

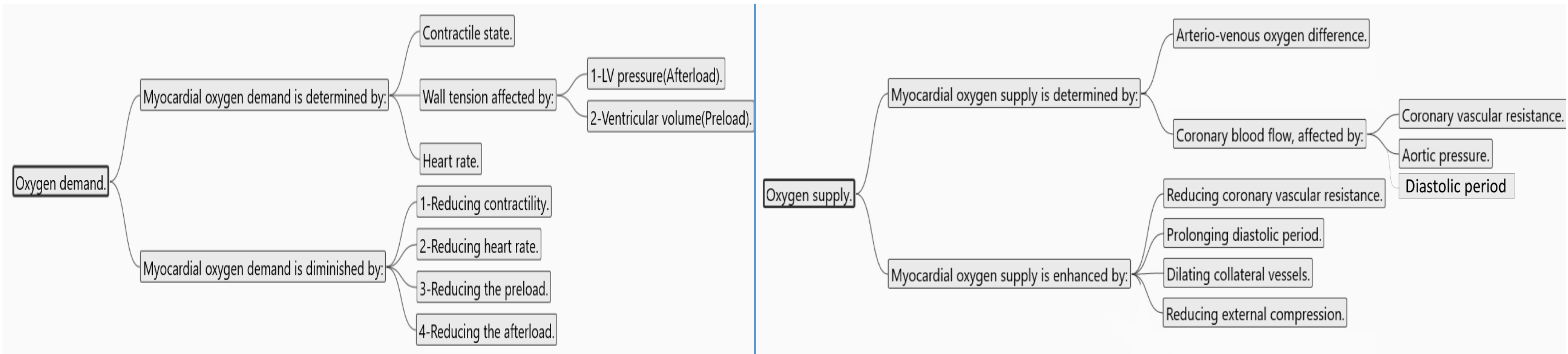
Antianginal drugs

- **Summary.** (Slides 2-6)
- **MCQs.** (Slides 7 and 8)
- **SAQ.** (slide 9)

المفروض انها حكمة

Signs and symptoms	the mechanism of angina pectoris	Types of angina pectoris:
1- chest pain (varying in severity) caused by ischemia of heart muscle 2- pain due to the accumulation of metabolites (K ⁺ ,PGs, kinins, adenosine) secondary to ischemia 3- pain due to either obstruction or spasm	Is a consequence of myocardial oxygen demand exceeding myocardial oxygen supply	1- stable angina 2- variant angina 3- Unstable angina

What are the determinants of oxygen demand and oxygen supply ?



Treatment of angina pectoris

Agents that improve :

- 1- symptoms and ischemia**
- NBC
 - Potassium channels openers.
 - Late Na⁺ current inhibition :ranolazine.
 - Sinus node inhibition. ex: Ivibradine.

- 2- Prognosis**
- Aspirin / other antiplatelet agents
 - ACE inhibitors
 - Statins
 - β-blockers

Classification : long acting and short acting

الأشياء الموحدة	
Mechanism of action	<ul style="list-style-type: none"> Nitric oxide binds to guanylate cyclase in vascular smooth muscle cell to form cGMP. cGMP activates PKG to produce relaxation.
Hemodynamic effects	<ul style="list-style-type: none"> <u>Venous</u> vasodilatation (Decrease the preload) at low dose <u>Coronary</u> vasodilatation (Increase the myocardial perfusion) <u>Arterial</u> vasodilatation (decrease afterload) at high dose Shunting (diverting) of flow from normal area to ischemic area by <u>dilating collateral vessels</u>
ADRs	Throbbing headache - Flushing in blush area - Postural hypotension, dizziness & syncope - Tachycardia & palpitation - Rarely Met-hemoglobinemia
contraindications	<ul style="list-style-type: none"> Known sensitivity to organic nitrates Glaucoma. nitrates increase synthesis of aqueous humor formation. Head trauma or cerebral haemorrhage = Increase intracranial pressure. Uncorrected hypovolemia Concomitant administration of PDE5 Inhibitors (phosphodiesterase type 5 inhibitor)(Sildenafil) Sildenafil + nitrates → Severe hypotension & death
tolerance	Loss of vasodilator response of nitrates on use of long-acting preparations (oral, transdermal) or continuous intravenous infusions, for more than a few hours without interruption.

