- ▶ Danazol inhibits the midcycle surge of LH and FSH

DANAZOL

- ▶ Danazol is slowly metabolized
- ▶ Half-life of over 15 hours.
- ▶ It is highly concentrated in the liver, adrenals, and kidneys
- ▶ Excreted in both feces and urine.



Danazol uses

- ▶ Danazol an inhibitor of gonadal function use in the treatment of **ENDOMETRIOSIS**.
 - ▶ Dose ; 600 mg/d.
 - ▶ Reduced to 400 mg/d after 1 month
 - ▶ Then to 200 mg/d in 2 months.
 - ▶ About 85% of patients show marked improvement in 3–12 months.
- ▶ Treatment of fibrocystic disease of the breast
- ▶ Hematologic Or Allergic Disorders, i.e.
 - ▶ Hemophilia, Christmas Disease,
 - ▶ Idiopathic Thrombocytopenic Purpura,
 - ▶ Angioneurotic Edema.

Adverse effects DANAZOL

- ▶ Major adverse effects
 - ▶ Weight gain, edema,
 - ▶ Decreased breast size,
 - ▶ Acne and oily skin,
 - ▶ Increased hair growth, deepening of the voice,
 - ▶ Headache, hot flushes,
 - ▶ Changes in libido, and muscle cramps.
- ▶ Mild adverse effects are very common
- ▶ May cause adrenal suppression.
- ▶ Great caution in hepatic dysfunction, produce mild to moderate hepatocellular damage
- ▶ Contraindicated during pregnancy & breast-feeding, (urogenital abnormalities)

Thanks

The background features a complex, abstract design of overlapping, semi-transparent green polygons. The colors range from light, pale greens to deep, dark forest greens. The shapes are angular and layered, creating a sense of depth and movement. The design is primarily concentrated on the right side of the frame, with some elements extending towards the center and bottom.