PHARMACOLOGY
TEAM 439

MED439
KING SAUD UNIVERSITY

Antianginal drug 1&2

Objectives:

- Recognize variables contributing to a balanced myocardial supply versus demand.
- Differentiate between drugs used to alleviate acute anginal attacks and those meant for prophylaxis & improvement of survival.
- Detail the pharmacology of nitrates and other drugs used as antianginal therapy.

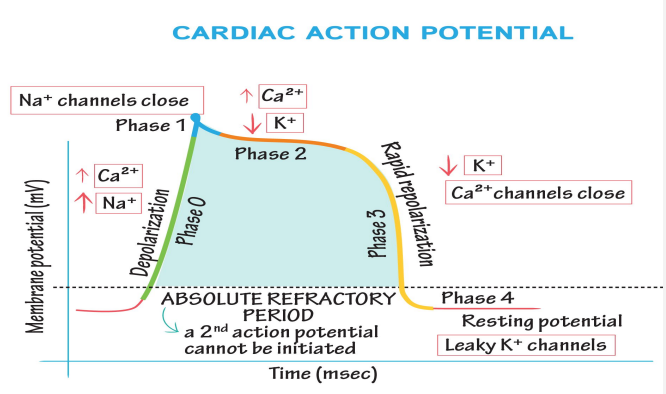
Important
In male and female slides
Only in male slides
Only in female slides
Extra information

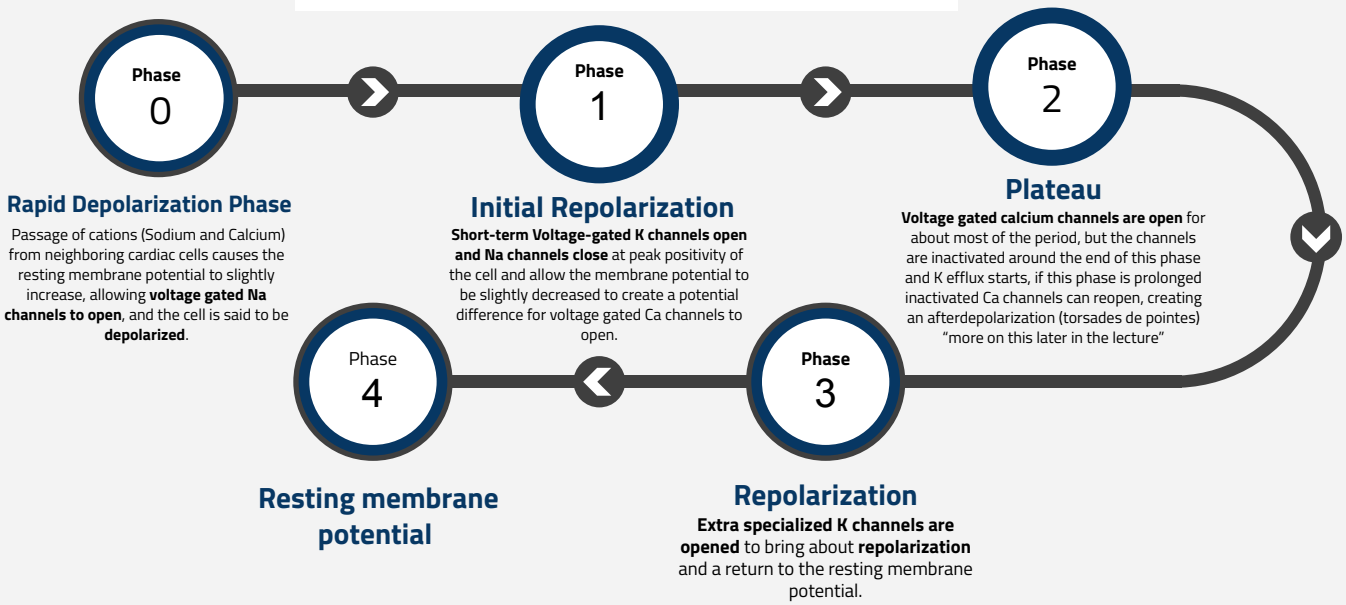
helpful video

Editing file

Extra information(recommended)

Special thanks for team 438





Rapid Depolarization Phase

Passage of cations (Sodium and Calcium) from neighboring cardiac cells causes the resting membrane potential to slightly increase, allowing **voltage gated Na channels to open**, and the cell is said to be **depolarized**.

