

Pharmacology 3rd year college of dentist medicine

Adrenocorticosteroid hormones :

CORTICOSTEROIDS

Betamethasone CELESTONE, DIPROLENE, LUXIQ

Cortisone CORTISONE ACETATE

Dexamethasone DECADRON

Fludrocortisone FLORINEF

Hydrocortisone

Methylprednisolone MEDROL

Prednisolone ORAPRED, PEDIAPRED

Prednisone

Triamcinolone KENALOG, NASACORT, ARISTOSPAN

INHIBITORS OF ADRENOCORTICOID BIOSYNTHESIS OR FUNCTION

Eplerenone INSPRA

Ketoconazole NIZORAL

Spironolactone ALDACTONE

✚ The adrenal gland consists of the cortex and the medulla.

✚ The medulla secretes epinephrine, whereas the cortex, synthesizes and secretes two major classes of steroid hormones-the adrenocorticosteroids (glucocorticoids and mineralocorticoids; and the adrenal androgens).

✚ The adrenal cortex is divided into three zones that synthesize various steroids from cholesterol and then secrete them .

✚ The outer zona glomerulosa produces mineralocorticoids (for example, aldosterone), which are responsible for regulating salt and water metabolism.

✚ The middle zona fasciculata synthesizes glucocorticoids (for example, cortisol), which are involved with normal metabolism and resistance to stress.

✚ The inner zona reticularis secretes adrenal androgens (for example, dehydroepiandrosterone).

✚ Secretion by the two inner zones and, to some extent, the outer zone is controlled by pituitary corticotropin adrenocorticotrophic hormone [ACTH; also called corticotropin], which is released in response to the hypothalamic corticotropin-releasing hormone (CRH; also called corticotropin-releasing factor).

Adrenocorticosteroids:-

✚ The adrenocorticoids bind to specific intracellular cytoplasmic receptors in target tissues.

✚ The glucocorticoid receptor is widely distributed throughout the body, whereas the mineralocorticoid receptor is confined mainly to excretory organs, such as the kidney, colon, and salivary and sweat glands.

Glucocorticoids:-

- ✚ Cortisol is the principal human glucocorticoid.
- ✚ Normally, its production is diurnal, with a peak early in the morning followed by a decline and then a secondary, smaller peak in the late afternoon.
- ✚ Factors such as stress and levels of the circulating steroid influence secretion.

Promote normal intermediary metabolism:

- ✚ Glucocorticoids favor gluconeogenesis.
- ✚ They stimulate protein catabolism (except in the liver) and lipolysis, thereby providing the building blocks and energy that are needed for glucose synthesis.
- ✚ [Note: Glucocorticoid insufficiency may result in hypoglycemia (for example, during stressful periods or fasting).]

Increase resistance to stress:

- ✚ By raising plasma glucose levels, glucocorticoids provide the body with the energy it requires to combat stress caused, for example, by trauma, fright, infection, bleeding, or debilitating disease.

Anti-inflammatory action:

- ✚ The most important therapeutic property of the glucocorticoids is their ability to dramatically reduce the inflammatory response and to suppress immunity.
- ✚ The exact mechanism is complex and incompletely understood.

Effects on other systems:

- ✚ Adequate cortisol levels are essential for normal glomerular filtration.
- ✚ High doses of glucocorticoids stimulate gastric acid and pepsin production and may exacerbate ulcers.
- ✚ Chronic glucocorticoid therapy can cause severe bone loss.

Mineralocorticoids:-

- ✚ Mineralocorticoids help to control the body's water volume and concentration of electrolytes, especially sodium and potassium.
- ✚ Aldosterone acts on kidney tubules and collecting ducts, causing a reabsorption of sodium, bicarbonate, and water.

Therapeutic uses of the adrenal corticosteroids:-

- ✚ Several semisynthetic derivatives of the glucocorticoids have been developed that vary in their anti-inflammatory potency, degree to which they cause sodium retention, and duration of action.

***Replacement therapy for primary adrenocortical insufficiency (Addison's disease):**

- ✚ This disease is caused by adrenal cortex dysfunction (as diagnosed by the lack of patient response to corticotropin administration).
- ✚ **Hydrocortisone** , which is identical to natural cortisol, is given to correct the deficiency.

Relief of inflammatory symptoms:

- ✚ Glucocorticoids dramatically reduce the manifestations of inflammations (for example, rheumatoid and osteoarthritic inflammations, as well as inflammatory conditions of the skin), including the redness, swelling, heat, and tenderness that are commonly present at the inflammatory site.
- ✚ The decreased production of prostaglandins and leukotrienes is believed to be central to the anti-inflammatory action.
- ✚ Glucocorticoids also influence the inflammatory response by their ability to reduce the amount of histamine that is released from basophils and mast cells, thus diminishing the activation of the kinin system.

Treatment of allergies:

- ✚ Glucocorticoids are beneficial in the treatment of the symptoms of bronchial asthma, allergic rhinitis, and drug, serum, and transfusion allergic reactions.
- ✚ These drugs are not, however, curative. [Note: **Beclomethasone dipropionate** , **triamcinolone** are applied topically to the respiratory tract through inhalation from a metered-dose dispenser.
- ✚ This minimizes systemic effects and allows the patient to significantly reduce or eliminate the use of oral steroids.]

Acceleration of lung maturation:

- ✚ Respiratory distress syndrome is a problem in premature infants. Fetal cortisol is a regulator of lung maturation.
- ✚ Consequently, a dose of beclomethasone is administered intramuscularly to the mother 48 hours prior to birth, followed by a second dose 24 hours before delivery.

Pharmacokinetics:-

Absorption and fate:

- ✚ Those that are administered orally are readily absorbed from the gastrointestinal tract.
- ✚ Selected compounds can also be administered intravenously, intramuscularly, intra-articularly (for example, into arthritic joints), topically, or as an aerosol for inhalation.

Dosage: In determining the dosage of adrenocortical steroids, many factors need to be considered, including

- 1-glucocorticoid versus mineralocorticoid activity,
- 2- duration of action,
- 3- type of preparation,
- 4-time of day when the steroid is administered.

Adverse effects:-

The common side effects of long-term corticosteroid therapy :-

- ✚ Osteoporosis is the most common adverse effect due to the ability of glucocorticoids to suppress intestinal Ca^{2+} absorption, inhibit bone formation.
- ✚ increased body hair growth, acne, insomnia, and increased appetite are observed when excess corticosteroids are present.
- ✚ Hyperglycemia may develop and lead to diabetes mellitus.



