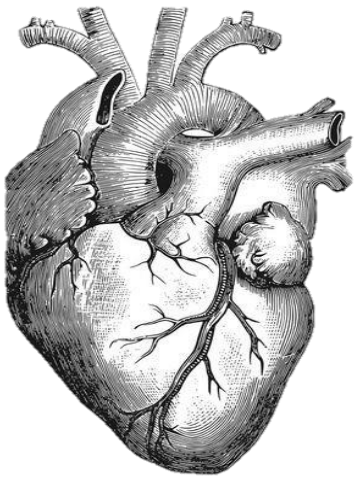
Pharmacology
Team 437

MED437
KING SAUD UNIVERSITY



Drugs of Cardiovascular Block

Important Notes Extra

Drugs of Cardiovascular Block

Drug	Key Point	Contraindications
Adrenergic Blockers & α Receptors Antagonists		
Adrenergic neuron blockers		
α-Methyl dopa (Formation of False Transmitters + Stimulation of presynaptic α2 receptors)	Treatment of hypertension in pregnancy	-
Reserpine	Depletion of storage sites	-
Guanethidine	Inhibition of release & enhance uptake	-
Clonidine	uses: - -Management of withdrawal symptoms -Hypertension complicated with renal disease -resistant hypertension ADRs: causes rebound hypertension	-
Apraclonidine	Used in open angle glaucoma as eye drops	-
Non-selective antagonists		
Phenoxybenzamine (irreversible)	Therapeutic Use: Pheochromocytoma Cause: - Vasodilation of blood vessels - Decrease peripheral vascular resistance - Postural hypotension - Increase CO - Reflex tachycardia. - Increase in GIT motility & secretions ADRS: male sexual dysfunction&headache	Patients with decreased coronary perfusion.
Phentolamine (reversible)		
Selective α1 adrenoceptor antagonists		
Prazosin (short half-life)	Therapeutic Uses: - Treatment of hypertension - Urinary retention associated with benign prostatic hyperplasia - Reynaud's disease	-
Doxazosin (long half-life)		-
Terazosin (long half-life)		-

Drugs of Cardiovascular Block

Selective $\alpha 1_A$ adrenoceptor antagonists

Drug	Key Point	Contraindications
Tamsulosin	Therapeutic Uses : - Treatment of benign prostatic hypertrophy - Help with the passage of kidney stones	-

Selective α2 adrenoceptor antagonists

Yohimbine	Used as aphrodisiac in the treatment of erectile dysfunction.	-

B Blockers

Non selective drugs (block B1 and B2)

Propranolol	Block Na channels(Antiarrhythmic like action). -Has local anesthetic effect -NO ISA USES: -Hypertension -anxiety (Social and performance type) -Pheochromocytoma(with a blockers "never alone") -chronic glaucoma -tremor -angina -Migraine headache prophylaxis -arrhythmia -Myocardial infarction -Thyrotoxicosis	-Bronchial Asthma,COPD -Raynaud's phenomenon & peripheral vascular disease (PVD). -Diabetics/ dyslipidemias -Variant Angina (coronary spasm) ^^ PREFERABLE TO USE BETA 1 BLOCKER in hypertensive patients with these complications
Sotalol	-	
Timolol	glaucoma as eye drops	
Pindolol	-	

Drugs of Cardiovascular Block

Selective drugs(block B2)

Drug	Key Point	Contraindications
Atenolol	uses: Hypertension arrhythmia Myocardial infarction	-
Bisoprolol	USES: supraventricular & ventricular arrhythmias Hypertension Congestive heart failure Myocardial infarction	
Metoprolol	USES: Hypertension Congestive heart failure Myocardial infarction	
Esmolol	USES: arrhythmia(ultra short acting)	
Acebutolol	-	

Mixed a and B receptors blockers

Carvedilol	-NO ISA and no anesthetic effect -has Antioxidant action USES: -Congestive heart failure -Hypertensive crisis ADRs: Orthostatic hypotension, Edema	-
Labetalol	-With intrinsic sympathomimetic activity (ISA) -block Na channels(Antiarrhythmic like action) has local anesthetic effect USES: -hypertension in pregnancy -Severe hypertension in pheochromocytoma -Hypertensive crisis (e.g. during abrupt withdrawal of clonidine). ADRs: Orthostatic hypotension, sedation & dizziness	-