Initial Repolarization

Short-term Voltage-gated K channels open and Na channels close at peak positivity of the cell and allow the membrane potential to be slightly decreased to create a potential difference for voltage gated Ca channels to open.

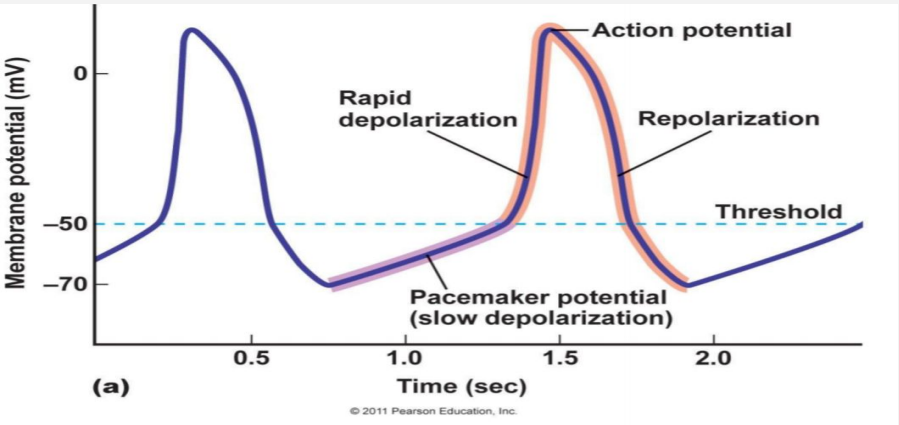
Plateau

Voltage gated calcium channels are open for about most of the period, but the channels are inactivated around the end of this phase and K efflux starts, if this phase is prolonged inactivated Ca channels can reopen, creating an afterdepolarization (torsades de pointes) "more on this later in the lecture"

Repolarization

Extra specialized K channels are opened to bring about **repolarization** and a return to the resting membrane potential.

Resting membrane potential



SA Node is made of specialized cardiac cells, (Modified Cardiomyocytes), the cells have high permeability to Na and K, allowing constant, spontaneous action potentials to be generated and a unique way of generating an action potential.

1

Pacemaker potential (slow depolarization): Slow Na influx and a decreased K efflux, makes the cells more positive gradually.

2

Rapid Depolarization: Calcium channels open, allowing the cells to be depolarized and action potential is reached.

3

Repolarization: Inactivation of calcium channels and K channels are open, the cell repolarizes and Na channels begin to open allowing the cycle to restart.

Angina Pectoris: extra #438

- Angina pectoris is a consequence of Myocardial oxygen demand exceeding myocardial oxygen supply.
- Mainly caused by obstruction of blood flow Resulting in ischemia

Which signs or symptoms suggest diagnosis of angina pectoris?

1

A clinical syndrome of chest pain (varying in severity) due to ischemia of heart muscle

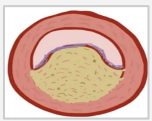
2

Pain is caused either by obstruction. (e.g. atherosclerotic plaque) or spasm

3

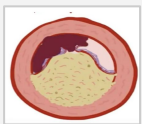
Pain is due to accumulation of metabolites (K + , PGs, Kinins, Adenosine....) secondary to the ischemia. These metabolites are body's response to ischemia as vasodilators.

Stable angina:
known as Effort-induced, typical, classical, chronic



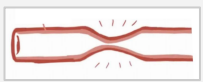
-Reduction of coronary perfusion due to a fixed obstruction of a coronary artery produced by **atherosclerosis**.
-Pain occurs upon exertion Exercise Emotion, Heavy meal.
Treatment:
Rest or nitroglycerin

Unstable angina:
Accelerated (Progressive) or crescendo Angina

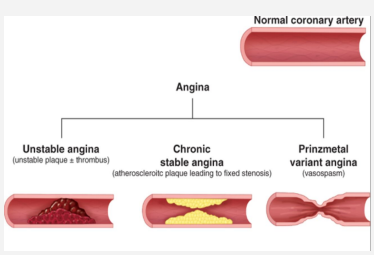


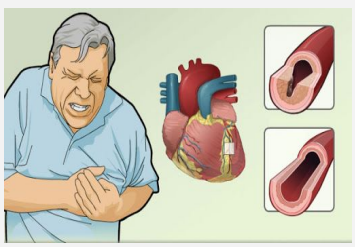
-A form of acute coronary syndrome, caused by rupture of an atherosclerotic plaque and partial or complete thrombosis of a coronary artery
-Sever type .
-There's increased frequency & duration of pain.
Treatment:
Hospital admission and more aggressive therapy.

