

Physiological Effects

- Estrogens, Progesterone, Placental lactogen & GH → stimulate breast development & prepare it for lactation.
- Prolactin induces growth & differentiation of ductal & lobulo alveolar epithelium.
- Lactation does not occur in absence of prolactin.
- During pregnancy, high levels of estrogen & progesterone # milk secretion.

Dept. of Pharmacology, GMC Amritsar

.....Physiological Effects

- After birth, declining estrogen & progesterone levels permit prolactin to induce lactation.
- Prolactin receptors hypothalamus, liver, testes, ovaries, prostate & immune system.
- Hyperprolactinemia ↓↓ Hypothalamicpituitary-gonadal axis, cause of infertility in women.

Prolactin

- No therapeutic uses.
- Hypothalamic or Pituitary disease → Hyperprolactinemia.
- Prolactin-secreting pituitary adenomas.
- Micro adenomas (<1cm diameter)
- Macro adenomas (≥1cm diameter).

Dept. of Pharmacology, GMC Amritsar

Prolactin

- Structurally related to GH & Placental lactogen – Somatotropin family.
- Encoded on human prolactin gene on Chromosome 6.
- Polypeptide- three intramolecular disulfide bonds, a portion of secreted prolactin is glycosylated.
- Synthesized in lactotropes.

Secretion

- Synthesis & Secretion in fetal pituitary starts in 1st few weeks of gestation.
- Levels decline after birth.
- · Levels normal in normal males.
- ↑ Levels in normal cycling females.
- Marked
 ↑ In pregnancy, maximum at term & decline unless mother breast-feeds the infant.
- Nursing mothers secretion stimulated by suckling stimulus or breast manipulation.

Dept. of Pharmacology, GMC Amritsar

.....Prolactin

- Circulating prolactin ↑ 10-100 fold within 30 min. of manipulation.
- After several months of breast-feeding, prolactin levels decline to pre pregnancy levels.
- Synthesized by decidual cells near end of luteal phase & in early pregnancy.
- High levels of prolactin in amniotic fluid in 1st trimester.

.....Prolactin

- Sleep, stress, hypoglycemia, exercise & estrogen ↑ prolactin.
- Secretion is pulsatile.
- Dopamine released by Tuberoinfundibular neurons in hypothalamus, interacts with D₂ receptors on lactotropes to inhibit prolactin secretion.

Dept. of Pharmacology, GMC Amritsar

Prolactin Releasing Factors

- TRH
- VIP
- Prolactin-releasing peptide.
- Pituitary adenylyl cyclase-activating peptide (PACAP).

Molecular & Cellular basis of Action

- Effects result from specific interaction with prolactin receptors.
- Prolactin receptor encoded by a single gene on chromosome 5.
- Multiple receptor forms short, long, intermediate.
- Like GH, hormone-induced dimerization recruits & activates Jak kinases.
- Phosphorylation of Jak 2 Kinase induces Phosphorylation dimerization & nuclear translocation of transcription factor STATs.

Dept. of Pharmacology, GMC Amritsar

11

Hyperprolactinemia

• <u>Women</u>

- Galactorrhoea
- Amenorrhea
- Infertility.
- <u>Men</u>
 - Loss of libido
 - Impotence
 - Infertility

Treatment of Prolactinomas

- Transphenoidal surgery.
- Radiation.

 Dopamine receptor agonists – suppress prolactin production via D₂ Dopamine

receptors.

- -Bromocriptine $\rightarrow 1^{st}$ Choice
- -Pergolide
- -Cabergoline
- -Quinagolide.

Dept. of Pharmacology, GMC Amritsar 13

THANK YOU