Drugs of Cardiovascular Block

Antiarrhythmic Drugs

Drug	Key Point	Contraindications
Class I drugs-Na channel blockers(Membrane stabilizing)		
Class IA (slow phase 0,4 + prolong action potential + slow conduction)		
Quinidine	-Use: Atrial flutter & fibrillation & ant-malaria -anticholinergic and a-adrenergic blocking effects -prolongs PR & QT interval (prolongation of QT is the cause of the following ADR) , widens QRS complex. -ORAL -ADRs: quinidine syncope due to torsades de pointes arrhythmia (at regular dose), anticholinergic ADRs "dry mouth + constipation" & hypotension.	-
procainamide	-Use: ventricular arrhythmia more than atrial arrhythmias -NO anticholinergic & a-blocking actions(so less toxic on heart) -ADRs: causes reversible lupus erythematous-like syndrome(SLE) torsades de pointes arrhythmia (at toxic dose)	-
Class IB (slow phase 0,4 & shorten action potential)		
Lidocaine	Use: Treatment of emergency ventricular arrhythmias (during surgery +following acute MI) NOT **effective orally** (Given I.V bolus/slow infusion) ADRs: hypotension/convulsions/Dysarthria	NOT effective in atrial arrhythmias
Mexiletine	Use: Ventricular arrhythmia & Digitalis-induced arrhythmias **effective orally** ADRs:hypotension/Nausea/vomiting/diplopia	-
Class IC (markedly slow phase 0 & slow phase 4)		
Flecainide	-Use:supraventricular arrhythmia/ Wolff-parkinson-white syndrome/ventricular arrhythmia -ADRs: Pro-arrhythmia/heart failure due to -ve inotropic effect / tremor / dizziness .	-

Drugs of Cardiovascular Block

Class II (Brenoceptors Blockers " slow conduction")

Drug	Key Point	Contraindications
Esmolol	Uses: given I.V. for rapid control of ventricular rate in patients with atrial flutter or fibrillation	-
Propranolol , Atenolol, Metoprolol	Used in patients who had myocardial infarction to reduce incidence of sudden death to ventricular arrhythmias	-

Class III (Drugs that prolong action potential duration)

Amiodarone	- prolongs RP, has additional class Ia, II & IV effects - Main use: serious resistant ventricular arrhythmias, WPW -many ADRs "patients should avoid sunlight" -active metabolite: N-desethylamiodarone	-Pregnant women - Breastfeeding women - with enzymes inducers or inhibitors (CYP3A4,CYP2C8) due to drug interaction
Ibutilide (Pure class III)	- Used for the acute conversion of atrial flutter or fibrillation to normal sinus rhythm - Causes QT interval prolongation **(may cause torsades de pointes).**	-

Class IV (Ca channel blockers)

Verapamil **Diltiazem**	-main site of action is A.V.N & S.A.N cause: slowing of conduction & prolongation of ERP Uses: atrial arrhythmias - WPW	NOT effective in ventricular arrhythmias.

Other drugs for Arrhythmia

Adenosine	-drug of choice for acute management of paroxysmal supraventricular tachycardia -half-life = less than 10 sec ADRs: shortness of breath , chest burning & brief AV block	- asthma patients - heart block

Drugs of Cardiovascular Block

Drug	Key Point	Contraindications
Dronedarone (New Antiarrhythmic Drugs)	- has antiarrhythmic properties belonging to all four classes - Used for maintenance of sinus rhythm following cardioversion in patients with atrial fibrillation	- NOT be used in patients with severe (class IV) heart failure. - NOT be used in patients with permanent atrial fibrillation
Bradyarrhythmias		
Atropine	Uses: sinus bradycardia after myocardial infarction & in emergency heart block with isoprenaline (with caution)	-
Drug Therapy of Heart Failure		
Class I (Drugs that decrease preload)		
Diuretics (reduce salt and water retention)		
Chlorothiazide	First line agent in HF therapy Used in: 1-volume overload 2- mild congestive HF	-
Furosemide	-Potent diuretic -Used for Immediate reduction of pulmonary congestion & severe edema,associated with: acute HF,moderate & severe chronic failure	-
Aldosterone antagonists		
Spironolactone	-Non selective -Potassium sparing diuretic -Improve survival in advanced HF	-

