DPT 4th
Course Title: Pharmacology I

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Note:
Attempt all questions
Each question carry equal marks
Pay attention to every point of question
Give to the point answers
Extra detail may leads to marks deduction

Q1. Explain the detailed neurotransmission process

Ans: **NEUROTRANSMISSION PROCESS:**

Process:

- Nerve cells pass massage from one cell to another cell tiny chemicals. When two nerve cells need to communicate, they can not just tap each other on the shoulder.
- These neurons pass information from one end of their body to the other as a tiny electrical signal. But one cell does not actually touch another and the signals can not jump across the tiny space in between.
- To cross those tiny gaps called synapses, they rely on chemical messenger. These chemicals are known as neurotransmitters. And their role in cell talk is called neurotransmission.

Synapses:

- The junction between two neurons is called synapses.

Vesicles:

- When an electrical signal reaches the end of a neuron, it triggers the release of tiny sacs that had been inside the cells called vesicles.
- As it moves through a nerve cell, an electrical signal will stimulate these sacs. Then the vesicles move and merge with their cells outer membrane. From there they spill their chemicals into the synapse.
- Those freed neurotransmitters then float across the gap and over to a neighboring cell. That new cell has receptors pointing towards the synapse. These receptors contain pockets, where the neurotransmitter needs to fit.
- A neurotransmitter docks into the proper receptor like a key in to a lock. And as a messenger chemical moves in the receptors shape will change. This change can open a channel in cell allowing charged particles to enter or exit.
- The shape change can trigger other actions inside the cell as well.

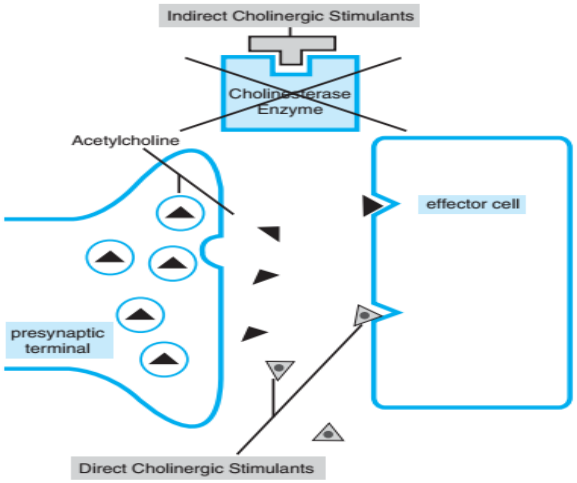
Q2. What does direct and indirect cholinergic agent means? Explain therapeutic application and adverse effects of cholinergic agents in detail.

Ans**: DIRECT CHOLINERGIC AGONISTS:**

- These drugs directly bind and activate nicotinic and muscarinic receptors with variable amount of selectivity.

INDIRECT CHOLINERGIC AGONISTS:

- These drugs inhibit anticholinesterase the enzyme which destroys acetylcholine secreted in to the synapse by the cholinergic neuron.
- By inhibiting destruction these drugs extend the half life of synaptic acetylcholine and thus boost systemic cholinergic activity.



THERAPEUTIC APPLICATION:

1. **Myasthenia Gravis;**

- Myasthenia gravis is an autoimmune disorder that attacks the nicotinic ACh receptors at the neuromuscular junction.
    - Leads to profound muscle weakness.
- Acetylcholinesterase Inhibitors increase the amount of acetylcholine in the neuromuscular junction.
    - Neostigmine is frequently used for the disorder.
- If muscarinic side effects are prominent, anticholinergics can be administrated. Example; atropine.
    - Tolerance usually occurs to the muscarinic side effects.

2. **Reversal of Neuromuscular Blockade:**

- By increasing levels of acetylcholine in the neuromuscular junction, the compounds are able to facilitate recovery from competitive neuromuscular blockade.

3. **Glaucoma:**

- Constriction of ciliary body promotes aqueous humor outflow it decrease intraocular pressure.

- Direct and indirect cholinomimetics can be used to treat glaucoma.

4. **Atonic GI/GU**

- The smooth muscle of the GI and GU system can show depressed activity in certain states.
    - Post operation ileus.
    - Congenital megacolon.
- Bethanechol and neostigmine are the most widely used agents.

ADVERSE EFFECTS:

The possible adverse effects of cholinergic drugs are;

- Slow heart beat, possible leading to cardiac arrest.
- Muscle weakness, Muscle cramps, and Muscle pain.
- Convulsions.
- Weak breathing, inability to breath.
- Increased stomach acid and saliva.

Q3.

(a) Explain the effects and adverse effects of organic nitrates in angina pectoris.
(b) Write down the treatment algorithm for improving symptoms of stable angina.

Ans: **(a)Part**

EFFECTS OF ORGANIC NITRATES IN ANGINA PATRICIA:

They are effective in all types of angina pectoris. At therapeutic doses; has two major effects.