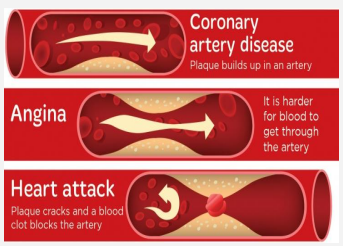
Variant angina: (Prinzmetal)
Or vasospastic

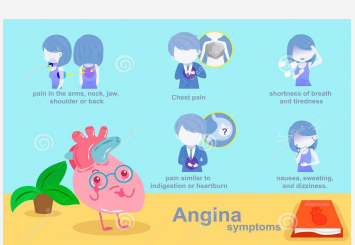


-Coronary artery spasm (Alpha receptor mediated vasoconstriction) With or without Atherosclerotic plaque
-**Pain even at rest.**
Treatment:
coronary vasodilators, such as nitroglycerin and calcium channel blockers.









What are the determinants of oxygen **demand** and **supply**?

Oxygen Demand

O_2 demand is determined by:	O_2 demand is diminished by:
1-Contractility 2-Heart rate 3-Wall tension(pressure exerted by the fibers itself) (affected by): -ventricular pressure (Afterload) Peripheral vascular resistance -Ventricular volume (Preload)	1-Reducing contractility 2-Reducing Heart rate 3-Reducing the Preload 4-Reducing the Afterload

Oxygen Supply

O_2 supply is determined by:	O_2 supply is enhanced by:
1-Arterio-Venous O_2 difference (Dr's note:difference between O2 content between atria and ventricles, it increases during exercise) 2-Coronary blood flow (affected by): -Aortic Driving pressure and diastolic period -Coronary vascular resistance is inverse relationship	1-Reducing coronary vascular resistance 2-Reducing external compression 3-Prolong diastolic period 4-Dilating collateral vessels 5-Optimizing hemoglobin & RBCs

It is important to point out that restoration of oxygen supply to ischemic tissue should be restored 3 hours after ischemia at most, after that period the cells will be overly acidic due to lactate accumulation from anaerobic metabolism, and the introduction of oxygen to the damaged mitochondria will result in the formation of free radicals, particularly H2O2, as a final product of ETC, causing further damage to the cells and possible inflammatory reaction. This is known pathophysiologically as Inadequate Tissue Reperfusion.

Treatment of angina pectoris

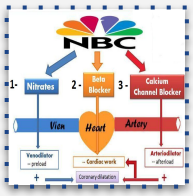
The Aim in this lecture is decrease contractility and HR and improve blood supply

1- Agents that improve symptoms and ischemia:

Traditional Approaches:

- **N**itrates. *Venodilator
- **B**eta-blockers. act on the heart
- **C**alcium channel blockers act on the heart and arteries

*venodilator↓venosus returns ↓heart volume ↓oxygen demand



New Approaches:

- Metabolic acting agents (modulation), e.g. Trimetazidine.
- Potassium channels openers, e.g. Nicorandil.
- Late Na+ current inhibition, e.g. Ranolazine.
- Sinus node inhibition, eg. Ivabradine. (↓ Heart rate, without effectinging force of contraction)

2- Agents that improve prognosis (Halt progression, prevent acute insult, improve survival):

أبعيش طووووول حياتي عزباء (ASBA)

- **A**CE inhibitors
- **S**tatins (stops cholesterol synthesis)
- **B**eta-blockers
- **A**spirin / other antiplatelet agents

General mechanism of antianginal drugs:

Oxygen Supply = **Oxygen Demand**

- Regional flow distribution
- Oxygen extraction
- Coronary blood flow
- heart rate
- cardiac contractility
- Myocardial wall tension: -preload -Afterload

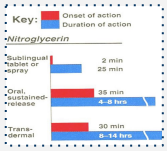
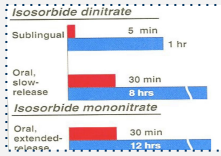
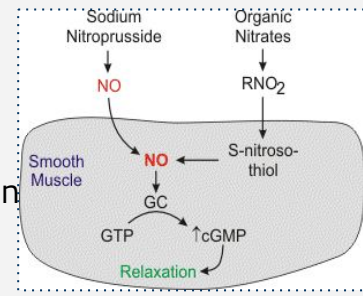
Regional flow distribution:
Flow to ischemic subendocardial tissue improved by nitrates, CCBs, B-blockers