Drugs of Cardiovascular Block

Drug	Key Point	Contraindications
Eplerenone	-Selective -Does not inhibit other hormones such as estrogen & androgen -improve survival of stable patients w/ congestive HF	-
Venodilators		
-Nitroglycerin -Isosorbide dinitrate	-Used IV for severe HF when main symptom is dyspnea -Dilates venous blood vessels & reduce preload	-
ClassII Drugs that decrease afterload (Arteriodilators)		
Hydralazine	-Used when main symptom is rapid fatigue due low CO -Reduce peripheral vascular resistance	حيدر الزين، بما انه زين فخدوده حمراء ويأثر على الارتريز "لونها احمر" الخدود الحمراء = ADR Lupus erythematosus like syndrome
Class III (Drugs that decrease both preload & afterload)		
ACE inhibitors (first-line in HF & Hypertension)		
Captopril	- rapidly absorbed from GIT after oral administration - food reduce their bioavailability ADR: - acute renal failure - hyperkalemia (especially in patients with renal insufficiency or diabetes) - severe hypotension in hypovolemic patients (due to diuretics, salt restriction or gastrointestinal fluid loss) - dry cough - angioneurotic edema - dysgeusia (reversible or altered taste)	- during the second & third trimesters of pregnancy (due to the risk of : fetal hypotension renal failure & malformations) - renal artery stenosis
Enalapril		
Ramipril		
active metabolites ونصيرون prodrugs لازم ينضجون فهم (Enala)، وبما انهم بزران ويتهاوشون (capto)اخته اينالا (Rami)كَبَت رامي		

Drugs of Cardiovascular Block

Drug	Key Point	Contraindications
Enalapril **Ramipril**	- prodrugs, converted to their active metabolites in liver - have long half-life & given once daily (Same ADR of previous)	(Same Contra. of previous)
Angiotensin receptor blockers (ARBs)		
Losartan **Valsartan** **Irbesartan**	**M.O.A:** - block AT_1 receptors - decrease action of angiotensin II	لو نجمع اول مقطع من كل درق يصير Lov al irbe انا احب العربي :)
α-Adrenoceptor Blockers		
Prazosin	- blocks α- receptors in arterioles and venules - decrease both afterload & preload	-
Direct acting vasodilators		
Sodium nitroprusside	- given I.V. for acute or severe heart failure - acts immediately and effects lasts for 1-5 min.	-
Class IV (Drugs that increase contractility) (+ve inotropic effect)		
β-adrenoceptor agonists		
Dobutamine	- Selective β1 agonist - **Uses:** Treatment of acute heart failure in cardiogenic shock.	-

Drugs of Cardiovascular Block

Cont: **Class IV** (Drugs that increase contractility)

Drug	Key Point	Contraindications
Cardiac glycosides (digitalis)		
Digoxin	-**M.O.A:** Inhibit Na+ / K+ ATPase enzyme **Therapeutic uses:** 1-Congestive heart failure (has narrow therapeutic index) **ADR:** 1-**(Cardiac):** **digitalis-induced arrhythmias:** extrasystoles - coupled beats (Bigeminal rhythm) - ventricular tachycardia or fibrillation - cardiac arrest **2-(GIT):**anorexia, nausea, vomiting, diarrhea **3-(CNS):**headache, visual disturbances, drowsiness. **Factors that increase its toxicity:** Renal diseases - Hypokalemia - Hypomagnesemia - Hypercalemia	-
phosphodiesterase -III inhibitors		
Milrinone	**M.O.A:** - Increase cardiac Contractility - dilatation of arteries & veins (reduction of preload & afterload) **Therapeutic uses:** - used only **IV** for management of acute heart failure - not safe or effective in the longer (> 48 hours) treatment of patients with heart failure. **ADR:** Hypotension and chest pain (angina)	furosemide"class I" should not be administered in I.V. lines containing milrinone due to formation of a precipitate (Due to chemical interaction)
Enoximone + Vesnarinone	new drugs in clinical trials.	-

Drugs of Cardiovascular Block

B adrenoceptors blockers

Drug	Key Point	Contraindications
Bisoprolol, Metoprolol	-Second generation: cardioselective (β1-receptors) -reduce the progression of **chronic** heart failure -attenuate cardiac remodeling	**not** used in **acute** heart failure.
Carvedilol , Nebivolol.	-Third generation: have vasodilator actions (α- blocking effect) -reduce the progression of **chronic** heart failure. -attenuate cardiac remodeling	

