Tikrit University
College of Veterinary Medicine

Pharmacology

Subject name: **Antianginal treatment**
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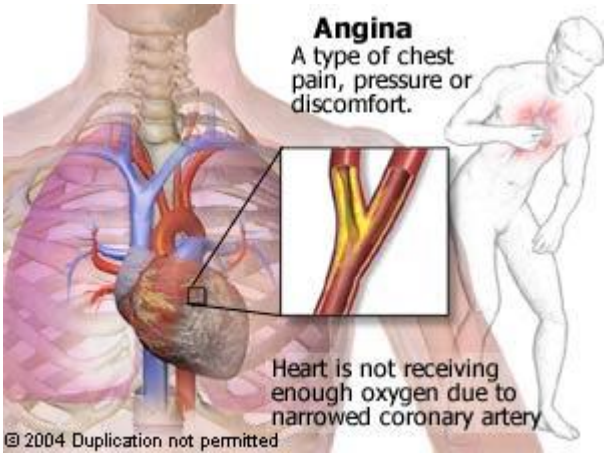
Lecturers link

Antianginal treatment

Angina (*angina pectoris*) is a type of temporary **chest pain**, pressure or discomfort that occurs when the heart is not getting enough oxygen. The most common underlying cause of angina is coronary artery disease, which occurs when the coronary arteries that supply the heart with oxygen-rich blood become blocked with plaque deposits.

Caused by coronary blood flow that is insufficient to meet the oxygen demands of the myocardium, the imbalance between oxygen delivery and utilization may result from a spasm of the vascular smooth muscle or from obstruction of blood vessels caused by atherosclerotic lesion.
If the angina occurs in predictable situations, such as during exertion or exercise, it is known as **stable angina**. However, if the painful episodes occur without warning, last longer than normal angina episodes and occurs more frequently, it is known as **unstable angina**. This is a dangerous medical situation that requires prompt medical attention. Unstable angina may signal that a **heart attack** is impending.

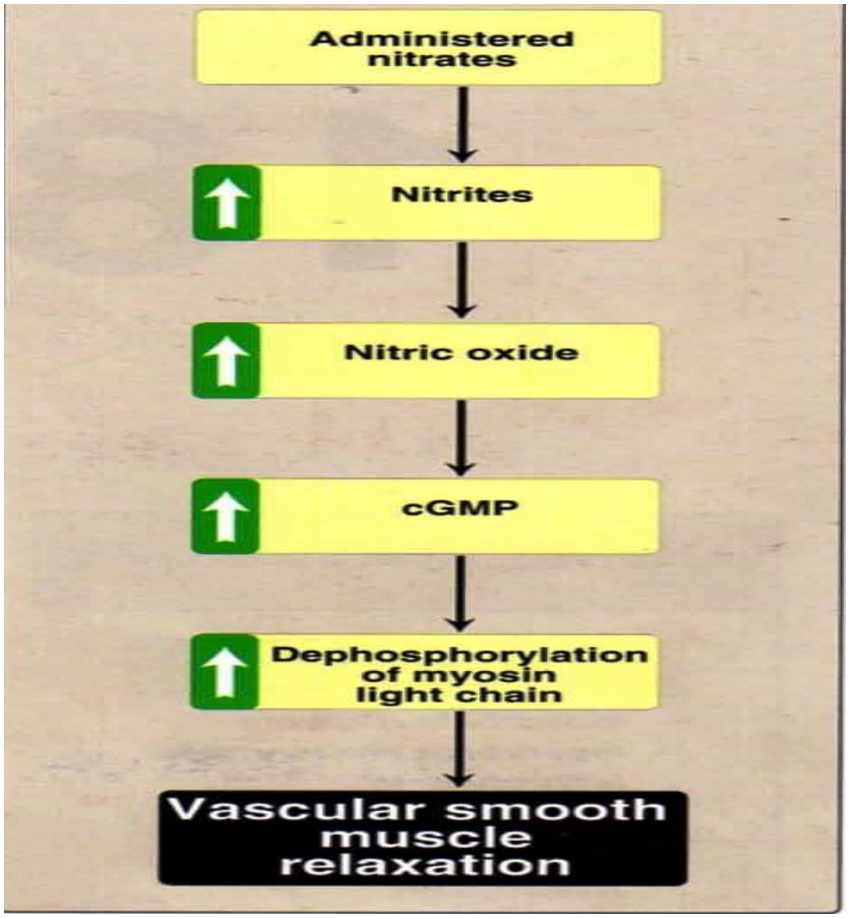


Basic aim of drugs treatment in angina are :-
1- reduce the work of the heart causes reducing O2 demand .
2- increase blood flow causes increasing O2 supply.
Antianginal druga:-
1- Nitrate:- decrease coronary vasoconstriction or spasm and increase perfusion of the myocardium by relaxing coronary arteries.
2- B-blocker :- decrease the O2 demands of the heart .
3- Calcium channel blockers :- vasodilator.