Coronary blood flow:
Increased by nitrates and CCBs

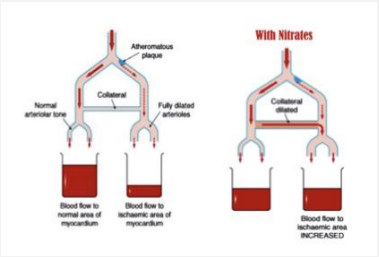
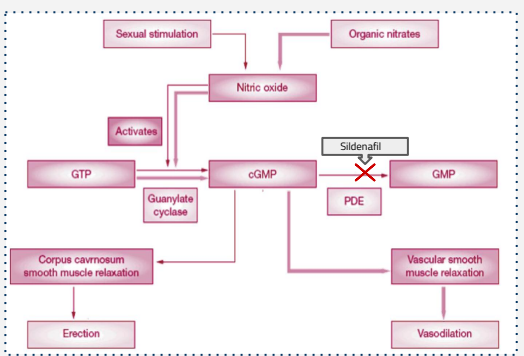
Heart rate + Cardiac contractility:
Decreased by B-blockers and some CCBs

Preload:
Decrease by nitrates
Afterload:
Decreased by CCBs

Antianginal drugs: 1.Organic Nitrates

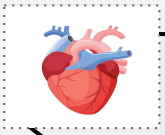
class	short acting	long acting
Drug	**Nitroglycerine (GTN)** -Prototype of organic nitrates -active ingredient of dynamite (explosive material)	**Isosorbide mononitrate & dinitrate**
P.k	▪Given sublingual or transdermal patch or parenteral. ▪ Can't be given orally, because it goes through Significant first pass metabolism in the liver ▪ Only (10-20%) bioavailability if given orally	▪ Very well absorbed . Mononitrate, 100% bioavailability ▪ The dinitrate undergoes denitration in liver to two mononitrates ➜ both possess antianginal activity which then conjugate to glucuronic acid in liver. ▪ T1/2= 1-3 hours. ▪ Excreted in urine.
Main use	▪ Rapid for terminating an acute attack of stable angina.	▪ For long-term persistent prophylaxis of stable angina.
Indications	IN STABLE ANGINA: ● Acute symptom relief ➜sublingual GTN ● Prevention; Situational prophylaxis➜sublingual GTN IN VARIANT ANGINA➜ sublingual GTN IN UNSTABLE ANGINA IV GTN ● Heart failure ● Refractory AHF[1] ➜IV GTN ● AMI[2]➜IV GTN	IN STABLE ANGINA: ● Prevention; Persistant prophylaxis ➜Isosorbide mono or dinitrate. IN UNSTABLE ANGINA: ● CHF[3]➜ Isosorbide mononitrate + hydralazine [if contraindication to ACE Is used] 1- Acute Heart Failure. 2- Acute myocardial infarction. 3- Chronic heart failure
Preparation	● Sublingual tablets or spray Have rapid onset of action and short duration (30min), ● Transdermal patch(8-14h) ● Oral or bucal sustained release ● I.V. Preparations 	● Dinitrate Sublingual tablets ● Dinitrate Oral sustained release ●Mononitrate Oral sustained release ● Infusion Preparations 
mechanism The damaged endothelium in angina patients can't produce NO, this group of drugs donate it	1. Release NO through interactions with intracellular SH groups and with further enzymatic degradation, NO is produced. Nitric oxide then binds to guanylate cyclase in vascular smooth muscle cell to form cGMP. 2. cGMP activates PKG (Protein Kinase G) to produce relaxation For the action of Nitrates we need SH groups.	

Antianginal drugs:
1.Organic Nitrates (cont.)