1. **Dilation of the large veins resulting in pooling of blood** in the veins which diminish the preload and reduces the work of heart.
2. **Dilates the coronary vasculature** providing increased blood supply to heart muscle;
    - Decrease preload
    - Decrease afterload
    - Relieving vasospasm
    - Redistribution blood flow

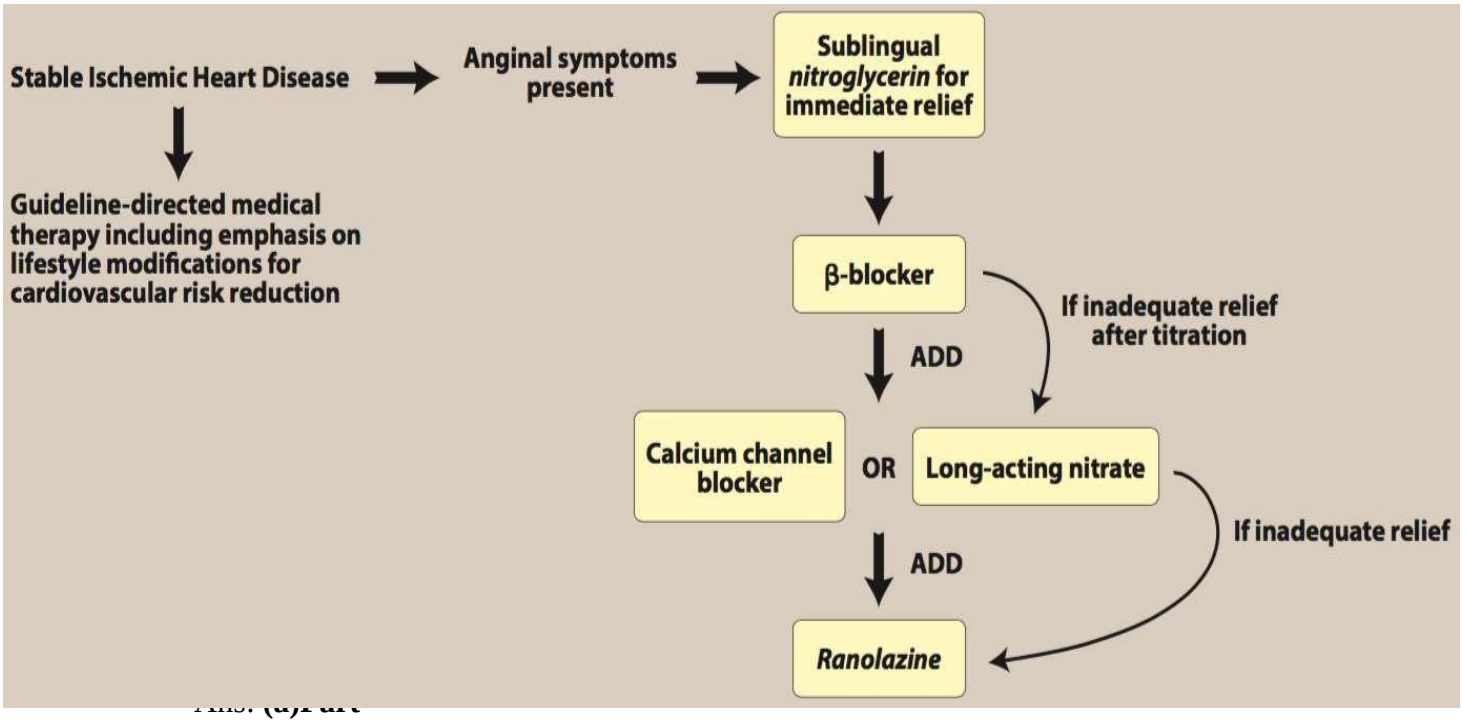
The total effect is a decrease in myocardial oxygen consumption because of decreased cardiac work.

ADVERSE EFFECTS OF ORGANIC NITRATES IN ANGINA PATRICIA:

- Nitrate can cause headache in about 30% to 60% of patients because of the pronounced vasodilation.
- High doses can cause Postural hypotension, Flushing and Tachycardia.

(b)Part:

TREATMENT ALGORITHM FOR STABLE ANGINA:



Ans: **(a)Part**

Q4: (a)Part

PRIMARY AND SECONDARY HYPERTENSION:

Hypertension is divided in to two forms;

1. Primary hypertension.
2. Secondary hypertension.

Primary hypertension:

- Primary hypertension has no single known cause but several mechanisms are linked to altered pathways in blood pressure control.
- These are genetic factors died especially increased salt intake, obesity, insulin, resistance, endothelial dysfunction, ageing , stress and sedentary lifestyle.
- The pressure against the blood vessel walls is affected by cardiac output and peripheral resistance. Altered pathways in BP control leads to sustained constriction of the arterioles resulting in increase peripheral resistance in the blood vessels.
- As the heart continue to pump normal, the pressure in the whole arterial system rises.