A- **organic nitrates**:- are simple nitric and nitrous acid they differ in their volatility.

Mechanism of action ;

The organic nitrates such as nitroglycerin are thought to relax vascular smooth muscle by their intracellular conversion to nitrite ions and then to nitric oxide (NO), which in turn activates gunylate cyclase and increase the cells cyclic GMP-----leads to dephosphorylation of the myosin light chain ,resulting in vascular smooth muscle relaxation.



Effects on the cardiovascular system:-

Therapeutic doses nitroglycerin has two major effects:-

1- it causes dilation of the large veins, resulting in pooling of blood in the veins ----- diminishes preload, reduce the work of the heart because decrease in the myocardial O2 consumption.

2- dilates the coronary vascular ,providing increased blood supply to the heart M.

Pharmacokinetics;- organic nitrate are absorbed from the gut, buccal or sublingual mucosa, and skin. The time onset of action varies from one minute(nitroglycerin) to more than hour (isosorbed mononitrate)--- significant first pass metabolism of nitro occurs in the liver .

Individual drug

drug	dose	Duration of action
Short acting Nitroglycerin (sublingual) Isosrbide (sublingual)	 0.15-0.2mg 2.5-5mg	 10-30min. 10-60min.
Long acting Nitroglycerin(oral) Nitroglycerin slow releasing transcutanus Isosorbide dintrate (sublingual) Isosorbide dinitrate (oral)	 6.5-13mg 10-25mg 2.5-10mg\2h. 10-60mg\ 4-6h .	 6-8h. 6-8h. 1-5h. 4-6h.

Adverse effects :
1- headache :most common.
2-reflex tachycardia postural hypotension and flushing .
3-prolong high dose may cause :-
a- metheamoglobiunaemia due to oxidation of Hb by NO.
b- formation of molecules called nitrosamines these are powerful carcinogenic in animals while there is no direct proof to cause cancer in human .

tolerance to nitrates:-
continues administration can result in loss of their antianginal effects(tolerance) in some patients the mechanism of such (homodynamic tolerance) are incompletely understood and may be mediated by:
1- impaired biotransformation of organic nitrate to NO.
2- Depletion of AH-group
3- Desensitization of guanylate cyclase receptor.

B- **Calcium channel blockers:**

activation of calcium channels by an action potential allows calcium to enter the cells. There follows a sequence of events which results in activation of the contractile proteins, myosin and action with shortening of the fiber and contraction of smooth M.
the calcium channel blockers by 1- inhibit the passage of calcium through the voltage gated L type membrane channels smooth and cardiac M.
2- reduce intracellular Ca ion----- cause the muscle to relax.
3- all Ca antagonists are vasodilators.

There are three structurally different classes of calcium channel blocker:
1- Dihydropyridines (nifedipin, amlodipine)
2- phenylakylamine(verapamil)
3-benzothiozopine(diltizem).

Selectively between heart and smooth M.varies:
1- verapamil-------is relatively cardio selective.
2- nifedipin-------is relatively smooth M. selective.
3- diltizem ------is intermediate in its selective.

Pharmacokinetics
1- all are well absorbed form (git) orally.
2- undergo first –pass metabolism.
3-they readily bind to plasma proteins.
4- have short elimination half-life (4-6h.).while amoldipine has long elimination half-life.
5- nifedipin and verpamil being excreted primarily in the urine while diltizen in the faces.

Nifedipine(procardia)

1-function mainly as an arteriolar vasodilator.
2-minimal effect on cardiac conduction or heart rate.
3-the drug may cause reflex tachycardia if peripheral vasodilatation is marked resulting in substantial decrease in blood pressure .
4- t(1\2):2h. give oral dose 30-90mg daily.
Can be taken sublingual.
Other uses hypertension, relaxation of visceral smooth m.spasm such as esophageal spasm ,peripheral vascular disease.

Side effects:-
1- flushing and headache(due to vasodilatation).
2-hypotension (overdose).
3-ankel edema(due to dilatation arterial).
4- tachycardia.
5-if use sublingual-----congestion and hypertrophy of the gum.

verapamil :t(1\2 4h.)

1-slows cardiac conduction directly----arterial vasodilator with some venodilator effects.
2- marked negative intropic and choronotropic action in myocardial .
3- not give to patient with bradycardia.
4- the drug increase AVblock.
Side effects: constipation, bradycardia.

Ditiazem: t 1\2 5h.