Classification : long acting and short acting

	الأشياء المختلفة تبعا للكلاسيكيشن	
	Long acting	short acting
Drug	Isosorbide mononitrate and dinitrate	Nitroglycerine
Preparations	<p>Isosorbide Dinitrate: Sublingual tablets - Oral sustained (extended) release – Infusion Preparations</p> <p>Isosorbide mononitrate: Mononitrate Oral sustained release</p>	Sublingual tablets – spray - Transdermal patch - Oral or bucal - sustained release - I.V. Preparations
pharmacokinetics	<ul style="list-style-type: none"> • Oral isosorbide • Very well absorbed & 100% bioavailability • The <u>dinitrate</u> undergoes <u>denitration</u> to two <u>mononitrates</u> → both possess antianginal activity (both pharmacologically active) • (t_{1/2} 1-3 hours) • Further <u>denitrated</u> metabolites conjugate to <u>glucuronic acid</u> in liver. Excreted in urine. 	<ul style="list-style-type: none"> • Significant (high) first pass metabolism occurs in the liver • (10-20%) bioavailability • Given sublingual or via transdermal patch, or parenteral
Indications	<p>In stable angina:</p> <ul style="list-style-type: none"> • <u>Persistent</u> prophylaxis • <u>Chronic</u> Heart Failure 	<p>In stable angina:</p> <ul style="list-style-type: none"> • Acute symptom relief (sublingual) • <u>Situational</u> prophylaxis • IN VARIANT ANGINA (sublingual) • IN UNSTABLE ANGINA (IV) • <u>Acute</u> Heart Failure • Refractory AHF and AMI (IV)

Effects	Results
↓ Arterial pressure	↓ O2 demand
↓ Ventricular volume	↓ O2 demand
↓ Diastolic perfusion time due to tachycardia	↓ myocardial perfusion
Reflex tachycardia	↑ O2 demand
Reflex ↑ in contractility	↑ O2 demand
↑ Collateral flow	Improved perfusion to ischemic myocardium
↓ Left ventricular diastolic pressure	Improve subendocardial perfusion
5 Vasodilation of epicardial coronary arteries	Relief of coronary artery spasm

كل الأسهم نازلة

كل أسهم الريفزلت طالعة

الريفزلت يبدأ ب (امبروفد)

Class	Drugs	Mechanism	Pharmacodynamics (Antianginal action)	Therapeutic uses	ADRs
Ca²⁺ channel blockers	Dihydropyridines Amlodipine Phenylalkylamines Benzthiazepines	Binding of [CCBs] to the L-type Ca channels ↓ their frequency of opening. in response to depolarization ↓ entry of Ca → ↓ Ca release from internal stores → No Stimulus-Contraction Coupling → RELAXATION	↓ Cardiomyocyte Contraction → ↓ cardiac work through their –ve inotropic & chronotropic action (verapamil & diltiazem) → ↓ myocardial oxygen demand ↓ VSMC Contraction → ↓ Afterload → ↓ cardiac work → ↓ myocardial oxygen demand Coronary dilatation → ↑ myocardial oxygen supply	IN VARIANT ANGINA : → Attacks prevented (> 60%) / sometimes variably aborted IN UNSTABLE ANGINA: Seldom added in refractory cases	
K⁺ CHANNEL blockers	Nicorandil	has dual mechanism of action: 1. Opens potassium ATP channels (arteriolar dilator) 2. NO donor as it has a nitrate moiety (venular dilator)	As K channel opener : 1. On vascular smooth muscles: opening K channels> hyperpolarization>vasodilation. 2. On cardiomyocytes: opening K channels> repolarization> decrease cardiac work. As NO donor: Increase in cGMP/PKG which leads to vasodilation.	1. Prophylactic 2nd line therapy in stable angina 2. Refractory variant angina	Flushing, headache, Hypotension, palpitation, weakness Mouth & peri-anal ulcers, nausea and vomiting.
β Adrenergic Blockers	Atenolol Bisoprolol Metoprolol (Selective β 1)		Decrease heart rate & contractility thus:-1-Increase duration of diastole > increase coronary blood flow > increase oxygen supply 2- Decrease workload > Decrease O2 consumption > Decrease oxygen demand	Stable , unstable angina and Myocardial infarction	
Metabolically acting agents	Trimetazidine	Oxygen requirement of glucose pathway is lower than FFA, during ischemia oxidized FFA levels rise, blunting the glucose pathway. Trimetazidine reduces oxygen demand without altering hemodynamics			GIT disturbances
	Ranolazine	Inhibits late sodium current which increases during ischemia Prolongs QT intervals so contraindicated with class Ia and III antiarrhythmatics		Used in chronic angina concomitantly with other drugs	dizziness , constipation
	Ivabradine	reduces slope of depolarization, slowing HR, reducing myocardial work, and oxygen demand If current is an inward Na/K current that activates pacemaker cells of the SA node, ivabradine selectively blocks it		Used in treatment of chronic stable angina in Patients with normal sinus rhythm with β-blockers Used in combination with beta blockers in people with heart failure with LVEF lower than 3 5 inadequately controlled by beta block whose heart rate exceeds 70/min	luminous phenomena

MCQs

1- What is the clinical term for angina caused by coronary vasospasm?