Hemodynamic effects of nitrates	▪ **Nitrates can treat angina pectoris by one of 4 mechanism:** 1- Decrease the preload (in low concentrations, it causes venodilation) 2-Increase the myocardial perfusion (O2 supply) by dilating the coronary vessels. 3- Arterial vasodilation → ↓Afterload. Decreasing the peripheral resistance(in higher concentrations) 4- Shunting of flow from normal area to ischemic area by dilating collateral vessels (blood in ischemic area increases). 
Nitrate tolerance	▪ **WHEN** ? 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. ▪ **How?, mechanism:** Like baroreceptors and RAAS #438 1. Compensatory neurohormonal counter-regulation due to continuous vasodilatation 2. Depletion of free-SH groups. (Nitrates are converted to NO through various intermediate reactions that require SH groups from tissues for the enzymes to function). ▪ **How to overcome tolerance? by:** free periods (Smaller doses at increasing intervals) & Giving drugs that maintain tissue SH group e.g. Captopril, N-acetyl cysteine.
Contra-indications	1. Known sensitivity to organic nitrates. 2. Glaucoma. nitrates increase synthesis of aqueous humor thus increase IOP. 3. Head trauma or cerebral haemorrhage → Increased intracranial pressure . 4. Uncorrected hypovolemia, because reduction of volume in the body will result in vasoconstriction. Hypovolemia must be corrected before administration of nitrates. 5. Concomitant administration of PDE5 Inhibitors. Sildenafil + nitrates → Severe hypotension & death Sildenafil (viagra), inhibit PDE which is responsible for inactivation of cGMP , thus increase the effect of NO> severe vasodilation lead to severe hypotension could cause death. 

Antianginal drugs: 1.Organic Nitrates (cont.)

ADRs

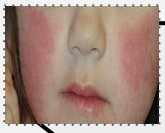


Reflex tachycardia and palpitation

Leading to increasing oxygen demand in high dose

Throbbing headache

(most common), due to dilation of cranial blood vessels)

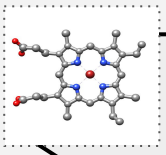


Flushing of blush area

(Leading to increasing oxygen demand)>>> ولأن الحبة تحت اللسان فأوعية الوجه هي الأكثر تأثراً

Postural hypotension, Dizziness and Syncope

(due to dilation of cutaneous blood dizziness and syncope. vessels)



Rarely Methemoglobinemia

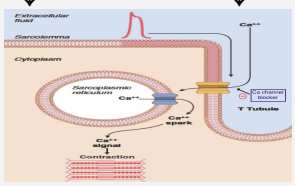
Nitrite bind to HB, converts ferrous "Fe+2" to ferric "fe+3" Methemoglobinemia >>which's not able to carry O2 in high dose

Effects of nitrates in treatment of angina and their results

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

2. Calcium channel blockers

Class	Dihydropyridine	Phenylalkylamine	Benzothiazepine
Drugs	• Nifedipine • Amlodipine • Nicardipine	Verapamil	Diltiazem
Selectivity	Dihydropyridine group act mainly on Vascular smooth muscle. (Thus, more selective as vasodilator than cardiac depressant)	act more on myocardium. (Cardiomyocytes) As cardiac depressant	has intermediate effect. Do both actions but with less effectiveness
M.O.A	Calcium channel blockers ➞Bind to L Type Ca channels (the most important type, involved in anginal pain) ➞ decrease their frequency of opening in response to depolarization ➞ ↓ entry of Ca ➞ ↓ Ca release from internal stores(sarcoplasmic reticulum) ➞ No Stimulus-Contraction Coupling ➞ RELAXATION		
P.D Antianginal actions	**1-verapamil & diltiazem** ↓ Cardiomyocyte Contraction ➞ ↓ cardiac work through their –ve inotropic & chronotropic action ➞ ↓ myocardial oxygen demand **2-Dihydropyridines** ↓ VSMC(vascular smooth muscle cell) Contraction ➞ arteriolar vasodilation ↓ Afterload ➞ ↓ cardiac work ➞ ↓myocardial oxygen demand **3-coronary dilatation** ↑ myocardial oxygen supply		
Indications in angina	Stable	Regular prophylaxis.	
	Unstable	Seldom (rarely) added in refractory cases.	
	Variant	Attacks are prevented (>60%)/sometimes variably aborted (stops pain)	



1. **Should the short acting dihydropyridines (Nifedipine , Nicardipine) be AVOIDED?**
Yes, because it could cause: 1- anginal attack 2- Vasodilation and hypotension which may result in Reflex tachycardia 3- ischemic heart disease . And it's short acting

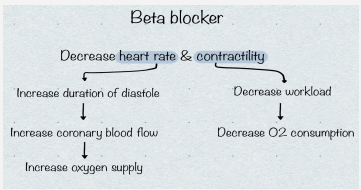
2. **Is a calcium channel blocker useful as antianginal in patients with CHF (Congestive heart failure)?**
Yes, dihydropyrdine.To reduce the preload and afterload (vasodilator) and thus decrease the cardiac workload.

