NAME: BRAIDE DIVINE

MATRIC NUMBER: 17/MHS/006

COURSE: PHA 304

Pharmacology of pituitary gland

The pituitary gland comprises three different structures arising from two different embryological precursors. The anterior pituitary and the intermediate lobe are derived from the endoderm of the buccal cavity, while the posterior pituitary is derived from neural ectoderm. The anterior and posterior lobes receive independent neuronal input from the hypothalamus, with which they have an intimate functional relationship.

The anterior and posterior pituitary gland receives neuronal input from the hypothalamus. The anterior gland; it secrets Growth Hormones (GH), Prolactin (PRL), Adrenocortropic hormone (ACTH), thyroid stimulating hormone (TSH), gonadotropins-follicle stimulating hormone (FSH) and luteinzing hormone (LH). Posterior gland secrets oxytocin, antdiuretic hormone (ADH, Vasopressin)

ANTERIOR PITUITARY GLAND

It is also called Adenohypophysis or master endocrine gland. It releases various peptide hormones which act on extracellular receptors located on their target cells. The secretion is controlled by the hypothalamus through releasing and releasing-inhibitory hormones. Each anterior pituitary hormone is produced by a separate group of cells, depends on their staining characteristics (acidophilic or basophillic). Acidophilic; somatotropes and lactotropes basophilic; gonadotropes, thyrotropes and corticotropes-lipo-tropes.

GROWTH HORMONES

It is secreted by somatotroph cells which contains 191 amino acids, single chain peptide has molecular weight 2200. Secretion is regulated by GHRF and modulated by somatostatin insulin like growth factor-l has inhibitory effect on growth hormone

Physiological role: main effect of Growth hormone to promotes growth by inducing hyperplasia but growth hormone is not responsible for growth of brain and eyes. It promotes retention of nitrogen and other constituents; GH promotes utilization of fat and carbohydrates and GH mediates some anabolic effect on skeletal muscle and cartilage at epiphysis of long bone hence promotes bone growth.

Pathological role

Deficiency of GH (lack of GHRF): resulting in pituitary dwarfism.

GH used in the treatment of turner’s syndrome (chromosomal disorder), chronic renal insufficiency in children.

hGH is also used illegally by athletes to increase muscle mass.

Excessive production of GH

It results in gigantism in children and acromegaly in adults

In adults, benign pituitary tumour resulting excessive production of GH, causes enlargement of facial structures and of hands and feet.

For the treatment of pituitary dwarfism -0.03-0.07mg/kg 3 times a week up to the age of 20-25 years is given. Treatment of excessive GH secretion is with dopamine agonist bromocriptine and octreotide is advised. Pegvisomant, a modified hormone prepared by recombinant technology selective antagonist of growth.

ADVERSE EFFECT

* Allergic reaction
* Pain at injection site
* Hand stiffness
* Glucose intolerance
* Hypothyroidism
* Salt and retention

GROWTH HORMONE INHIBITORS: somatostain, octreotide pegvisomant

PROLACTIN

It is a 199 amino acid, single chain peptide having MW2300, similar to GH. The hormone is responsible for secretion of milk from crop gland of pigeon. Prolactin secreted from cells action of prolactin increased by influence of oestrogen.

SECRETION AND SECRETION: Release takes place after stimulation like suckling, sound of hungry pups and its inhibited by dopamine

Physiological role: prolactin receptors are not only found in the mammary gland but are widely distributed throughout the body, including the brain, ovary, heart and lungs. Along with estrogen, progesterone and several other hormones, causes growth and development of breast during pregnancy. It causes proliferation of ductal as well as acinar cells in the breast and induces synthesis of milk proteins and lactose

PATHOLOGICAL ROLES:

* Hyper prolactinaemia is responsible for the galactorrhea amenorrhea infertility syndrome.
* Disorders of hypothalamus decreases inhibitory control over pituitary
* Antidopaminergic and DA depleting drugs

PROLACTIN INHIBITORS

Bromocriptine: it is a synthetic ergot derivative 2-bromo-aergocryptine is a potent dopamine agonist weaken an adrenergic blocker.

Cabergoline: it is a newer D2 agonist more potent, mor D2 selective and longer acting than bromocriptine less side effect than bromocriptine

MECHANISM OF ACTION

Activating dopaminergic receptors and decreases prolactin release. I normal individuals increase GH release but decreases the same from pituitary tumours that causes acromegaly. It has levodopa like action in CNS- antiparkinsonian and behavioral effects produces nausea and vomiting by stimulating dopaminergic receptors. Hypotension due to central suppression of postural refluxes and weak adrenergic blockers. Decrease in GI motility.

