Physio CVS lec 9

Hormonal control of calcium blood levels :

➢ Functions of calcium :

1-Mineralization of bone and teeth .

2-activation of blood clotting factors .

3-Release of neurotransmitters .

4-Neoromuscular excitability .

5-Muscle contraction .

6-Acts as second messenger for hormone actions .

➢ Calcium distribution in the body :

1)Plasma :

*The concentration of calcium in plasma is about 10mg/dl its in three forms :

-Ionized : free calcium (Ca+2) 47%

-Complexed with phosphate : 6-8%

-Bound to plasma proteins (mainly albumin) : 47%

*The complexed and ionized are **diffusible** , while the bound form is **non-diffusible** (عشان كدا لو مستواه قل مش بياثر جامد زي التاني لانه مش دايب)

2)Bone :

*More than 99% of total body calcium is present in bone & teeth .

*Bone is formed of :

-*Protein* : mainly Collagen **type I**

-*Calcium & phosphate* as **Hydroxy apatite** crystals .

-*Bone cells* .

*Types of bone cells :

1- **osteoblast (bone forming cells)** that promote deposition of calcium , so their stimulation leads to a **decrease** in plasma calcium level .

2-**osteoclasts (bone eroding or resorption cells)** they erode previously formed bone and dissolve calcium crystals resulting in diffusion of calcium to blood so **increasing** its plasma level .

➢ Calcium Homeostasis :

***Three** hormones control Ca++ level in plasma :

(فيه تلات هرمونات بتتحكم في مستوى الكالسيوم في الجسم عن طريق انها بتاثر ع الأعضاء الي بتفرز الكالسيوم او بتنقله من مكان لمكان و هم العضم و الأمعاء و الكلية)

1)Parathyroid hormone (PTH) :

- Its secreted from **4 parathyroid glands** embedded in the thyroid gland . (بيتم افرازه من 4 غدد موجودين ع ضهر الغدة الدرقية)
  (في حالة إزالة ال thyroid ممكن تتشال معاها غدة او اكتر من الي بيفرزوا الهرمون و بيدخل المريض ف حالة hypoparathyroidism و دي بتسبب tetany)
- It **elevates** plasma calcium level to reach its normal level .
- Its secretion is related to plasma Ca++ level , a *drop in Ca++ level stimulates PTH secretion and vice versa .*
- **PTH increases plasma Ca++ level by :**
  1)Stimulation of osteoclasts . (so patients with hyperparathyroidism have weak bones)

2)increasing calcium reabsorption by renal tubules .
3)increasing calcium absorption through the intestine by stimulating the activation of Vitamin D .

2) Active Vitamin D (1,25 dihydroxycholecalciferol) :

- **Synthesis of Vitamin D :**
  -Skin cells when exposed to sun , starts to change cholesterol into cholecalciferol (inactive vitamin D) , which become hydroxylated and changed into 25- cholecalciferol .
  -By **1-alpha hydroxylase** enzyme (from kidney) hydroxyl group added to the compound which become *1,25-dihydroxycholecalciferol (active vitamin D) .*
- Active Vitamin D **increases t**he availability of calcium and phosphate for *bone mineralization and remodeling* , **through** :
  1)increasing calcium & phosphate absorption by the intestine .
  2)increasing calcium & phosphate reabsorption by the renal tubules .
  3) it both deposits and mobilizes calcium and phosphate in bone leading to its remodeling .

3)Calcitonin :

- A hormone secreted from the **parafollicular cells of the thyroid gland.**
- It's a plasma calcium **lowering** hormone *, its secretion is increased by a rise in plasma calcium level .*
- It decreases plasma calcium level **through** :
  1) Stimulation of osteoblasts .
  2) Inhibits activity of osteoclasts .
  3) Decreases calcium and phosphate reabsorption by the renal tubules , and increases Ca++ loss in urine .

➢ Tetany :

*it's a condition of **increased neuromuscular excitability** caused by a **decrease of plasma ionized (free)** calcium level which increases sodium permeability .

*The muscle show **spasmodic contractions** .

*it may be caused by :

1)Hypoparathyroidism .

2)Vitamin D deficiency .

3) Alkalosis (increased ph of blood) : decreases Ca++ solubility leading to a decrease in ionized Ca++ .

4)Renal disease : decreased calcium reabsorption .

*فكرة حدوث المرض :

ان الكالسيوم بيشتغل زي حارس على Na+ channels بينظم دخولها و بالتالي اما يقل مستوى الكالسيوم في الدم هيزيد دخول الصوديوم جوه الخلايا و بتالي هيزيد ال depolarization و هتزيد ال excitability بتاعة العضلة ف هتفضل منقبضة و يحصلها شلل .

The suprarenal gland (Adrenal gland) :

- The suprarenal gland consists of two distinct parts :

1)The central part (adrenal medulla) : which is considered a sympathetic ganglion supplied by preganglionic neurons .

-On activation it secretes **adrenaline and noradrenaline** (catecholamine)

-Secretion of catecholamine from suprarenal medulla cause *diffusion of sympathetic action (sympathetic over activity all over the body)*

2) The outer part (adrenal cortex) : is further divided into 3 zones :

-**The outer zone (zona glomeruloza**) : secrets mineralocorticoids (aldosterone) .