3. **Can we combine Calcium Channel Blocker with a beta blocker?** Dr's note:**Except verapamil**
Yes, dihydropyridine: because beta blockers work on the heart so we can not combine it with CCB that also works on the heart (cardiomyocyte), it may cause heart block. but we can give something that works on the blood vessel like the long acting dihydropyridine:amlodipine

4. **Can we combine Calcium Channel blocker with Nitrate ?**
Yes, Verapamil: Because Nitrate is a vasodilator, that causes hypotension which leads to reflex tachycardia (increasing in the heart rate) and increasing in the force of contraction, so we can combine it with a CCB that works on the heart (cardiomyocyte) like verapamil to reduce the heart rate and the contraction.

β Adrenergic blockers

3. β1 Selective blockers

Drugs	Atenolol Bisoprolol Metoprolol	
P.D	**Acts on cardiomyocyte:** **1. Negative inotropic effect (force of contraction)** ↓cardiac work →↓ myocardial oxygen demand **2. Negative chronotropic effect (Heart rate = bradycardia)** Increase diastolic duration Due to the bradycardia(give time for filling) → Increase coronary blood flow →↑ myocardial oxygen supply 	
Indications as antianginal	Stable	1. Cardioselective (beta 1 blockers) are preferred to avoid affecting lung (bronchiole) and blood vessels 2. First choice for Chronic use with **nitrate**.
	Unstable	halts (stops) progression to MI, improve survival
	Variant	Contraindicated, because they are ineffective and may actually worsen symptoms.
Indications as acute Myocardial infarction	Given early to ↓ Infarct size, morbidity & mortality (↓ incidence of sudden death) ↓Arrhythmia and ↓ O2 demand	

1

Are Cardioselective beta blockers preferred in angina?

Yes, beta 1 blockers are preferred, and non-selective beta blockers are better avoided as they block vasodilatory effects of sympathetic stimulation that tend to increase afterload & O2 consumption.
(Especially if the patient has tachycardia)

2

should Beta blocker be withdrawn gradually?

Yes, (because sudden stoppage will give rise to a withdrawal syndrome)
Increase pain, Rebound angina, arrhythmia, myocardial infarction & Hypertension (due to stimulation or Up-regulation of beta-receptors).

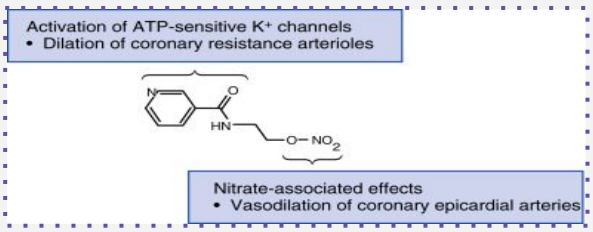
3

Can we give a beta blocker to a diabetic patient with ischemic heart disease?

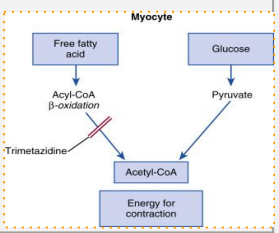
(We should change the drug because it's not good to give beta blocker in diabetes why ? Because the beta blockers)
1-inhibit glycogenolysis 2- inhibit insulin release 3- inhibit recovery of hypoglycemia 4-beta blocker will mask hypoglycemia symptoms like tremor and palpitations so not recommended

New Approaches:

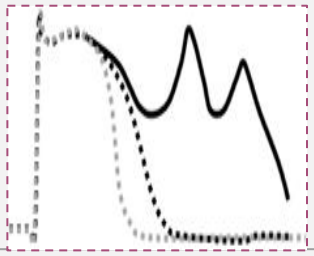
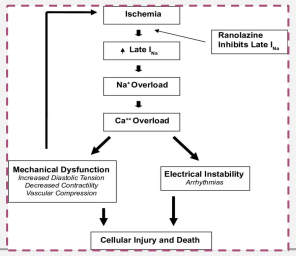
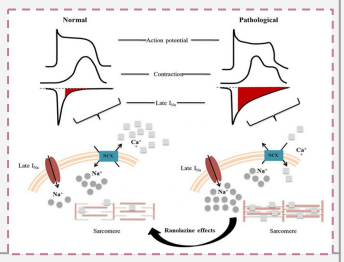
1-Potassium Channel Openers