Secondary hypertension:

In secondary hypertension blood pressure is raised due to a known underlying cause.

- Renal disorder
- Vascular disorder
- Endocrine disorder
- Drugs
- Miscellaneous causes example; scleroderma, obstructive sleep apnoea.

(b)Part

EFFECTS OF RENIN ON HYPERTION:

- The renin angiotensin system regulates blood pressure and fluid balance in the body.
- When blood volume or sodium levels in the body are low or blood potassium is high cells in the kidney release the enzyme, renin.
- Renin convert angiotensinogen, which is produced in the liver, to the hormone angiotensin I. An enzyme Know as ACE or angiotensin converting enzyme found in the lungs metabolize angiotensin I in to angiotensin II.
- Angiotensin II causes blood vessels to constrict and blood pressure to increase. Angiotensin II Stimulate the release of the hormone aldosterone in the adrenal glands which causes the renal tubules to retain sodium and water and excrete potassium.
- Together angiotensin II and aldosterone work to raise blood volume, blood pressure and sodium levels in the blood to restore the balance of sodium, potassium, and fluids.
- If the renin angiotensin system become overactive, consistently high blood pressure results.

(C)Part

PHARMACOLOGICAL TREATMENT OF HYPERTENSION:

There are several types of drugs used to treat high blood pressure including;

- Angiotensin converting enzyme (ACE) inhibitors
- Angiotensin II receptor blockers (ARBs)
- Diuretics
- Beta blockers
- Calcium channel blockers
- Alpha blockers
- Renin inhibitors
- Combination of medications

Diuretics are aften recommended as the first line of therapy for most people who have high blood pressure.

Q5.

(a) Differentiate between right heart failure and left heart failure
(b) Summarize the pharmacotherapy of heart failure.

Ans: **(a)Part**

Left heart failure and Right heart failure:

LHF Definition:

Left CHF happens when the left ventricle can't pump blood to the body and fluids build up leak into the lungs resulting in shortness of breath.

RHF Definition:

Right CHF happens when the right ventricle can't properly pump blood to the lungs.

Fluid and blood may backup in the veins that transport blood into the heart. This can result in fluid to leak into organs and tissues thus causing CHF right.

LHF Cause:

- Decreased cardiac output
- Pulmonary congestion

RHF Cause:

- Congestion of peripheral tissues.

LHF Sign and symptoms:

- Fatigue
- Orthopnea
- Restlessness
- Confusion
- Extreme weakness
- Cyanosis

RHF Sign and symptoms:

- Bloating
- Anorexia
- Nausea
- Distended neck vein
- Cool legs
- Oliguria

LHF Fluid retention:

- Pulmonary edema
- Pleural effusion

RHF Fluid retention:

- Abdomen (ascites)

LHF Back flow:

Back flow to pulmonary veins.

RHF Back flow:

Back flow to vena cave

LHF Neck veins:

Mild to moderate raised jugular venous pressure.

RHF Neck veins:

Severe jugular venous pressure.

Neck veins are distended.

LHF Clinical manifestation:

Pulmonary congestion, crackles

RHF Clinical manifestation:

Peripheral and visceral congestion.

LHF Final result:

Pulmonary congestion/ edema is the final result.

RHF Final result:

Peripheral generalized edema is the final result.

(b)Part:

Summarize the pharmacotherapy of heart failure.

PHARMACOTHERAPY:

The basic goal of pharmacotherapy in congestive heart failure is to improve the heart's pumping ability.

Strategies:

There are two types of strategies of pharmacotherapy.

Strategy 1:

Drugs increases the cardiac contractile performance and produces a positive inotropic effect.

Positive inotropic effect: "inotropic" means force of muscular contraction, so positive inotropic effect means the effect of increasing the muscular contraction and cardiac contractile performance.

Example: primary drugs used to exert a positive inotropic effect are cardiac glycosides.

1. Cardiac glycosides:

Mechanism of action: they inhibits the Na/K ATPase which results in a small increase in intracellular sodium, due to which driving force of sodium calcium exchange is altered and less calcium is removed from the cell. The increased calcium is stored in the sarcoplasmic reticulum and upon release increases contractile force.

Specific agents:

- Digoxin (Lanoxin)

- Digitioxin (Digitaline)

2. Phosphodiesterase inhibitors:

Mechanism of action: These agents cause a cAMP-mediated increase in intracellular calcium, which subsequently increases the force of contraction within the myocardial cell.

Specific agents:

- Inamrinone
- Milrinone

3. Beta-1 agonists:

Mechanism of action: Dopamine and dobutamine stimulates the beta-1 receptor on myocardium, and exerts a fairly specific positive inotropic effect.

Specific agents:

- Dopamine
- Dobutamine

Strategy 2:

Drugs decrease workload through an effect on the heart or peripheral vasculature (vasodilation), or by controlling fluid volume.

Examples:

- Angiotensin converting enzyme inhibitors
- Beta blockers.
- Diuretics
- Vasodilation.