- A. Classic angina. B. Myocardial infarction. C. Prinzmetal angina. D. Unstable angina.

2- All of the following medications can be useful for managing stable angina in a patient with coronary artery disease except:

- A. Amlodipine. B. Atenolol. C. Immediate-release nifedipine. D. Isosorbide dinitrate

3- A 72-year-old male presents to the primary care clinic complaining of chest tightness and pressure that is increasing in severity and frequency. his current medications include atenolol, lisinopril, and nitroglycerin. Which intervention is most appropriate at this time?

- A. Add amlodipine. B. initiate isosorbide mononitrate. C. initiate ranolazine. D. refer the patient to the nearest emergency room for evaluation

4- A 62-year-old patient with a history of asthma and vasospastic angina states that he gets chest pain both with exertion and at rest, about ten times per week. one sublingual nitroglycerin tablet always relieves his symptoms, but this medication gives him an awful headache every time he takes it. Which is the best option for improving his angina?

- A. Change to sublingual nitroglycerin spray. B. Add amlodipine. C. Add propranolol. D. Replace nitroglycerin with ranolazine.

5- Which side effect is associated with amlodipine?

- A. Bradycardia. B. Cough. C. Edema. D. QT prolongation.

6- Which medication should be prescribed to all anginal patients to treat an acute attack?

- A. Isosorbide dinitrate. B. Nitroglycerin patch. C. Nitroglycerin sublingual tablet or spray. D. Ranolazine

C-9
C-5
4-B
3-D
2-C
1-C

7- A 65-year-old male experiences uncontrolled angina attacks that limit his ability to do household chores. He is adherent to a maximized dose of B-blocker with a low heart rate and low blood pressure. He was unable to tolerate an increase in isosorbide mononitrate due to headache. Which is the most appropriate addition to his antianginal therapy?

- A. Amlodipine. B. Aspirin. C. Ranolazine. D. Verapamil.

8- A 68-year-old male with a history of angina had a MI last month, and an echocardiogram reveals heart failure with reduced ejection fraction. He was continued on his previous home medications (diltiazem, enalapril, and nitroglycerin), and atenolol was added at discharge. He has only had a few sporadic episodes of stable angina that are relieved with nitroglycerin or rest. What are eventual goals for optimizing this medication regimen?

- A. Add isosorbide mononitrate. B. Increase atenolol. C. Stop atenolol and increase diltiazem. D. Stop diltiazem and change atenolol to bisoprolol.

9- Which of the following medications would be safe to use in a patient taking ranolazine?

- A. Carbamazepine. B. Clarithromycin. C. Enalapril. D. Quetiapine.

10- A patient whose angina was previously well controlled with once-daily isosorbide mononitrate states that recently he has been taking isosorbide mononitrate twice a day to control angina symptoms that are occurring more frequently during early morning hours. Which of the following is the best option for this patient?

- A. Continue once-daily administration of isosorbide mononitrate but advise the patient to take this medication in the evening.
B. Advise continuation of isosorbide mononitrate twice daily for full 24-hour coverage of anginal symptoms.
C. Switch to isosorbide dinitrate, as this has a longer duration of action than the mononitrate.
D. Switch to nitroglycerin patch for consistent drug delivery and advise him to wear the patch around the clock.

10-A
9-C
8-D
7-C

A 57-year-old patient with a history of hypertension over the last 5 years, diabetic since he was 20 years old came to the ER with 8/10 substernal chest pain. While taking history the patient says that the pain comes with emotional stress and physical activity. The ER consultant called the cardiologist to help stabilize the patient and to check up with him after being diagnosed with variant angina.

Q1: What is the drug of choice to stabilize the patient in such a scenario?

Nitroglycerine

Q2: What is the best route of administration of this drug? And why?

Sublingual or parenteral due to its high first pass metabolism.

Q3: Are there any contraindicated groups of drugs in this case? And why?

Yes, there is, beta blockers are contraindicated in patients with diabetes because beta blockers cover the signs of hypoglycemic state.

Q4: What is the drug of choice in long-term prophylactic therapy in this patient?

K channel blockers



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