Drug	Nicorandil	
P.D (dual mechanisms)	**1.Opening of KATP channels**	**2. Acting as NO donor**
	On VSMCs :K+ channel opening → Hyperpolarization and stabilization of the excitable cell membrane near to resting potential → VASODILATATION (Improves coronary blood flow)	On VSMCs: NO donner → increase cGMP/ PKG → VASODILATATION 
	On Cardiomyocyte : K channel opening Repolarization → relaxation of myocardial cells → ↓ Cardiac work	
Indications	1. Prophylactic 2nd line therapy in stable angina. 1st is the traditional drug : nitrate ,BB, CCB. 2. Refractory (not responding) variant angina if not responding to nitrate and CCB.	
ADRs	Flushing, headache, Hypotension, palpitation due to nitrate effect Weakness, Mouth & peri-anal ulcers Dr's note:special ADR for nicorandil , nausea and vomiting	

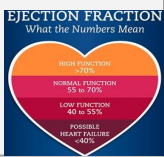
2-Metabolically Acting Agents

Drug	Trimetazidine
Pharmaco dynamics (dual mechanism	During ischemia, metabolism shifts to oxidation of FFA (fatty acids), which provides more energy but requires more O2 than Glucose utilization. So, to decrease O2 consumption & demand, we can enhance utilization of glucose (less O2 requirement) by giving Partial FFA Oxidation Inhibitors (e.g. Trimetazidine) 
Indications	Used as an add on therapy
ADRs	GIT disturbances
Contraindications	▪Hypersensitivity reaction ▪In pregnancy & lactation

3-.Late Na+ current inhibition

Drug	Ranolazine
Pharmaco -logical effect	▪Inhibits the late sodium current(which opens in phase 4 depolarization), which increases during ischemia and affects Na dependent-Ca Channels. Due to ischemia **only** will be activation of sodium current in phase 4 . Inward of Na >>>> overload of Ca++ >>>> inhibit the relaxing of ventricle in ischemic patient>>>>diastolic failure +extravascular compression >heart tired >>>>**Give Ranolazine and will inhibit late sodium current >>more time to ventricle to relax**   
Indication	Used in chronic angina concomitantly with other drugs (it can be used in the treatment of cardiac arrhythmia, as well as **diastolic heart failure**)
ADRs	dizziness & constipation
Precautions	▪It prolongs the QT interval so contraindicated with Class Ia (Na blocker) & III antiar rhythmic drugs . ▪ Toxicity develops due to interaction with CYT-p450 inhibitors as; diltiazem, verapamil, ketoconazole, macrolide antibiotics, grapefruit juice

4-Sinus node inhibition

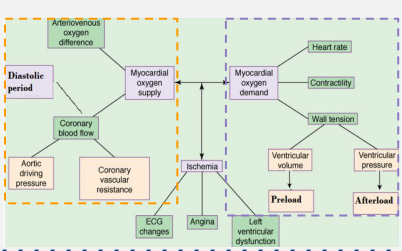
Drug	Ivabradine
M.O.A	-Selectively blocks I_f (I_f current is an inward Na+/K+ current that activates pacemaker cells of the SA node)
Pharmaco dynamic effect	-Acts on the " Funny Channel" a special Na channel in SAN, **reduces slope** of depolarization, slowing HR, reducing myocardial work & Myocardial O2 demand *funny channels are abundant in SA node cells. through these channels, both sodium and potassium can enter. Blocking these channels will reduce SA node automaticity, thus, longer time is required for the action potential to take place; which will decrease the heart rate
Indication	-Used in treatment of chronic stable angina in patients with normal sinus rhythm who cannot take ß-blockers.(Ivabradine decreases heart rate ONLY, does not affect the contractility > Good in HF)>>>Ivabradine case decrease in HR (Bradycardia) -Used in combination with beta blockers in people with heart failure with LVEF * lower than 35 percent inadequately controlled by beta blockers alone and whose heart rate exceeds 70/min *left ventricle ejection fractions 
ADRs	luminous phenomena (described as a transiently enhanced brightness in a limited area of the visual field, halos, image decomposition (stroboscopic or kaleidoscopic effects), colored **bright** lights, or multiple images (retinal persistency)

Helmi's case :

Helmi, a 62-year-old male smoker with type 2 diabetes mellitus and hypertension presents with a 4-month history of exertional chest pain. Physical examination shows a blood pressure of 152/90 mm Hg but is otherwise unremarkable. The ECG is normal, and laboratory tests show a fasting blood glucose value of 110 mg/dL, glycosylated hemoglobin 6.0%, creatinine 1.1 mg/dL, total cholesterol 160, LDL 120, HDL 38, and triglycerides 147 mg/dL. He exercises for 8 minutes, experiences chest pain, and is found to have a 2-mm ST-segment depression at the end of exercise.

