

ANGINA PECTORIS

Angina - strangling

Pectoris – the chest

An attack of angina pectoris occurs when myocardial demand for oxygen exceeds supply from the coronary circulation.

Angina is commonly experienced as a heavy, pressing, acute substernal discomfort, (complained by the patient as pain) often radiating to left shoulder and flexor aspect of left arm, neck, teeth, abdomen and intrascapular region. It may be described as aching, burning, or even indigestion.

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Forms of Angina

❖ Unstable

angina (preinfarction, crescendo)

❖ Variant Angina of exercise (commonest) classical/effort

❖ Angina (Prinzmetal / vasospastic)

vasospasm of large coronary artery may occur at rest or awakens the patient from sleep

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ANGINA PECTORIS: How drugs act

Angina – Problem of blood supply

Drugs – Increase supply of oxygen

- Reduce demand for oxygen
- or both

INCREASED SUPPLY OF OXYGEN

- ❖ Dilating coronary arteries
- ❖ Slowing the heart (coronary flow uniquely occurs in diastole lengthens as heart rate falls)

Demand can be reduced by

Reducing preload (i.e.venous filling pressure)

Slowing the heart

Reducing afterload (i.e.peripheral resistance))

Antianginal Drugs

ORGANIC NITRATES:

➤ Reduce preload, afterload and dilate main coronary arteries

- Glyceryl trinitrate:
(GTN or NITROGLYCERIN)
- Isosorbide dinitrate
- Isosorbide mononitrate
- Pentaerythritol tetranitrate
- Amyl nitrite
- Sodium nitrite

Nitrate Tolerance

- Interrupt therapy for 8 to 12 hr. each day
- Omit night dosing in pt. of exertional angina
- Adjust oral or buccal dose
- ❑ Removing cutaneous nitroglycerin
- Nocturnal angina: Continue at night and omit in day time

GTN

- Vessels $>200 \mu\text{m}$ in D- responsive
- Vessels $<100 \mu\text{m}$ in D-minim responsive
- Coronary microcirculation improves due to dilatation of cardiac veins
- Reduced myocardial oxygen demand determinants:-
 - Left vent. wall tension
 - Heart rate
 - Myocardial contractility
 - Decrease in preload and afterload
 - GTN increase cGMP in platelets
 - Increase exercise tolerance

Myocardial oxygen consumption

= Aortic pressure x Heart rate x Ejection time

Mech. of relief of symptom of angina pectoris

- Decrease in cardiac work secondary to fall in B.P.
- Dilatation of epicardial coronary arteries
- High dose may aggravate ischaemia

Calcium Channel Blockers

- Reduce cardiac contractility, dilate coronary arteries, reduce afterload.
- Amlodipine
- Diltiazem
- Nifedipine
- Nicardipine
- Verapamil
- Felodipine
- Nisoldipine

Beta-Adrenoceptor Blocking Agents

- Reduce myocardial contractility and slow heart rate
- May increase spasm in variant angina
- Propranolol
- Atenolol
- Metoprolol
- Acebutolol
- Bisoprolol

Potassium Channel Activators

- Nicorandil
- Pinacidil
- Cromakalin

Management- Angina Pectoris

- Treatment of contributory cause, e.g. anaemia, arrhythmia
- Changes in life style, e.g. weight reduction, stop smoking
- Immediate preexertional prophylaxis: GTN sublingual or nifedipine(bite the capsule and hold the liquid in mouth or swallow it)
- Acute attack: GTN (S/L) or nifedipine (Bite capsule)

Management of an acute attack of angina

- GTN is the drug of choice
- 0.5 mg tab. should be chewed and dissolved under tongue or place in buccal sulcus for rapid and reliable absorption.
- Repeated every 5 minutes for three doses till relief of pain. Spit out the tablet on pain relief or
- Nitrolingual spray one metered dose every 5 min. for 3 doses

GTN in Acute Angina

Action begins in 2 min. and lasts upto 30 min.

Dose is 300-600 μ gm in standard tab.

GTN taken at onset of pain or as immediate preexertional prophylaxis

Metered aerosol spray under the tongue

(Nitro lingual spray)

GTN

$t_{1/2} = 3$ min.