New drugs

Nesiritide (Natriuretic Peptides group)	-Purified preparation of human BNP - indicated (IV) for the treatment of patients with acute decompensated heart failure (ADHF) who have dyspnea at rest or with minimal activity.	-
Levosimendan (Calcium sensitisers group)	-used in the **management** of ADHF -Calcium sensitization (improves cardiac contractility without increasing oxygen consumption) - potassium-ATP channel opening (cause vasodilation, improving blood flow to vital organs)	-

Drugs of Cardiovascular Block

Antihypertensive drugs

Drug	Key Point	Contraindications
1-Diuretics		
Hydrochloro-thiazide Chlorthalidone	-mild to moderate hypertension MOA: initial diuresis lasts 4-6 weeks and then replaced by a decrease in PVR	
Furosemide	Loop diuretic are useful in hypertensive patients with either renal impairment or heart failure(edema)	
2-Drugs acting on the renin- angiotensin-aldosterone (RAAS) system		
Angiotensin-converting enzyme inhibitors (ACEIs)		
Enalapril **Lisinopril** **Ramipril** **Captopril**	- The antihypertensive effect of ACE inhibitors results primarily from vasodilatation with little change in cardiac output effective when hypertension results from excess renin production. - Hypertension in patient with **chronic renal disease,ischemic heart disease,diabetes.** -ADRS Dry cough,Angioneurotic edema.First dose effect (severe hypotension). - adrs specificto **captopril** Dysgeusia (reversible loss or altered taste). Proteinuria and neutropenia.	-Renal artery **stenosis.** -**Potassium-sparing** diuretics. -During the second and third trimesters of **pregnancy** due to the risk of: fetal hypotension,anuria ,renal failure& malformations.

Drugs of Cardiovascular Block

Drug	Key Point	Contraindications
Angiotensin receptors blockers (ARBs)		
Losartan **Valsartan** **Candesatran** **Telmisartan**	-Cause selective block of AT1 receptors. -No effect on bradykinin, no cough,no angioedema. -Produce more,complete inhibition of angiotensin as,there are other enzymes(not only ACE) that can generate angiotensin. **Losartan**; Has a potent active metabolite,Long half-life,taken once daily, Orally effective,Do not cross BBB. **Valsartan**; No active metabolites.	Same contraindicat-ions as ACEI.
3- Calcium Channel Blockers		
Very Nice Drugs Verapamil - Nifedipine - Diltiazem		
Verapamil **Nifedipine** **Diltiazem**	-**Verapamil** acts more on myocardium. -Dihydropyridine group act mainly on smooth muscle, **Nifedipine** -**Diltiazem** has intermediate effect **M.O.A:** -peripheral vasodilatation -decrease cardiac contractility. **P.K:** - **verapamil** and **nifedipine** are highly bound to plasma proteins while **diltiazem** is less. -**verapamil** & **diltiazem** have active metabolites but **nifedipine** has not. **Uses:** -treatment of chronic hypertension. -**nicardipine** can be given by I.V. route in hypertensive emergency. **ADRs:** -**nifedipine:** Tachycardia -**verapamil:** constipation -**verapamil & diltiazem:** peripheral edema	-

Drugs of Cardiovascular Block

Drug	Key Point	Contrain dications
Vasodilators(IMPORTANT)		
Hydralazine	MOA:Direct on SM ADRs: lupus erythematosus like syndrome Uses: hypertensive pregnant woman(2nd line)	
Minoxidil	MOA:opening of K channels in SM membranes by minoxidil sulfate(ACTIVE METABOLITE) Uses: baldness ADRs: hypertrichosis	females
Diazoxide	MOA:opening of K channels Uses: treatment of hypoglycemia due insulinoma ADRs: hyperglycemia	diabetics
Sodium Nitroprusside	MOA: Arterio&venodilator Uses: severe heart failure ADRs: severe hypotension Methomoglobin during infusion cyanide toxicity /thiocyanate toxicity	
4-Sympatholytic Drugs		
β-adrenoceptor blockers		
Propranolol (Non-selective)	-used in mild to moderate hypertension, In severe cases used in combination with other drugs. -May take two weeks for optimal therapeutic response -Evidence support the use of ß-blockers in patients with concomitant coronary artery disease -When discontinued, ß- blockers should be withdrawn gradually -M.O.A lower BP by: -Decreasing cardiac output -Inhibiting the release of renin -Central mechanism ADRs: Fatigue, Hypoglycemia, Mask the symptoms of hypoglycemia in diabetes, Increased triglycerides, Aggravate peripheral arterial disease, Erectile dysfunction	**Diabetics and Asthma patients**
Atenolol (Selective)		
Metoprolol (Selective)		