Uses: it is used in the treatment of condition like hyperprolactinemia; which causes infertility in women and impotence and sterility in men. Acromegaly and parkinsonism

ADVERSE EFFECT: Nausea, vomiting, constipation, nasal blockage, postural hypotension in patients taking antihypertensives. Other effects can be mental confusion, abnormal movement, psychosis and behavioral alteration.

ADRENOCORTICOTROPHIC HORMONCE (ACTH)

ACTH is the anterior pituitary secretion that controls the synthesis and release of the glucocorticoids of the adrenal cortex. It is a 39- residue peptide derived from the precursor pro opiomelanocortin. The principle effects are increased production and release of cortisol by the cortex of the adrenal gland.

PYSIOLOGICAL ROLE

* ACTH plays a role in glucose metabolism and immune function.
* The circadium rhythm influences cortisol secretion. The highest levels of cortisol are seen in the early morning and the lowest level are in the evening.
* Promotes steroidogenesis in adrenal cortex by stimulating CAMP supply formation in the cortical cells.

PATHOLOGICAL ROLE

Hyperfunctioning or hyperfunctioning of pituitary gland resulting in pathological consequences

Addison disease

Cushing’s disease

Uses

* ACTH is used for the diagnosis of disorders of pituitary adrenal axis
* Direct assay of plasma ACTH level is now preferred
* For therapeutic purpose

THYROID STIMULATING HORMONE (TSH)

It is a 210 amino acid, two chain glycoprotein, MW 30000

PYSIOLOGIAL FUNCTION

TSH stimulates thyroid to synthesize and secretes thyroxine(T) and triiodothyronine

Induces hyperplasia and hypertrophy of thyroid follicles and increases blood supply to the gland

Promotes processes helpful for synthesis of thyroid hormones

PATHOLOGICAL ROLE: Hypo-or hyperthyroidism are due to inappropriate TSH secretion

Uses: Thyrotropin has no therapeutic use only used for diagnosis purpose of myxedema

GONADOTROPIN

Follicle stimulating hormone (FSH) and luteinizing hormone (LH): both are glycoprotein containing 23-28% sugar of two peptide chains having total of 207 amino acid residues. Having molecular weight FSH-32,000 while LH-30,000.

PYSIOLOGICAL ROLE: both hormones promote gametogenesis and secretion of gonadal hormones

FSH: in female it induces follicular grow causes development of ovum and secretion of estrogen. In male supports spermatogenesis and has trophic influence o seminiferous tubules.

LH: In female induces preovulatory swelling of the ripe graafian follicle and triggers ovulation. Also responsible for progesterone secretion. In male stimulates testosterone secretion

PATHOLOGICAL ROLE: Hypo secretion of gonadotrophins resulting delayed puberty precocious puberty in girls and boys. Also, amenorrhea and sterility in women, impotence and sterility in men. Excessive production of gonadotrophins causes polycystic ovaries.

Uses: it is used in the treatment of cryptorchism, amenorrhea and infertility and hypogonadotropic hypogonadism in males and to aid in vitro fertilization menotropins.

ADVERSE EFFECTS

* Ovarian hyperstimulation
* Allergic reaction
* Hormone dependent malignancies
* Precocious puberty
* Edema, headaches and mood changes

GONADOTROPIN RELEASING HORMONE (GnRH)

GnRH injected induces prompt release of LH and FSH but causes rapid enzymatic degradation so shorter plasma. It is used for testing pituitary gonadal axis in male as well as female hypogonadism. Example includes; Nafarelin Goserelin, Triptorelin and Leuprolide

Advantages of Synthetic Analogues are:

* 15-150 times more potent than natural GnRH
* High affinity for GnRH receptor
* Resistance of enzymatic hydrolysis so longer acting having half life -6 hours
* Used as nasal spray or injected subcutaneously

GnRH antagonist

* Substituted GnRH analogues acts as GnRH receptor antagonist. They inhibit Gn secretion without causing initial stimulation
* The early GnRH antagonist causes histamine release.

Advantages Over Long-Lasting GnRH Agonist Include

* They produce quick Gn suppression by competitive antagonism
* They carry a lower risk of ovarian hyperstimulation syndrome
* They achieve more complete suppression of endogenous Gn secretion
* However,pregnancy rates are similar or may even be lower