UNIT-V

Cardiovascular System (CVS)

Prototype Drugs Affecting The CVS

In this chapter we will discuss the prototype drugs used in major diseases of CVS.

Major Diseases Related To Cardiovascular System

1. **Heart Failure**
2. **Arrhythmias**
3. **Angina**
4. **Hypertension**

Now we will discuss prototype drugs of each disease.

Heart Failure

Heart is a unique organ that starts functioning before birth and continues till the death occurs. Heart acts as a pump to supply blood and thus oxygen and nutrients to all the body tissues.
Heart failure is a complex, progressive disorder in which the heart is unable to pump sufficient blood to meet the needs of the body. HF is due to the impaired ability of the heart to properly fill with blood or eject blood. It is often due to abnormal increases in blood volume and interstitial fluid.

Prototype Drugs Used To Treat Heart Failure

Renin Angiotensin System Blockers
➔Captopril (ACE inhibitor)
➔Losartan (angiotensin receptor blockers)

B-Blockers
➔Propranolol

Diuretics
(See in Genito Urinary System)

Direct Vasodilators
➔Sodium nitroprusside

Inotropic Agents
➔Digoxin/Digitalis

Available Brands in the Market

Capotein Tab. (Captopril)
Losar-k, Tab. (Losartan)
Losartan Tab. (Losartan)
Inderal Tab. (Propranolol)
Betanol Tab. (Propranolol)
Spiromide Tab. (Spironolactone)
Aldactone Tab. (Spironolactone)
Digox Tab. (Digoxin)

Captopril (ACE Inhibitors)

Captopril is ACE inhibiters agents that block the ACE activity. As ACE convert angiotensin-I into angiotensin-II, which is a powerful vasoconstrictor.
These agents also diminish the rate of bradykinin inactivation, which is a vasodilator.

Action On Heart
Captopril and other ACE inhibitors decrease vascular resistance and blood pressure.

Adverse Effect
Dry cough, abdominal pain, skin rash, hypotension, and renal insufficiency. ACE inhibitor should not be used in pregnant women, because they are fetotoxic.

Pharmacokinetics
ACE inhibitors absorbed in GIT. The presence of food may decrease absorption so they should be given empty stomach except for Captopril.

Losartan (Angiotensin Receptor Blocker)

Losartan and other angiotensin receptor blockers are competitive antagonist of angiotensin type 1 receptor (AT1 receptor).
Losartan have the advantage of more complete blockade of angiotensin action. These agents do not affect bradykinin level.

Action On CVS
All the angiotensin receptor blockers approved for treatment of hypertension. This agent is very useful in HF as they reduce the blood pressure.

Pharmacokinetics
All drugs are orally active and require only once a day dosing. Losartan undergoes extensive first pass hepatic metabolism. All drugs are highly plasma protein bound.

Adverse effects
Angiotensin receptor blockers have similar adverse effect of ACE inhibitor. However angiotensin receptor blockers do not produce cough.

Propranolol (B-Blockers)

See, B-Blocker prototype drug in adrenergic antagonist chapter.

Diuretics

(See in Genito Urinary System)

Sodium Nitroprusside (Direct Vasodilators)

Vasodilators are used in the treatment of heart failure and hypertension. Vasodilators cause relaxation of smooth muscle of blood vessels by direct action. Sodium Nitroprusside is a mixed vasodilator.

Pharmacological Action
Sodium Nitroprusside is an emergency drug, which, acts directly to relax smooth muscle of both arterioles' and veins.

Pharmacokinetics
Onset of action occurs within 1 minute of intravenous administration.

Therapeutics Uses
Sodium Nitroprusside is used for treatment of heart failure and hypertension.

Adverse Effects
Headache, nausea, vomiting

Inotropic Agents (Digoxin or Digitalis)

Positive Inotropic agents enhance cardiac muscle contractility and thus increase cardiac output.

Mechanism Of Action

These agents increase cytoplasmic calcium concentration that enhances the contractility of cardiac muscle.

Pharmacological Action Of Digitalis

Digitalis has direct and indirect action on cardiovascular. The important actions are increasing contractility, conductivity and rate of the heart. Digitalis increases the cardiac output.

Therapeutic Uses

Digitalis is used for treatment of congestive heart failure. The drug is effective in right, left or both ventricular failures. In badly damaged heart the drug may not be so effective.