Both Drugs in hypertensive emergency

Drugs of Cardiovascular Block

Drug	Key Point	Contraindications
α Adrenoceptor blockers (in arterioles & venules)		
Prazosin **Doxazosin** (Preferred Long half-life)	-Reduce blood pressure by decreasing both afterload & preload **Prazosin**, short- acting causes first dose hypotension & postural hypotension	-
Centrally- acting		
Clonidine	-α2-agonist, diminishes central adrenergic outflow & ↑ parasympathetic outflow -Abrupt withdrawal may lead to rebound hypertension -Does not decrease renal blood flow or glomerular filtration -Useful in the treatment of hypertension complicated by renal disease and resistant hypertension	-
α- methyldopa	-An α- 2 agonist, is converted to methyl noradrenaline centrally to diminish the adrenergic outflow from the CNS -Lead to reduced total peripheral resistance, and a decrease in blood pressure -first line treatment of hypertension in pregnancy	

Drugs of Cardiovascular Block

Thrombolytic drugs

Drug	Key Point	Contraindications
Non fibrin-specific thrombolytic drugs		
Streptokinase	-acts indirectly by forming plasminogen-streptokinase complex(THE ONLY INDIRECTLY ACTING plasminogen activator) -Given by IV infusion -It is the least expensive. -ADRs: Antigenicity/Allergic reactions//Bleeding	Not used in patients with: Recent streptococcal infections or Previous administration of drug due to antistreptococcal antibodies.
Anistreplase	-Anisoylated Plasminogen Streptokinase Activator Complex (APSAC) -prodrug, de-acylated in circulation & active -Given as a bolus I.V. (Longer duration) -More thrombolytic activity, greater selectivity. **ADRS:** like streptokinase but to lesser degree -more expensive than streptokinase	could be the same(?)
Urokinase	-Human enzyme synthesized by the kidney(embryonic cell) & urine -given by I.V infusion. -Used in **acute** massive pulmonary emboli. -no anaphylaxis. **Disadvantages:**-Minimal fibrin specificity/Systemic lysis /Expensive	-

Drugs of Cardiovascular Block

Fibrin specific agents thrombolytic drugs

Alteplase.	-They activate fibrin-bound plasminogen rather than free plasminogen in blood. -They bind to fibrin in a thrombus and convert the entrapped plasminogen to plasmin followed by activated local fibrinolysis with limited systemic fibrinolysis. -Reduced risk of bleeding -Not-antigenic (**can be used in patients with recent streptococcal infections or antistreptococcal antibodies**).	-**use:** ➢ In ST-elevation myocardial infarction (STEMI) ➢ Pulmonary embolism.
Reteplase		
Tenecteplase		-It is only approved for use in acute myocardial infarction. - It is more fibrin-specific & longer duration than alteplase.

Fibrinolytic Inhibitors (Antiplasmins)

inhibit plasminogen activation & inhibit fibrinolysis and promote clot stabilization.

-Aminocaproic Acid **-Tranexamic Acid** **(competitive inhibition)**	**Uses:** -Adjuvant therapy in hemophilia -Fibrinolytic therapy-induced bleeding (antidote) -Post-surgical bleeding	-
Aprotinin **(plasmin antagonist)**		

Drugs of Cardiovascular Block

hyperlipidemia

Agents targeting exogenous cholesterol

Bile Acid Sequestrants (Resins)
(form an insoluble complex with bile acids and salts, preventing their reabsorption from the intestines)

Colestipol **Cholestyramine** **Colesevelam**	- prevents enterohepatic cycling of bile acids - obligates the liver to synthesize replacement bile acids from cholesterol -increase LDL receptors to obtain more cholesterol - decrease serum LDL-C - Excellent choice for people that cannot tolerate other types of drugs ADRs: - constipation - Decreased absorption of fat soluble vitamins (A,D, K) - The concentration of HDL-C is unchanged - Colesevelam is a better choice for patients on multiple drug regimens. (Doesn't affect their absorption, unlike other two)	- Complete biliary obstruction - Chronic constipation - Severe hyper-triglyceridemia

