Adrenal medulla

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Learning outcomes:

- **At the end of the lecture, you will be able to:**

1. Describes the innervation of adrenal medulla
2. Describes the synthesis and metabolism of catecholamines
3. Explain the control of secretion of catecholamines
4. Explain the physiological actions of catecholamines
5. Explain the phyeochromocytoma and hyposecretion of adrenal medulla

Adrenal Medulla

- The adrenal medulla represents an enlarged and specialized **sympathetic ganglion**.

❑ Innervation of adrenal medulla:

- It is innervated by long **sympathetic preganglionic cholinergic neurons** that form synaptic connections with the chromaffin cells.

❑Histology of adrenal medulla:

Adrenal medulla consist of **chromaffin cells** which contain adrenaline and noradrenaline (stored in granules).

- **Adrenaline:** 80%.
- **Noradrenaline:** 20%.

❑Synthesis of catecholamines:

- Catecholamines are synthesized from **L-tyrosine** through a series of enzymatic reactions

- In plasma, about **95%** of the **dopamine** & **70%** of the **norepinephrine and epinephrine** are **conjugated to sulfate**.

- Sulphate conjugates are **inactive**, and their function is **unsettled**.

- The plasma **half-life** of epinephrine and norepinephrine is **2-3 minutes**.

❑Metabolism of catecholamines:

A) Neuronal uptake:

- Sympathetic nerve endings take up amines actively from the circulation➔

* **nonenzymatic inactivation** by intraneuronal storage

* **enzymatic inactivation** by monoamine oxidase (MAO) enzyme.

B) Extra neuronal uptake: by different tissues (as liver, kidney, lung, gut) where they are destroyed by **COMT (catechol-O- methyl transferase)**.

C) Inactivation: Circulating catecholamines are metabolized mainly in the **liver** and **kidney**.

- **N.B: vanillyl mandelic acid** (VMA) is the major metabolic waste product for catecholamines found in urine

❑Control of catecholamine secretion:

- by: **adrenaline secreting center (ASC)** in the medulla oblongata.
- **A.S.C** → impulses descend through **reticulospinal tract (RST)** → LHCs in T_5-T_9 → sympathetic **preganglionic** fibers through **greater splanchnic nerve** → adrenal medulla.
- **Catecholamine secretion**:
  - **Low** → in basal states.
  - **↓ further** → at sleep.

➢ ASC is stimulated by:

1) ***Hypothalamus:*** **e.g.** pain, emotions, cold and hypoglycemia.

2) ***Arterial baroreceptors in carotid sinus & Ao arch:*** ↓ ABP

e.g haemorrhage ➔ release of ASC from baroreceptor inhibitory impulses ➔ ↑ catecholamine secretion ➔ ↑ ABP.

3)Peripheral chemoreceptors in carotid & aortic bodies as during hypoxia.

4)Volume receptors in right and left atria and in pulmonary vessels: In hypovolemia, ASC is released from inhibition of these receptors ➔ ↑ catecholamine secretion.

- **N.B:** Catecholamine synthesis is dependent on **cortisol;** thus, the functional integrity of adrenal medulla indirectly depends on a functional hypothalamic – hypophysial – adrenocortical axis.

❑Physiological actions of catecholamines:

1-On heart: ↑ all cardiac properties:

- ↑ heart rate.
- ↑ force of myocardial contraction.
- ↑ cardiac metabolism and O_2 consumption.
- Coronary VD due to ↑ metabolites.

2-Vascular effect:

VC in all organs except blood vessels of skeletal muscle and liver ➔ VD via β_2 receptors.

3-Respiratory effects:

- **Initially** ➔ **adrenaline apnea** occur **because:** adrenaline ➔ ↑ ABP ➔ stimulate arterial baroreceptors ➔ inhibit resp. center ➔ apnea.
- **Then** ➔ adrenaline ➔ stimulate resp. center ➔ ↑ **rate & depth of resp**.

4-Renal effects:

- ***VC of renal arterioles*** ➔ ↓ GFR.
- ***Stimulate Na^+ reabsorption***.
- ***Stimulate renin secretion*** from juxtaglomerular cells (β_1) ➔ stimulate renin – angiotensin – aldosterone system ➔ ↑ distal Na^+ reabsorption.

5-Effect on skeletal muscles:

↑ strength of skeletal muscle contraction & delay fatigue (**Orbelli phenomenon**) **due to:**

- VD and increased BF to muscle.
- Stimulate metabolism and energy production.

6-Effects on skin:

- Cutaneous VC ➔ ***pallor***.
- Contraction of pilomotor muscle ➔ ***erection of hair***.

7-Effects on smooth muscles:

- Relaxation of smooth muscles of bronchi & bronchioles (β_2) ➔ **bronchodilatation**.
- Relaxation of walls **(β_2)** and contraction of sphincters **(α)** in the **GIT**.
- Relaxation of wall of **urinary bladder (β_2) & contraction of internal urethral sphincter (α)**.
- **Dilatation of pupil** due to contraction of dilator pupillae muscle **(α)**.

8-Nervous effects:

- ↑ ***excitability of CNS***.
- ***Shortens the response time***.
- ↑ ***alertness, awareness & mental activity*** by stimulating reticular activating system (RAS).

9-Effect on blood clotting: Shortens clotting time due to:

- ↑ production of ***fibrinogen and prothrombin***.
- ***Activate clotting factor V***.

10-Effect on pancreatic islets: ↑ **secretion of insulin and glucagon** (via **β** adrenergic mechanism) and **inhibit their secretion** (vie **α** adrenergic mechanism).

11-Effect on fat metabolism:

- Stimulate **lipolysis** by activating **triglyceride lipase**.
- **Mobilization of FFA** from adipose tissue → **ketogenesis** in liver.
- **Cardiac muscle** and **renal cortex** use **FFA** in preference to glucose whereas **resting skeletal muscles** use **FFA** as major source of energy.

12-Effect on carbohydrate metabolism: ***hyperglycemia*** due to:

- Stimulation of ***glycogenolysis*** in liver and skeletal muscles.
- Stimulate ***glucagon*** secretion which ***amplify its hyperglycemic effect***.
- Stimulate ACTH secretion ➔ stimulate cortisol secretion ➔ ***gluconeogenesis.***
- ***Inhibit glucose uptake*** by:
  - ***Blockade of insulin secretion***.
  - ***Inhibition of glucose transporter*** proteins in cell membranes (skeletal and cardiac muscles and adipocytes).

❑Pheochromocytoma:

➢***Cause:*** Tumour of chromaffin cells.

➢***Manifestations:***

- Headache. - Sweating. - Hypertension
- Pale skin due to cutaneous VC .
- Palpitation due to tachycardia.
- Chest pain due to increased work of heart.
- Hyperglycemia and glucosuria.
- Blurred vision due to papillary dilatation.

➢ ***Diagnosis of pheochromocytoma:***

- By measuring **urinary catecholamines**.
- Normally ➔ **10 – 100 µg/day**.
- Pheochromocytoma ➔ ↑ to **300 µg/day**.

❑Hyposecretion of adrenal medulla hormones:

- **Occur during** T.B, malignant destruction of adrenal gland, adrenalectomy.
- **No manifestations**.
- **Catecholamine production from sympathetic nerves is satisfactory** as **adrenal medulla is not essential for life**.
- Adrenalectomized patient **do not require epinephrine replacement therapy**.

References

1. Costanzo, Linda S. "BRS Physiology (Board Review Series)." (2018).

2. Ganong, William F. "Review of medical physiology." (2020).

3. Hall, John E and Hall, Micheal E. “Guyton and Hall Textbook of medical physiology." (2021).