Questions and answers:

- **Q1) Which signs or symptoms of Helmi suggest diagnosis of angina pectoris?**
  -Exercise induced chest pain and depression of ST segment.
  -Pain is caused either by obstruction,or spasm.
- **Q2) What triggers the onset of symptoms in Helmi case?**
  -The main triggers is the Exercise.(increase in cardiac demand)
- **Q3)What factors worsen the symptoms in case of Helmi?**
  - Smoking, hypertension >>vasoconstriction this will increase compression on the heart so reduce in blood supply, hyperlipidemia case AS ,diabetes
- **Q4) What lifestyle modifications should Helmi carry out?**
  -Quit smoking, control of diabetes, diet control and moderate exercise.
- **Q5)What is the possible underlying cause of Helmi's exertional pain?**
  atherosclerotic and blood obstruction
- **Q6)What are the determinants of oxygen demand & supply?**



- **Q7)If Helmi was prescribed nitrates & tolerance developed to their effects, how to overcome tolerance to nitrates?**
  -Nitrate tolerance can be overcome by: Smaller doses at increasing intervals (Nitrate free periods twice a day) & Giving drugs that maintain tissue SH group e.g. Captopril.
- **Q8) Which antianginal drug is the best choice for the case of Helmi? And Why?**
  - We should avoid B-blocker because he is Diabetic , we can start with Nitrate and Ca++ channel blocker.
- **Q9)If Helmi does not respond to monotherapy, what other drug should be added to his regimen?**

  بدون ما يستنوا responding good or not they should
  give traditional drugs (nitrate,CCB)+add on drugs like Nicorandil,trimetazidine ,Ranolazine,Ivabradine .
- **Q10)Which antihyperlipidemic drug should be prescribed to Helmi?**
  -Statins + Fibrates

Special Thanks For #438

MCQ

1-One of these drugs can induce luminous phenomena			
A- Ranolazine	B- Nicorandil	C-Ivabradine	D-Trimetazidine

2-A 62 years old women came to the clinic with variant angina, history showed that the patient does not respond to nitrate and CCB, what is the drug of choice?			
A-Dihydropyridine	B-Atenolol	C-Trimetazidine	D-Nicorandil

3- 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.

4-The chest pain that occurs in angina pectoris is due to what?			
A-ischemia of heart muscle	B-obstruction or spasm of vessel	C-accumulation of metabolite	D- A,B & C

5-Which of the following is contraindicated in variant angina?			
A-Diltiazem	B-bisoprolol	C-Amlodepine	D-Verapamil

6-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 β-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

Answers

1	2	3	4	5	6
C	D	C	D	B	C

SAQ

Q1)what are the factors that determine O_2 supply?

Q2) A 54 years old asthmatic patient came to your clinic complaining from chest pain which comes after any physical activity and relieves if he rest , investigations showed that the patient is atherosclerotic and diabetic. Heart investigations showed that his sinus rhythm is normal.
1- what is the drug of choice? 2- what is the mechanism of action? 3- mention one ADR

Q3) what's the mechanism of Organic Nitrates?

Q4) name a calcium channel blocker that is useful as antianginal in patients with CHF?and why?

Q5)why we use beta blocker CAUTIOUSLY to a diabetic patient with ischemic heart disease?

Q6) what are the Agents that improve symptoms and ischemia?

Answers:

A1)1-Regional myocardial distribution 2-Arterio-Venous O_2 difference 3-Coronary blood flow

A2) 1-Ivabradine 2- in slide 12 3- luminous phenomena

A3) slide 6

A4) dihydropyridine.because it reduce the afterload (vasodilator) and thus decrease the cardiac workload.

A5) because it masks hypoglycemia in diabetics and mask its symptoms, they also inhibit the counter-regulatory mechanism and thus prevent recovery of hypoglycemia

A6) 1- nitrate 2-beta blocker 3-ca channel blockers

GOOD LUCK!

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