-the middle zone (zona fasciculate) : secretes glucocorticoids (mainly cortisol) .

-The inner zone (zona reticularis) : secretes androgens and estrogens .

N.B: androgen hormone is present in males and females but with less amount in females , so when it increases than normal level it causes hirsutism (appearance of hair in an abnormal sites in females)

1. Glucocorticoids :

- The **hypothalamus** secretes **corticotrophin releasing factor (CRF)** which stimulates the secretion of **adenocorticotrophic** hormone (ACTH) from the anterior **pituitary** .
- **ACTH** in turn stimulates the **adrenal cortex to secrete cortisol** .
- Cortisol exerts **negative feedback** inhibition on both CRF & ACTH .
- CRF secretion shows a diurnal pattern (نمط نهاري) it reaches a peak in the early morning and is lowest at night (circadian rhythm) , this rhythm is related to the sleeping hours and is reversed if the sleeping hours is reversed .

(افراز هرمون CRF ليه نمط نهاري يعني بيزيد الصبح و بيقل بالليل لكن هو مرتبط بعدد ساعات نوم الشخص يعني لو الشخص بينام الصبح و يصحى بالليل ف معدل افراز الهرمون بيتعكس)

➢ Actions of glucocorticoids (cortisol) :

1)On metabolism :

-Carbohydrate : it **increases gluconeogenesis** especially from amino acids , so it **increases blood glucose level** .

*Gluconeogenesis : is synthesis of glucose from non carbohydrates materials .

-Proteins : it **increases protein catabolism** and inhibits protein synthesis.

-Lipids : it increases lipolysis and fat mobilization .

(عشان كدا الناس الي بتاخد كورتيزون بيكون عندها ترسيب دهون ف أماكن كتير و مش متساوي)

2)Anti inflammatory & anti allergic action :

-stabilizes lysosomes .

-decrease capillary permeability .

-inhibits release of histamine .

-inhibits the immune response by inhibiting B & T lymphocyte production , so the patient become more available for infections , but it helps patients who transplant organs to accept the new organ .

3) Permissive effect :

-cortisol is important for **catecholamines** to produce their vasoconstrictor effect .

2. Mineralocorticoids :

- **Control of secretion :**

1)Renin angiotensin system :

-Renin (secreted from the **juxtaglomerular apparatus** in the kidney in response to decreased renal blood flow) acts on a plasma globulin (angiotensinogen) to produce **angiotensin I** .

-**Angiotensin I** is further converted in the lung to **angiotensin II** by **angiotensin converting enzyme (ACE)** .

-**Importance of angiotensin II** :

*vasoconstrictor . *salt retention .

*stimulate the **formation of aldosterone** .

2)Hyperkalemia (increased K+ blood levels): increases aldosterone secretion .

(من وظائف الaldosterone انه يتخلص من البوتاسيوم الزيادة و ينزله ف البول و بالتالي اما تزيد نسبة البوتاسيوم في الدم هيزيد افراز الaldosterone)

- **Actions of aldosterone :**

-Aldosterone acts on the **distal and collecting renal tubules** to **increase sodium & water reabsorption and K+ secretion .**

-Through sodium and water reabsorption aldosterone helps in keeping a **normal extracellular fluid volume** and **increase blood pressure** , so its considered as a compensatory reaction during shock .

- **Disorders of suprarenal hormone secretion :**

1)Cushing syndrome :

-its due to excessive secretion of **glucocorticoids** or more commonly due to pharmacologic use of cortisol .

-its characterized by :

1.Accumulation of fats in face and upper trunk (moon face & buffalo hump)

2.increased protein catabolism leading to :

*thin and fragile skin .

*delayed wound healing .

*muscle wasting & weakness .

*weakness of bones and osteoporosis .

3.Hyperglycemia (increased gluconeogenesis) .

4.increased anti-inflammatory effect leading to increased availability to infection .

5.through the mineralocorticoid effect it causes sodium & water retention leading to hypertension .

6.through the and androgenic effect it causes hirsutism (increased body hear in females) .

2) Hyperaldosteronism (Conn's disease) :

-Hypertension (الي حصل هنا اننا بنسحب صوديوم و مياه كتير و نفقد بوتاسيوم كتير)

-Hypokalemia .

3)Addison's disease:

-its due to **adrenal insufficiency** with **deficiency of both mineralocorticoids and glucocorticoids** resulting in :

*Sodium loss .

*low blood pressure (hypotension) : due to low aldosterone .

*Hypoglycemia .

Endocrine functions of the pancreas :

➢ Glucagon :

-secreted by **alpha cells** of islets of Langerhans .

-the main stimulus for glucagon secretion is a **drop of blood glucose level below normal . (hypoglycemia) .**

- **Actions of glucagon :**

1.On carbohydrate metabolism :

-it increases blood glucose levels through increasing **glycogenolysis** .

*Glycogenolysis : is breaking down of glycogen to increase glucose level.

