

05-Drugs used to induce ovulation

Drug	MOA	USES	Method of Administration	ADRs
Clomiphene <div style="border: 1px solid black; padding: 5px; margin: 10px 0; text-align: center;"> 1-ANTIESTROGENS (SERMs) </div>	compete with the endogenous estrogen receptors in hypothalamus & ant.pituitary , thus removing the negative feedback effect of estrogens from the hypothalamus & Ant.pituitary leading to an increase in gonadotrophs' (FSH & LH) release . This will result in ovulation	<ul style="list-style-type: none"> ➤ Female infertility that is not due to ovarian or pituitary failure → Normogonadotrophic ➤ The success rate for ovulation → 80% & pregnancy → 40%. 	<ul style="list-style-type: none"> ✓ Clomiphene given → 50 mg/d for 5 days from 5th day of the cycle to the 10th day. ✓ If no response give 100 mg for 5 days again from 5th to 10th day (double the dose) ✓ The drug can be repeated not more than 6 cycles. 	1. Hot Flashes & breast tenderness (Anti-estrogenic effect) 2. Gastric upset (nausea and vomiting) 3. Visual disturbances (reversible) 4. ↑ Nervous tension & depression 5. Skin rashes 6. Fatigue 7. Weight gain 8. Hair loss (reversible) 9. Hyperstimulation of the ovaries & high incidence of multiple birth. (10%) Are due to the hormonal imbalance but not the drug
2. TAMOXIFEN Is similar & alternative to clomiphene, But differ in being Non Steroidal	Tamoxifen also has an antiestrogenic effects in the breast	Used in palliative treatment of hormone-dependent / estrogen receptor- positive advanced breast cancer		
2. GONADOTROPIN RELEASING HORMONE (GnRH) Analogue with agonist activity: Leuprolin, Goserelin	GnRH agonist & Analogue	-GnRH and agonists, given S.C. in a pulsatile(drip) to stimulate gonadotropin release (1 – 10 µg / 60 – 120 min) Start from day 2-3 of cycle up to day 10 . -Given continuously, when gonadal suppression is desirable e.g. precocious puberty and advanced breast cancer in women and prostatic cancer in men	Uses: Induction of ovulation in patients with hypothalamic amenorrhea (GnRH deficient)	-GIT disturbances, abdominal pain, nausea....etc -Headache -Hypoestrogenism on long term use → <ul style="list-style-type: none"> ◆ Hot flashes ◆ ↓ Libido ◆ Osteoporosis -Rarely ovarian hyperstimulation → (ovaries swell & enlarge)
3. GONADOTROPHINS (FSH & LH) extracted forms are available as; 1. Human Menopausal Gonadotrophin(hMG) → extracted from postmenopausal urine → contains LH & FSH → MENOTROPIN 2. Human Chorionic Gonadotrophin(hCG) extracted from urine of pregnant women → contains mainly LH → PREGNYL		<ul style="list-style-type: none"> ➤ Stimulation & induction of ovulation in infertility 2ndry to gonadotropic deficiency (pituitary insufficiency) Success rate for inducing ovulation is usually ≥ 75 %	hMG is given i.m every day starting at day 2-3 of cycle for 10 days (to induce the development of the follicle) followed by hCG on (10 th - 12 th day) for OVUM RETRIEVAL (Ovulation or rupture of the follicle).	FSH containing preparations (MENOTROPIN) ; Fever, Ovarian enlargement(hyper stimulation) , Multiple Pregnancy (approx. 20%) LH containing preparations; Headache & edema
4-Dopamine (2) Receptor Agonists (BROMOCREPTINE) Uses: Female infertility 2ndry to hyperprolactinaemia		D₂ R Agonists binds to dopamine receptors in the anterior pituitary gland & inhibits prolactin secretion.	<ul style="list-style-type: none"> ➤ GIT disturbances; nausea, vomiting, constipation ➤ Headache dizziness & orthostatic hypotension ➤ Dry mouth & nasal congestion ➤ Insomnia 	

