

# Anti anginal drugs

## □ Learning objectives

- ❖ Definition of angina pectoris
- ❖ Nitrates, pharmacological features of GTN  
mechanism of action
- ❖ rout of drug administration
- ❖ side effects and tolerance
- ❖ other drugs useful in treatment of angina
- ❖ as calcium channel blockers and beta blockers ,role

# Anti anginal drugs

Pathophysiological definition of angina pectoris

is imbalance between oxygen demand or requirement by heart and oxygen supply to it ; due to defect in coronary arteries through partial block by thrombus or atherosclerosis ; sometimes coronary arteries are normal , but there is spasm of arteries lead to inadequate blood supply to myocardium

So, anti anginal drugs act by:-

1) Increase oxygen supply to heart by:-

a- dilating coronary arteries.

b- Slowing the heart rate (because coronary blood flow occur during diastole).

2) Reduction the demand by:-

a- reducing after load (peripheral resistance).

b- Reducing pre load (venous filling pressure).

c- Slowing heart rate

# 1) Nitrate group; include

## A) Glycerol trinitrate (Angesid)<sup>R</sup>

- Is a drug of choice in treatment acute form of angina pectoris, it is potent vasodilator, it relaxes smooth muscles of blood vessels (on venous side more than arterial side), lead to decrease in preload and after load on the heart lead to reduce myocardial oxygen and energy demand
- On venous side lead to decrease venous return to heart, lead to decrease ventricular volume and consequently lead decrease left ventricular diastolic pressure
- On arterial side lead to decrease arterial blood pressure lead to reduction ejection time by this decrease heart work and decrease oxygen and energy demand and overcome on the anginal pectoris
- Beside increase oxygen supply to heart by increase coronary vasodilatation

- ❖ GTN, has very quick onset of action within 5 minutes when taken sublingually
- ❖ its half life is 5 minutes and duration of action 20-30 minutes
- ❖ GTN, not used orally because it has extensive first effect in the liver ,
- ❖ it is given sublingually 0.5 mg at beginning of anginal pectoris or when there is anticipated of angina .

## Side effects:-

- 1)** Headache (throbbing or bursting in nature) occur due to stretching of pain sensitive tissues around the meningeal arteries.
- 2)** Flushing.
- 3)** Reflex tachycardia.
- 4)** Hypotension.
- 5)** Methaemoglobinaemia occur with heavy dosage.

GTN; present as tablet ,lingual spray , ointment or cream for skin on chest ,transdermal patch or paste (5-10mg ) once or twice per day

## B) Oral preparation of nitrate is called Isosorbide mononitrate and Isosorbide dinitrate

- ❖ Specific for oral use because it is not destroyed by hepatic enzymes
- ❖ It causes relaxation of blood vessels
- ❖ Longer half life than GTN (about 20 minutes ) , duration of action 2 hours .
- ❖ used in chronic cases of angina pectoris and as prophylaxis to prevent further attack.
- ❖ Tolerance, occur by frequent use of Nitrate group, so either by withdrawal for short time (12 hours) or by using Nicorandil which is specific for resistant cases.

## 2) $\beta$ – adrenoceptor antagonists

- ❖ Mechanism of action through lowering cardiac oxygen demand by reducing heart rate ,blood pressure and myocardial contractility
- ❖  $\beta_1$ - blockers advisable to use one daily as cardioselective drugs e.g. Atenolol 50-100 mg , Metoprolol 200mg daily , Bisoprolol (5-10mg daily
- ❖ while  $\beta_2$  receptor of heart will be free and mediated vasodilatation and bronchodilatation .

## 2) $\beta$ – adrenoceptor antagonists

- ❖  $\beta$ - Blockers should not withdrawal abruptly, because this precipitate dangerous arrhythmias, worsening angina or M.I. (The  $\beta$  –blockers withdrawal syndrome).
- ❖ Oxprenolol and Pindolol have partial agonist (intrinsic sympathomimetic activity) and therefore; tend to cause less bradycardia.
- ❖ Propranolol ; needed high doses because extensive first pass effect ,beside it lipid soluble can cross the BBB and cause side effects like nightmares ,drowsiness .
- ❖ Other possible side effects of beta-blockers; exacerbate cardiac failure and peripheral vascular diseases; provoke bronchospasm in patients with obstructive airway disease.



### 3) Calcium –channel blockers:-

- ❖ Mode of action by inhibiting the slow current of calcium ions to the smooth muscles of arteries and myocardium lead to reduce myocardial contractility and reduce blood pressure
- ❖ This decrease the oxygen demand of heart and therefore; useful in coronary spasm e.g. Amlodipine; Nifedipine and Nicardipine; cause reflex tachycardia counteract by using  $\beta$  –blockers
- ❖ While Diltiazem and Verapamil useful for patient not used  $\beta$  –blocker because they inhibit conduction through AV node and cause bradycardia.

# Side effects

- ❖ Calcium channel blockers reduce the heart contractility and may precipitate heart failure
- ❖ peripheral edema
- ❖ flushing
- ❖ headache
- ❖ dizziness

## 4) Potassium $\text{-}$ channel activators e.g. Nicorandil

- has venous dilatation and arterial dilatation without tolerance as seen with nitrate.
- For treatment of angina; low dose of Aspirin +GTN sublingually +  $\beta$   $\text{-}$ blocker; then added calcium channel blocker or long acting nitrate.