2.On lipid metabolism : it promotes lipolysis .

3.On protein metabolism : it's a **catabolic** hormone leading to protein breakdown .

➢ Insulin :

-Secreted by **Beta** cells of islets of Langerhans .

- **Regulation of Insulin secretion :**

-The primary stimulus for insulin secretion is a **rise in blood glucose level (hyperglycemia) .**

- **Actions of insulin :**

1.On Carbohydrate metabolism :

-Insulin **increases glucose uptake into liver, skeletal and cardiac muscles and adipose tissue** by increasing the number of **glucose transporters** in their cell membranes which **decreasing its concentration in blood** . *(in insulin dependent cells)*

(الجلوكوز مش بيقدر يدخل الخلية الا عن طريق ناقل خاص بيه بيدخله جوه , بس الناقل دا بيكون متخزن جوه السيتوبلازم مش موجود على السطح , فلازم الانسولين يجي يمسك في مستقبلات على سطح الخلية عشان الناقل بتاع الجلوكوز يتحرك لسطح الخلية و يقدر يدخل الجلوكوز جوه و يقلل تركيزه في الدم)

-Insulin also **promotes glycogenesis** (synthesis of glycogen) in muscle and liver cells .

-In *insulin in-dependent cells* , insulin **doesn't increase** glucose uptake because **their glucose transporters are already present at the cell membrane** , as :

*RBC's . *brain cells .

*intestinal cells . *renal tubular cells .

2.On protein metabolism :

-Insulin is an **anabolic** hormone , it **increases** transport of amino acids into cells and increases protein synthesis .

3.On lipid metabolism :

-Insulin is the **only lipogenic** hormone (it promotes fat synthesis)

4. On growth :

-Due to its anabolic action insulin is essential for normal growth .

➢ Diabetes Mellitus (poly urea) :

-A disease caused by a **deficiency in insulin** secretion .

-**Type I (insulin dependent diabetes mellitus):** is mainly due to **destruction of the beta cells by autoimmune disease** with a resulting lack of insulin .

*its usually develops early in life **(in children)** .

*patients should take insulin injections throughout life .

-Type II (non-insulin dependent diabetes mellitus) : it's the common form of diabetes and is characterized by **impaired insulin secretion plus decreased insulin sensitivity (insulin resistance)** .

*it usually occurs after the age of 40 .

*__obesity__ is a major cause of insulin resistance and main cause of type II diabetes .

*patients are treated by __oral hypoglycemic drugs__ until their pancreas get exhausted then they take __insulin injections__ .

(في النوع التاني من مرض السكري المريض عنده حساسية قليلة للانسولين يعني الخلايا مش بتحس بيه ع الرغم من وجوده ف هنا بيبدأ المريض ياخد ادوية تزود انتاج البنكرياس للانسولين عشان يزيد إحساس الخلايا بيه لحد اما يحصل اجهاد للبنكرياس ف يبدأ المريض ياخد حقن انسولين)

-Manifestation : (علامات الإصابة بالمرض)

1.Hyperglycemia : a high blood glucose level .

2.Glucosuria : the appearance of glucose in urine .

*when the blood glucose level exceeds 180mg\dl (renal threshold) it starts to appear in urine .

3.polyuria : producing a large volume of urine .

*increased water excretion due to increased urinary osmotic pressure caused by increased glucose in renal tubules .

4.polydipsia : drinking a large volume of water .

*polyuria causes dehydration , resulting in an increased thirst sensation and drinking a large water volume .

5.Hyperphagia : increased appetite and food intake .

*decreased glucose utilization **inhibits the satiety center** (مركز الشبع) *“which is the only insulin dependent cells in the brain “* causing an increased activity of the feeding center .

(مركز الشبع هو الجزء الوحيد في المخ الي بيعتمد ع الانسولين عشان يستخدم الجلوكوز , ف اما يقل الانسولين هيحصل خمول ف مركز الشبع و بالتالي المريض هيفضل ياكل كتير)

*in spite of increased food intake there is loss of weight due to increased lipolysis . (more fat is used as a source of energy)

6.diabetic coma : which may result due to the acidosis resulting from increased fat breakdown with increased ketone body production (ketoacidosis) , this type of coma is associated with **increased blood glucose levels .(hyperglycemic coma)**

***hypoglycemic coma** may also occur in diabetics treated with insulin due to **insulin overdose** .

➢ Glucose Homeostasis :

-blood glucose should be maintained within a certain range .

- **Mechanisms controlling blood glucose level :**

1)Glucostatic role of the liver :

-After meals the absorbed glucose passes to different body organs to be utilized , the unused glucose is either **transformed to glycogen in the liver or converted into lipids in adipose tissues .**

-Between meals , as the blood glucose level decreases the liver glycogen is changed back into glucose and released in the blood to prevent hypoglycemia .

-So the liver acts as a blood glucose buffer preventing both hyper and hypoglycemia .

2)Hormonal control :

-Hormones decreasing blood glucose level ***: INSULIN***

-Hormones increasing blood glucose level **: anti-insulin effect , growth hormone , adrenaline , glucocorticoids and glucagon .**