Oily non inflammable liquid

Tab. fairly stable

Discard tab. 8 weeks old or exposed to heat or air due to loss of potency

Nitroglycerin spray as aerosol is available

Management of Angina

Pectoris

For long term prophylaxis

Bisoprolol (cardioselective beta-1#) given continuously

Adjust dosage by response:

- Increase dosage provided heart rate does not fall below 55/min.
- Prefer pure antagonists like Propranolol in severe anginal prophylaxis
- Warn the patient on sudden withdrawal

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Alternatively

CCB Drugs:

- Nifedipine or Amlodipine
- Use especially if coronary spasm suspected
- If myocardial insufficiency
- Bronchospastic disease
- Can be combined with a Beta # or
- A long acting Nitrate: ISDN or ISMO or GTN { transdermal patch, oint., oral(S/R prep.)} or
- Potassium channel opener-Nicorandil

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Long term prophylaxis

Nocturnal angina prophylaxis

Transdermal GTN, Oral ISMO

Antiplatelet therapy :-

Low dose Aspirin / Clopidogrel

Surgical revascularisation:-

PTCA, CABG

Mech. of Action - Nitrates

- Denitration in smooth muscle cells
- Release of Nitric Oxide (NO) from endothelial cells
- Activates soluble guanylyl cyclase
- Increased i/c cGMP conc.
- Decrease stored calcium
- Vasodilatation

Cont.....

- Generalized dilatation of venules
- Arteriolar dilatation
- Fall in B.P.
- Dilatation of large coronary arteries
- Redistribution of blood
- Decrease venous return
- Reduces SV
- CO / min sustained
- Fall in left vent. filling pressure

Pharmacokinetics

- Well absorbed across skin, mucous membrane of mouth and gut
- Extensive first-pass hepatic metabolism
- Oral dose > S/L dose

Nitrates - Clinical Uses

- Acute attack of angina
- Acute left vent. failure
- Long term prophylaxis of angina
- Immediate preexertional angina
- Unstable angina
- CHF due to IHD
- Biliary colic
- Esophageal spasm
- Cyanide poisoning

Nitrates - ADRs

- Collapse due to fall in B.P.
- Nitrate headache
- Methaemoglobinaemia
- Contraindications:-
- Angina due to anemia
- Pregnancy
- Hypertrophic obstructive cardiomyopathy

Nitrates - Overdose

- Palpitations
- Dizziness
- Blurred vision
- Headache
- Flushing followed by pallor
- **AVOID ACCIDENTAL OVER DOSE**

Combination Therapy

- Use of lower doses
- Increasing effectiveness
- Reducing the side effects
- Nitrates and Beta- receptor antagonists
- Beta- receptor antagonists and Calcium channel blockers.
- Calcium channel blockers and Nitrates
- Calcium channel blockers, Nitrates and Beta-receptor antagonists

Nitrates and Beta- receptor antagonists

- Very effective in typical exertional angina.
- Additive efficacy on net myocardial oxygen consumption
- Beta- blockers block reflex tachycardia and positive inotropy of nitrates

Nitrates and Calcium Channel Blockers

- Severe exertional or vasospastic angina
- Nitrates reduce preload & calcium blockers reduce afterload
- Net effect is reduction in oxygen demand
- Nitrate and Nifedipine in exertional angina with heart failure, Sick- Sinus syndrome, or A-V conduction defect
- Excessive tachycardia and hypotension occurs

Calcium Channel blockers & Beta - blockers

- Nifedipine and propranolol in severe stable angina
- Nifedipine and metoprolol
- Amlodipine and atenolol

Nitrates, Calcium Channel blockers & Beta-blockers

- Exertional angina not responding to two antianginals
- Nifedipine and GTN dilate epicardial coronary arteries
- Nifedipine decrease afterload & nitrates decrease preload
- Beta blockers decrease heart rate and myocardial contractility

Future Strategies

- Nolsidomine
- Nitrendipine
- Gallopamil
- Flunarizine
- Trimetazidine
- Ranolazine
- Vascular Endothelial Growth Factor (VEGF)

Thank You