Drug Treatment of Ischemic Heart Disease

1) Nitroglycerine (GTN)

- Nonspecific smooth muscle relaxant, action is due to release of NO, leading to activation of guanylyl cyclase.
- Can be administered by various routes, Fast onset of action(1-3minutes, Peaks at 10 minutes), Short duration (15-30minutes).
-Reductase enzyme, in liver, breaks down the drug.

- Causes general vasodilation:

a) **Arteriolar dilation**: short lived (5-10 min) , Decreases systemic blood pressure (afterload), but causes reflex tachycardia and increased contractility.

b) **Venous dilation**: more intense, even with low doses, lasts for 30 minutes. Decreases venous return (preload) and decreases MVO2.

***Side Effects:**

- Headache, Hypotension , tachycardia, Increased intraocular and intracranial pressures.
- Methemoglobinemia, Tolerance: only for the arteriolar effects.
- Withdrawal: in workers in ammunition industry.

Drug	Duration of Action
Short-acting:	
Nitroglycerin, sublingual	10–30 minutes
Isosorbide dinitrate, sublingual	10–60 minutes
Amyl nitrite, inhalant	3–5 minutes
Long-acting:	
Nitroglycerin, oral sustained-action	6–8 hours
Nitroglycerin, 2% ointment, transdermal	3–6 hours
Nitroglycerin, slow-release, buccal	3–6 hours
Nitroglycerin, slow-release patch, transdermal	8–10 hours

2) Beta Adrenergic Blockers

- Prevent actions of catecholamines, so more effective during exertion.
- Do not dilate coronary arteries, might constrict them, do not increase collateral blood flow.
- Cause subjective and objective improvement: decreased number of anginal episodes, nitroglycerine consumption, enhanced exercise tolerance, and improved ECG.

3) Calcium Channel Blockers

- Particularly beneficial in vasospasm, can affect platelets aggregation.
- May be dangerous in the presence of heart failure and in patients susceptible to hypotension.

- L-type calcium channel can be blocked by Verapamil , T-type calcium channel can be blocked by flunarizine and mibefradil.

Drug	Oral Bioavailability (%)	Half-Life (hours)	Indication
Dihydropyridines			
Nimodipine	13	1–2	Subarachnoid hemorrhage
Nicardipine	35	2–4	Angina, hypertension
Nifedipine	45–70	4	Angina, hypertension, Raynaud's phenomenon
Nitrendipine	10–30	5–12	Investigational
Nisoldipine	< 10	6–12	Hypertension
Isradipine	15–25	8	Hypertension
Felodipine	15–20	11–16	Hypertension, Raynaud's phenomenon
Amlodipine	65–90	30–50	Angina, hypertension
Miscellaneous			
Diltiazem	40–65	3–4	Angina, hypertension, Raynaud's phenomenon
Verapamil	20–35	6	Angina, hypertension, arrhythmias, migraine

***Side Effects:** Hypotension, Headache, dizziness, Flushing, Peripheral edema.

Effects of Nitrates Alone and with Beta Blockers or Calcium Channel Blockers in Angina Pectoris.			
	Nitrates Alone	**Beta Blockers or Calcium Channel Blockers**	**Combined Nitrates with Beta Blockers or Calcium Channel Blockers**
Heart rate	***Reflex[1] increase***	**Decrease**	**Decrease**
Arterial pressure	**Decrease**	**Decrease**	**Decrease**
End-diastolic volume	**Decrease**	Increase	Non or decrease
Contractility	***Reflex[1] increase***	**Decrease**	Non
Ejection time	**Decrease**	Increase	Non

4) Dipyridamole

- Inhibits the uptake of adenosine and inhibits adenosine deaminase enzyme.
- good coronary dilator, increases the blood flow to the normal area i.e. “Coronary Steal Phenomenon”.
-Still used as an antiplatelet drug but not better than aspirin.

5) Others

ACEI, Anticoagulants and/or Thrombolytic Therapy, Cholesterol Lowering Agents, Angioplasty ,Surgery.

6) Newer Antianginal Drugs

Metabolic modulators: **Ranolazine.**
Direct bradycardic agents: **Ivabradine.**
Potassium channel activators: **Nicorandil.**
Rho-kinase inhibitors: **Fasudil.**
Sulfonylureas: **Glibenclamide.**
Thiazolidinediones.
Vasopeptidase inhibitors.
Nitric oxide donors: L- arginine.
Capsaicin.
Amiloride.