Lecture 3
Ovulation Induction

Pharmacology 434

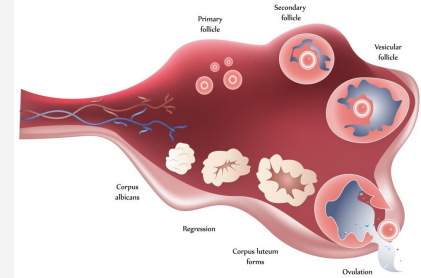## Objectives:

★ how ovulation occurs and specify its hormonal regulation

★ Classify ovulation inducing drugs in relevance to the existing deficits

★ Expand on the pharmacology of each group with respect to mechanism of action, protocol of administration, indication, efficacy rate and adverse effects.

- ▪ Additional Notes
- ▪ Important
- ▪ Explanation –Extra-

★ before starting, please check our Reproductive block correction

For any correction, suggestion or any useful information do not hesitate to contact us: Pharmacology434@gmail.com

Ovulation Induction

Ovulation induction is the stimulation of ovulation by medication. It is usually used in the sense of stimulation of the development of ovarian follicle to reverse anovulation or oligoovulation, but can also be used in the sense of triggering *oocyte release* from relatively mature ovarian follicles.

1-Antiestrogens	3-GnRH	3.Gonadotrophins
SERMs; **Clomiphene** **Tamoxifen**	**GnRH-agonists;** **Leuprolin** **Goserelin**	**HMGs;Menotropin** **HCGs; Pregnyl**

4-D$_2$ R agonists

Use it in <u>hyperprolactinemia</u>:
Bromocreptine

5. Rx POLYCYSTIC OVARIAN SYNDROME (PCOS):

★   Most common cause of infertility

★   Inulin resistance may play a role ???

WE GIVE **Metformin**

1-Antiestrogen (1-Clomiphene)

MOA	★ <u>**Compete with estrogen on the hypothalamus and anterior pituitary gland**</u>; ⬇ **negative feed back of endogenous estrogen→⬆ GnRH→⬆ production of FSH & LH → OVULATION**
Indication	➜ **Female infertility; due to <u>anovulation</u> or <u>oligoovulation</u> . not due to ovarian or pituitary failure→Normogonadotrophic** ➤ **The success rate for ovulation→ 80% & pregnancy→ 40% .**
Method of Administration	● **Clomifene 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** ● **Each dose can be repeated not more than 3 cycles .**
ADRs	**1-Hot Flushes & breast tenderness** **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.**

1-Antiestrogen (2-Tamoxifen)

- Similar & alternative to clomiphene but differ in being **Non Steroidal**.
- Tamoxifen is a good alternative to clomiphene in women with **PCOS** and **clomiphene-resistant cases**
- Used in **palliative** treatment of hormone-dependent / estrogen receptor- positive advanced breast cancer. **palliative:** relieving pain or alleviating a problem without dealing with the underlying cause.:

2-GNRH (GnRH-agonists; Leuprolin, Goserelin)

MOA	**Native GnRH i**s naturally produced by hypothalamus in a pulsatile manner. It is triggered when the negative feedback inhibition of ovarian hormones is lost by the end of the cycle. This activates FSH release from pituitary that stimulate growth and maturation of ova early during the follicular phase of the cycle. It also mediates estrogen induced LH surge that triggers ovulation. **GnRH-Agonists** bind to the receptors & mimic the native hormones provided it is given PULSATILE
Indication	- In OVULATION INDUCTION In patients with **hypothalamic amenorrhea** (GnRH deficient) - **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**
ADRs	- **GIT disturbances**, abdominal pain, nausea.. - Headache - **Hypoestrogenism** on long term use such as Hot flashes, decLibido, Osteoporosis, Vaginal bleeding - Rarely ovarian hyperstimulation (ovaries swell & enlarge)

3-Gonadotropins: (HMGs;Menotropin and HCGs; Pregnyl)

- Naturally produced by the pituitary gland
- For therapeutic use, extracted forms are available as; (CHEEP)

1. Human Menopausal Gonadotrophins (hMG) extracted from **postmenopausal urine** contains LH & FSH **MENOTROPIN**

2. Human Chorionic Gonadotrophins (hCG) extracted from **urine of pregnant women** contains mainly LH **PREGNYL**

- N.B. New available preparations by recombinant technology

MOA	- Preparations of FSH act on ovary directly, stimulating growth & maturation of Graafian Follicle(s). - Preparations of LH act just to induce ovulation Therefore, Given sequentia
Indication	stimulation and **induction of ovulation** in fertility **2ndry to gonadotropin deficiency**. (pituitary insufficiency)
Administration	**hMG is given i.m or subcut**. every day starting at **day 2-3 of cycle for 10 days** followed by **hCG on (10th - 12th day) for OVUM RETRIEVAL** within 36 hrs.
ADRs	**FSH containing preparations:** - Fever - Ovarian enlargement (hyperstimulation) - Multiple Pregnancy (approx. 20%) **LH containing preparations:** - Headache - edema

D2 Agonist (Bromocreptine)
Ergot derivative (not a hormone)

MOA	D2 R Agonists bind to dopamine receptors in anterior pituitary -ve Prolactin secretion.
Indication	Female infertility 2ndry to **hyperprolactinemia** (hypogonadotropic)
ADRs	**GIT disturbances**; nausea, vomiting, constipation - Headache , dizziness **orthostatic hypotension** **Dry mouth & nasal congestion** - Insomnia

MCQs

1- The most prominent action of bromocriptine is:
A) Dopamine D2 agonist
B) Dopamine D2 antagonist
C) GnRH agonist

2-The Drug pregnyl contains:
A) FSH
B) LH
C) FSH & LH

3-When should you retrieve the ovum after giving hCG:
A) Immediately
B) 36h
C) 60h

4-In which of the following formulas should you give GnRH- agonists as In case of infertility treatment :
A) Continuous
B) Sequentially
C) Pulsatile

5-which of the following true about method of administration of clomiphene ?
A) 50 mg/d for 5th day of the cycle to the 10th day
B) the drug can be repeated not more than 6 cycles
C) given on 10th to 12th day of the cycle
D) A & B

1-A
2-B
3-B
4-C
5-A

Good luck!

Done by Pharmacology team 434

Done by:
- ★ Hussain alkaff

Reviewed by:
- ★ Rawan Ghandour
- ★ Ahmed Alsaleh