- ✓ The main Cause of Failure to Ovulate (Female infertility) is hormonal imbalance e.g high estrogen, low gonadotrophs(FSH & LH) due to pituitary or hypothalamic disorders, or high prolactin levels usually due to prolactinoma.
- ✓ **1-Selective Estrogen Receptor Modulators [SERMs] E.g. Clomiphene & Tamoxifen**
- ✓ Clomiphene is a partial agonist at estrogen receptors.
- ✓ **Clomiphene:** compete with the **endogenous estrogen receptors** in hypothalamus & ant.pituitary ,thus removing the negative feedback effect of estrogens from the hypothalamus & Ant.pituitary leading to an increase in gonadotrophs' (FSH & LH) release.
- ✓ Clomiphene is used in **Female infertility that is not due to ovarian or pituitary failure** ➔ **Normogonadotrophic**
- ✓ **Clomiphene given** ➔ **50 mg/d for 5 days from 5th day of the cycle to the 10th day. (we repeat this method of dosing for 3 cycles)**
- ✓ **If no response for 3 cycles:** the dose is doubled in the next 3 cycles with the same method of administration.
- ✓ **The drug can be repeated not more than 6 cycles .**
- ✓ Its main ADRs : **Visual disturbances, hair loss which can be reversible** , .Hot Flushes & breast tenderness that are due to the Antiestrogenic effect of Clomiphene
- ✓ Tamoxifen Is similar & alternative to clomiphene ,But **differ in being Non Steroidal**
- ✓ Tamoxifen has an Antiestrogenic effects on the breast (**Used in cases of breast cancer**)
- ✓ **2-Leuprolin, Goserelin are synthetic analogues of GnRH with agonistic activity**
- ✓ given S.C. in a pulsatile(drip) to stimulate gonadotropin release
- ✓ **Start from day 2-3 of cycle up to day 10.**
- ✓ Given continuously, when **gonadal suppression is desirable** e.g. precocious puberty and advanced breast cancer in women and prostatic cancer in men
- ✓ **It's main ADR** is Hypoestrogenism on long term use ➔ **Hot flashes, decreased Libido ,Osteoporosis**
- ✓ **3-Gonadotrophs**
- ✓ **1. Human Menopausal Gonadotrophin(hMG)** ➔ extracted from postmenopausal urine ➔ **contains LH & FSH** ➔ **MENOTROPIN**
- ✓ **2. Human Chorionic Gonadotrophin(hCG)** extracted from urine of pregnant women ➔ **contains mainly LH** ➔ **PREGNYL**
- ✓ They are used in Stimulation & induction of ovulation in infertility **2ndry to gonadotropin deficiency (pituitary insufficiency)**
- ✓ **hMG (MENOTROPIN)** is given i.m every day starting at day 2-3 of cycle for 10 days **(to induce the development of the follicle)** followed by
- ✓ **hCG (PREGNYL)** is given on (10th - 12th day) for OVUM RETRIEVAL **(Ovulation or rupture of the follicle)** .
- ✓ **ADRs:**
- FSH containing preparations (MENOTROPIN);**
 - ✓ Fever
 - ✓ Ovarian enlargement (hyper stimulation)
 - ✓ Multiple Pregnancy (approx. 20%)
- LH containing preparations (MENOTROPIN or Pregnyl);** Headache & edema
 - ✓ **MENOTROPIN, Leuprolin, and Goserelin may lead to ovarian swelling or enlargement**
- ✓ **4-BROMOCREPTINE: D₂ R Agonists** binds to dopamine receptors in the anterior pituitary gland & inhibits prolactin secretion .
- ✓ **Used in Female infertility 2ndry to hyperprolactinaemia**
- ✓ **5-METFORMIN** is used in **IN POLYCYSTIC OVARIAN SYNDROME** to ↓ body weight & ↑ response to ovulation induction drugs