Adverse Effects

Nausea, vomiting, headache, blurred vision

Antianginal Drugs

Angina pectoris (pain or discomfort in the chest),(pectoris= chest or breast) is on of the major symptoms of heart disease. It is sudden, severe, pressing chest pain radiating to the neck, jaw and arms. It is caused by coronary blood flow that is insufficient to meet the oxygen demand of the myocardium leading to ischemia.

Types Of Angina

Angina occurs in the following forms

1. **Stable Angina/ Typical Angina**
2. **Unstable Angina**
3. **Variant Angina**

Stable Angina

It is the most common form of angina and therefore is called typical angina pectoris. It is characterized by a burning and heavy feeling in the chest. It is produced by physical activity, emotional excitement or any other cause of increased cardiac workload. Typical angina pectoris is promptly relieved by rest or nitroglycerin (a vasodilator).

Unstable Angina

Unstable angina lies between stable angina and myocardial infarction. In unstable angina chest pains occur with increased frequency. The symptoms are not relieved by rest or nitroglycerin. Unstable angina requires hospital admission.

Variant Angina

Variant angina is an uncommon pattern of episodic angina that occurs at rest and due to coronary artery spasm. Symptoms are caused by decreased blood flow to the heart muscles due to the spasm of coronary artery. Variant angina relieved by coronary vasodilators such as nitroglycerine and calcium channel blockers.

Antianginal Prototype Drugs

Organic Nitrate
➔Nitroglycerine

B-Blockers
➔Propranolol

Ca2+ Channel Blockers
➔Verapamil

Available Brands in the Market

Angised Tab. (Nitroglycerine)
Cardnit Tab. (Nitroglycerine)
Inderal Tab. (Propranolol)
Betanol Tab. (Propranolol)
Calan Tab. (Verapamil)

Nitroglycerine (Organic Nitrates)

Organic nitrates and nitrites used in the treatment of angina pectoris. These are simple nitric and nitrous acid esters of glycerol. These compounds cause a rapid reduction in myocardial oxygen demand, followed by rapid relief of symptoms. They are effective stable and unstable angina as well as in variant angina pectoris.

Pharmacological Effect
Nitrates decrease coronary vasoconstriction or spasm and increase blood flow by relaxing coronary arteries. In addition they relax veins, decreasing preload and myocardial oxygen consumption. Nitroglycerine, which is also known as glyceryl trinitrate, relaxes vascular smooth muscle by their intracellular conversion to nitrite ions and then to nitric oxide.

Pharmacokinetics
Nitroglycerine is commonly given by sublingually or via a transdermal patch because it has significant first pass metabolism.

Adverse Effects
The most common adverse effect of nitroglycerine and other organic nitrates are headache, postural hypotension, facial flushing and tachycardia.

Propranolol (B-Blockers)

(See in Adrenergic Antagonists)

Verapamil (Ca2+ Channel Blockers)

(See in Antiarrhythmic)

Antiarrhythmic Drugs

Any cardiac rhythm other than the normal is called arrhythmia. For example cardiac arrhythmias may cause the heart to beat too slowly (bradycardia) or to beat too rapidly (tachycardia) or to beat irregularly.

Causes Of Arrhythmias
Most arrhythmias arise due to abnormal automaticity or due to defect in impulse conduction.

Prototype Drugs

Class I (Na+ channel blockers)
➔Quinidine

Class II (B-Adrenoceptor blockers)/ B-Blockers
➔Propranolol

Class III (K+ channel blockers)
➔Amiodarone

Class IV (Ca2+ channel blockers)
➔Verapamil

Available Brands in the Market

Inderal Tab. (Propranolol)
Betanol Tab. (Propranolol)
Cordarone Tab. (Amiodarone)
Sedacoron Tab. (Amiodarone)
Calan Tab. (Verapamil)

Quinidine (Class-I Anti Arrhythmic Drug Or Na+ Channel Blockers)

Quinidine is an alkaloid and shows many of the action of quinine such as anti malarial, antipyretic, depression. The action on the heart is more marked and specific as compared to quinine.

Pharmacological Action
In general quinine is a cardiac depressant. It decreases automaticity, excitability and conduction velocity and depressed contractility.

Mechanism Of Action
Quinidine blocks sodium channels. It reduces the maximal rate of depolarization (phase o) depresses spontaneous phase 4 diastolic depolarization slow conduction and prolong the effective refractory period of arterial and ventricular.