1- has cardiovascular effects that are similar to those of verapamil.
2-it reduce the heart rate----lesser extent than verapamil, also decrease blood pressure.
3- relive coronary artery spasm, therefore useful in patient with variant angina.
4- the incidence of adverse effects is low.

B-adrenergic blocker (cardio protective agents).

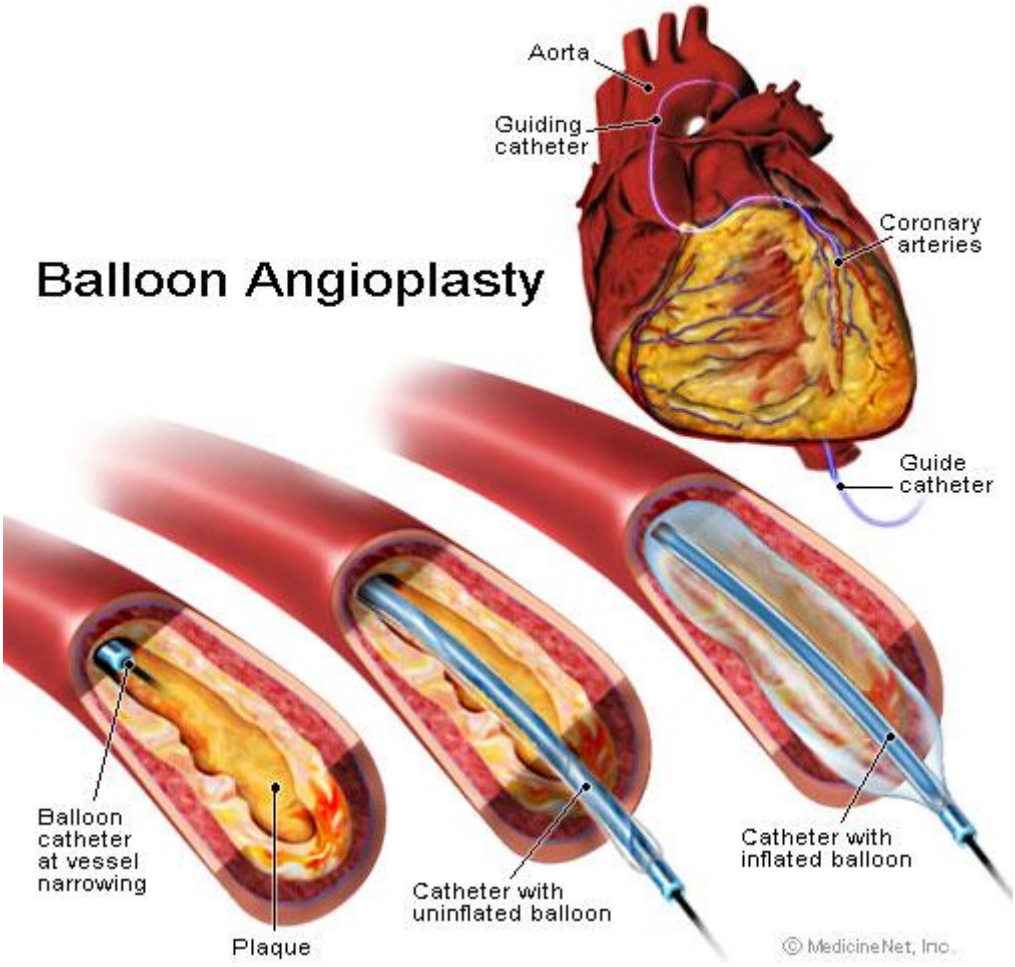
1-selective beta 1-receptor blocker (atenolol, metaprolol)
2-non selective beta-receptor blocker (propranolol) anderol.
3-beta –receptor blocker with sympathomimetic activity(pindolol, acebutolol).

They have good value in the management of angina pectoris-
1- relief pain in 60%of patients.
2-reduce the number of episodes 75% .they are used of prophylactic treatment of angina.

Mechanism of action

1-decrease cardiac O2 demand as result of:
-negative choronotropic effects.
-negative intropic effects.
Both result in decreasing of cardiac output \ min. So the blood pressure leading to reduction of the work heart.
2-may increase coronary blood flow and oxygen supply by reducing heart rate.
Contraindication.:
Asthma ,peripheral vascular disease, sever bradycardia, artioventricular node blocker, and sever heart failure.

Management of angina:-
1- advices to patients with angina don't smoke, reach the ideal body weight and take regular exercise.
2-identification and control of signification risk factors hypertension, obesity, hyperlipidemia.


Balloon Angioplasty
Aorta
Guiding catheter
Coronary arteries
Guide catheter
Balloon catheter at vessel narrowing
Plaque
Catheter with uninflated balloon
Catheter with inflated balloon
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