

ANTIANGINAL AGENTS

1. What is Angina? Angina is pain resulting from myocardial ischemia and is the principal symptom of ischemic heart disease.

- a. Induced by exercise, emotion, eating when the underlying pathology is atherosclerosis of the coronary arteries
- b. Vasospasm of the coronary artery

2. What is an antianginal drug? These are drugs that are used to relieve the symptoms of angina by restoring balance between oxygen supply and demand.

- a. Organic nitrates (-C-O-NO₂) and nitrites (-C-O-NO)
- b. Calcium channel blockers
- c. Beta-adrenergic antagonists (exertional angina)

3. Nitrates and nitrites

- a. Nitroglycerin is the prototype of this group; other examples are isosorbide dinitrate, erythritol tetranitrate, and amyl nitrate
- b. Mechanism of antianginal effect
 - i. decrease in peripheral vascular resistance (decrease of afterload)
 - ii. venodilatation (decreased preload)
 - iii. redistribution of flow to subendocardium without overall change in coronary flow
 - iv. preferential dilatation of larger coronary vessels and collaterals favoring distribution of blood to ischemic areas
- c. Side effects related to peripheral actions
 - i. headache (cerebral arteries)
- d. nitrite ions: oxidation of hemoglobin to methemoglobin causing reduced blood oxygen content
- e. Route of administration (sublingual for nitroglycerin)

4. Calcium channel blockers

5. Prototypes: verapamil and nifedipine

- a. Mechanism of action
 - i. peripheral vasodilatation, reducing total peripheral resistance due to direct effect on calcium channels of arteriole smooth muscle cells
 - ii. diminished afterload
 - iii. inhibition of coronary artery vasospasm

6. Beta-adrenergic blockers

a. Prototype: propranolol

b. Mechanism of action

i. reduction of sympathetic stimulation of the heart, leading to reductions of heart rate, myocardial contractility, and myocardial oxygen consumption

c. Side effects

i. can worsen congestive heart failure

ii. asthmatics: can worsen bronchospasm (beta₂ receptor); metoprolol or other beta¹ blocker preferred

7. Commonly used combinations of antianginal agents

a. Rationale: to diminish dosages of individual agents to reduce side effects, while keeping therapeutic effectiveness

b. Beta-blocker plus nitrate against exertional angina: interruption of sympathetic reflexes that compensate for vasodilation, reduced blood pressure, and lower cardiac output

c. Nifedipine and beta-adrenergic blocker

d. Nitrates and calcium channel blocker (vasospastic and exertional angina)