Cholesterol Absorption Inhibitors

Ezetimibe	- reduces C absorption and it's flux from intestine to the liver. - reduced flux of C to VLDL particles will lower LDL-C. - reduce LDL ,TG / increases HDL slightly -Absorbed & conjugated in intestine to active glucuronide - lowering LDL will = prevention of low risk CHD (As monotherapy) **- As combination therapy:** -With statins:synergistic in moderate/severe increase in LDL - Or If must lowering statin dose because of side effects - Or with other lipid lowering drugs; as fibrates	-

Drugs of Cardiovascular Block

Drug	Key Point	Contraindications
HMG-Co reductase inhibitors		
Statins	Statins are considered as first-line drugs when lowering LDL -PLEIOTROPIC EFFECTS: cardioprotective -Pravastatin and fluvastatin are the statins of choice in patients taking other drugs metabolized by cytochrome 3A4 system. -orally at bedtime because of hepatic C synthesis except atorvastatin taken at any time because of its long half-life -Used alone or with antihyperlipidemic drugs(ezetimibe) -Combination therapy in mixed dyslipidaemias (added to fibrates or niacin) & in diabetics and patients with insulin resistance -given from the 1st day of ischemic attack & in Type IIa Hyperlipoprotinemia. ADRs: Teratogenicity Hepatotoxicity, raised concentrations of liver enzymes (serum **aminotransferases**) Myopathy (increased ck) discontinue lead to rhabdomyolysis	-Pregnant -Drugs that increase the risk of statin-induced myopathy include: ➢ Other antihyperlipidemics (fibrates) ➢ Drugs metabolized by 3A4 isoform of cytochrome P450: erythromycin, verapamil, cyclosporin, ketoconazole
Niacin (Nicotinic Acid)		
Niacin	- Niacin is the most effective medication for increasing HDL **-M.O.A:** 1- In adipose tissue: binds to adipose nicotinic acid receptors will lead to decrease in free fatty acids resulting in TG and thus VLDL synthesis 2- In liver: diacylglycerol acyltransferase-2, akey enzyme for TG synthesis so it will decreases VLDL production (decreased TG synthesis and estrification) 3- In plasma: it increases LPL activity that increases clearance of VLDL & chylomicron. **-ADRs:** cutaneous flushing - GIT disturbances" Dyspepsia , nausea , vomiting & reactivation of peptic ulcer" -**Uses:** - type IIa, IIb hypercholesterolemia & any combined hyperlipidemia - patient with hypertriglyceridemia & low HDL-C	-Gout -Peptic ulcer -Hepatotoxicity -Diabetes mellitus -pregnancy

Drugs of Cardiovascular Block

Drug	Key Point	Contraindications
Fibrates		
-Clofibrate **-Gemfibrozil** **-Fenofibrate**	-intracellular metabolism receptors that modulate fat -They **increase genes transcription for lipoprotein lipase (LPL)** leading to increased catabolism of TG in VLDL and chylomicrons. -Increased risk of myopathy when combined with statins. -Displace drugs from plasma proteins (e.g. oral anticoagulants and oral hypoglycemic drugs) -1st-line defense for Patients with low HDL and high risk of atheromatous disease (often type 2 diabetic patients) -**ADRS:** -Myalagia, Myositis, Rhabdomyolysis Acute renal failure Occurs > -In alcoholics, -If combined with statins -Or In impaired renal function -Gallstones (especially Clofibrate so its use is limited to patients who have cholecystectomy)	• Patients with impaired renal functions • Pregnant or nursing women • Preexisting gall bladder disease
Adjuvants in hyperlipidemia		
Omega -3-FA	**-M.O.A:** enzymes involved in TG synthesis. beta-oxidation of FFA platelet function Prolongation of bleeding time Anti-inflammatory effects **-Uses:**Approved as adjunctive for treatment of very high TGs	-
β-Sitosterol	**-M.O.A:** Compete with dietary & biliary C absorption levels LDL levels **-Uses:** Given as food supplement before meal in hypercholesterolemia	