Therapeutic Uses
Quinidine is used in the treatment of a wide variety of arrhythmias.

Pharmacokinetics
Quinidine is rapidly and almost completely absorbed after oral administration. It undergoes extensive hepatic metabolism forming active metabolites.

Adverse Effects
Quinidine may cause SA and VA block or a systole. At toxic level the drug may induce ventricular tachycardia. Nausea, vomiting and diarrhea are commonly observed.

Propranolol (Class-II, B-Adrenoceptor Blocker)

See in Adrenergic Antagonists

Amiodarone (Class-III, K+ Channel Blockers)

Action
Amiodarone contains iodine and is related structurally to thyroxin. It has complex effect showing class I, II, III and IV actions.
Its dominant effect is prolongation of the action potential duration and the refractory period. Amiodarone has anti anginal as well as anti arrhythmic activity.

Therapeutic Uses

Amiodarone is effective in the treatment of severe refractory supra ventricular and ventricular trachy arrhythmias. Despite its side effect Amiodarone is the most commonly employed antiarrhythmic.

Pharmacokinetics

Amiodarone is incompletely absorbed after oral administration. The drug is unusual in having prolonged half-life of several weeks and it distributes extensively in adipose tissue.

Adverse Effects

Amiodarone shows a variety of toxic effects. Some common side effects are GIT disturbance, tremor, dizziness, lover toxicity, photosensitivity, muscle weakness, skin discoloration caused by iodine accumulation in the skin.

Verapamil (Class-IV, Ca2+ Channel Blockers)

Mechanism Of Action

Verapamil inhibits slow channel calcium ion transport across the myocardial cell membrane it also reduces intracellular calcium concentration in smooth muscle cells of the coronary and peripheral vasculature.

Pharmacological Action

Verapamil depress SA and AV nodal functions. Slow AV conduction is its major action making it useful as anti arrhythmic agent. It reduces coronary and peripheral vascular resistance. It increases coronary blood flow. Verapamil increases myocardial oxygen supply by increasing coronary blood flow. Simply we can say Verapamil has anti arrhythmic, anti anginal and antihypertensive properties.

Pharmacokinetics

Verapamil is rapidly and almost completely absorbed after oral administration. It undergoes extensive first pass metabolism in the liver. It is highly bound by plasma proteins. Its half-life is 3 to 6 hours.

Therapeutics Uses

Verapamil is more effective in the treatment of arterial arrhythmias than ventricular arrhythmias. It is also very useful in the treatment of angina pectoris and hypertension.

Adverse Effects

Constipation is the most common side effect. Nausea, vomiting, headache, weakness and gastric disturbance may occur when given IV; Verapamil may cause severe hypotension, and bradycardia.

Antihypertensive

Hypertension is group of symptoms, characterized by elevated blood pressure. Cardiac output and total peripheral resistance determine the blood pressure.

Anti hypertensive therapy involves non-pharmacological intervention as well as specific drugs treatments. Dietary sodium restriction, exercise, weight loss, behavior are some factors that effect B.P.

Prototype Drugs Of Hypertension

Diuretics
(See in Genito Urinary System)

B-Blockers
➔Propranolol

ACE Inhibitors
➔Captopril

Angiotensin Receptor Antagonist
➔Losartan

Rennin Inhibitors
➔Aliskiren

Ca2+ Channel Blocker

Alpha Blockers

Available Brands in the Market

Spiromide Tab. (Spironolactone)
Aldactone Tab. (Spironolactone)
Acetofen Tab. (Acetazolamide)
Acetopril Tab. (Acetazolamide)
Osmotol Tab. (Mannitol)
Medisol Tab. (Mannitol)
Inderal Tab. (Propranolol)
Betanol Tab. (Propranolol)
Capotein Tab. (Captopril)
Losark-k Tab. (Losartan)
Rasilez Tab. (Aliskiren)

Diuretics

➔See in Genito urinary system

Propranolol (B-Blockers)

➔See in adrenergic antagonist

Captopril (ACE inhibitors)

➔See in Heart failure

Losartan (Angiotensin Receptor Antagonist)

➔See in Heart failure

Alpha Blockers

➔See in adrenergic antagonist

Ca2+ Channel Blockers

➔See in antiarrhythmic