Drugs of Cardiovascular Block

Angina

Drug	Key Point	Contraindications
Organic Nitrates		
Isosorbide mononitrate or dinitrate Nitroglycerin	**-M.O.A:** Nitric oxide binds to guanylate cyclase in vascular smooth muscle cell to form cGMP, cGMP activates PKG to produce relaxation. **-Hemodynamic effects:** *Venous vasodilation (Decrease the preload) *coronary vasodilation (Increase the myocardial perfusion) *Arterial vasodilation (decrease afterload) *Shunting of flow from normal area to ischemic area by dilating collateral vessels. **-Uses:** ***isosorbide mononitrate or dinitrate "in stable angina":** Persistent prophylaxis - Congestive Heart Failure - when there is ACE inhibitor contraindications ***nitroglycerin"in stable angina":**Acute symptom relief - Situational prophylaxis - In variant angina (sublingual) - In unstable angina (IV) - Acute Heart Failure-Refractory AHF,and AMI (IV) **ADRs:** -Throbbing headache -Flushing in blush area -Postural hypotension, dizziness & syncope-Tachycardia & palpitation -Rarely Methemoglobinemia	-sensitivity to organic nitrates. - Glaucoma - Head trauma or cerebral haemorrhage - Uncorrected hypovolemia. - Concomitant administration of PDE_5 Inhibitors. -Sildenafil + nitrates = severe hypotension & death **If Tolerance develops:** give smaller doses at longer intervals (Nitrate free periods twice a day) & drugs that maintain tissue SH group e.g.Captopril.

Drugs of Cardiovascular Block

Calcium channel blockers (low Ca = Relaxation)

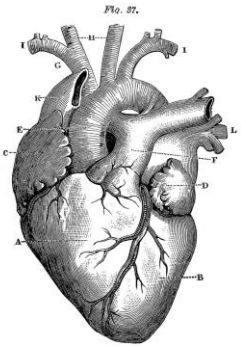
Dihydropyridines: **-Nifedipine** (Vascular smooth muscle) **-Nicardipine** **-Amlodepine**	**Antianginal Action:** - (**verapamil** & **diltiazem**) ↓ Cardiomyocyte Contraction > ↓ cardiac work (-ve ino/chronotropic) > ↓ myocardial O_2 demand - ↓ VSMC contraction > ↓ afterload > ↓ cardiac work > ↓ myocardial O_2 demand - Coronary dilatation>↑myocardial O_2 supply **Uses:** **- Variant Angina**> Attacks prevented (>60%) /sometimes variably aborted **- Unstable Angina**> Seldom added in refractory cases **- Stable Angina**> Regular prophylaxis	-
Phenylalkylamines: **-Verapamil** (cardiomyocytes)		
Benzthiazepines: **-Diltiazem** (intermediate)		

β Adrenergic Blockers

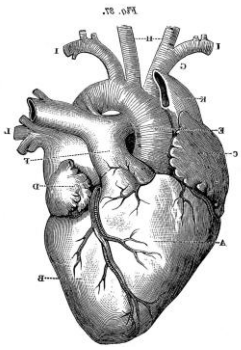
Atenolol, Bisoprolol , Metoprolol	-**Decrease heart rate & contractility** thus: 1- Increase duration of diastole >increase coronary blood flow >increase oxygen supply 2-Decrease workload > Decrease O2 consumption. **-use**: Stable ,unstable angina and Myocardial infarction .	-variant **Contraindicated**

Drugs of Cardiovascular Block

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 -Prophylactic 2nd line therapy in stable angina -Refractory variant angina	-**ADRS** Flushing,headache, Hypotension, palpitation, weakness Mouth & peri-anal ulcers, nausea and vomiting.
Metabolically acting agents		
Trimetazidine	shift oxidation to glucose instead of free fatty acids to reduce oxygen demand of heart no haemodynamic effect+add-on therapy	Hypersensitivity pregnancy & lactation
Ranolazine	inhibits late Na current which increase during ischemia -used in chronic angina patients w/other drugs	-in class Ia & III antiarrhythmics -toxicity develop due interaction with CYT450 inhibitors
Ivabradine	treatment of chronic stable angina in patients with normal sinus rhythm who can't take b-blockers + with b-blockers in heart failure with LVEF < 35% and HR>70 -in combination with b blockers in heart failure	



"It is not hard, you just made it to the end!"



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References:

✓ Doctors' notes and slides

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