Managing IHD and acute Myocardial Infarction
In Ireland - 1 out of every 10 deaths (22% of all premature deaths) in 2006 were due to CVD.

Source: Central statistical office
RATIONAL FOR THERAPY

ASYMPTOMATIC PHASE
PRIMARY PREVENTION

VASCULOPROTECTIVE THERAPY

ANGINA
ANTIANGINAL THERAPY

PLAQUE INITIATION

PROGRESSION

PLAQUE RUPTURE

Myocardial Infarction; Death

MANAGING ACUTE MI
Learning Objectives

• Managing Angina
• Managing Acute MI
• Acute coronary syndromes
Focus on the therapeutics/ rationale.
Treating angina

Anti-anginal agents

Nitrates
β – blockers
Calcium channel blockers

Improve exercise tolerance

No role in prevention of MI

Vasculo-protective agents

Aspirin, Clopidogrel, Statin, ACE-I
β – blockers

Lower rate of progression to complicated plaque

Prevention of MI

Re-vascularisation
Anti-anginal agents

- Nitrate; beta-blockers; calcium channel blockers; K⁺ channel blockers
- Antianginals typically increase effort tolerance on treadmill testing by 30-60 seconds
- Very similar in efficacy
- Anticipate the need for treatment with two or three agents in many patients
Therapeutic targets: antianginal medications

- Contractile state
- Heart rate
- Wall tension
- L.V. filling
- L.V. PRESSURE

O2 DEMAND
O2 SUPPLY
BLOOD FLOW
ARTERIAL O2
NITRATES

- C-gmp mediated relaxation of vascular smooth muscle in veins more than arteries
- Mimics actions of endothelium derived nitrous oxide
NITRATES

L.V. WORKLOAD

Contractile state
Heart rate
Wall tension

O2 DEMAND
O2 SUPPLY

BLOOD FLOW

ARTERIAL O₂

L.V. filling
L.V. PRESSURE
Pharmacological properties

• Tolerance (tachyphylaxis)
  - reduced therapeutic effects
• “Monday morning sickness”
• ? due to depletion of free tissue –SH
• Long-acting preparations
  /infusions/transdermal patches
• “Nitrate free period”
Indications

- Relief of acute angina attack
- Prophylaxis of stable angina
  (prior to exercise GTN or long-acting)
- Left ventricular failure
Cautions/Contraindications

- Hypotension
- Aortic stenosis
- HOCM
- Constrictive pericarditis
- Co-administration with phospho-diesterase inhibitors can lead to life threatening hypotension
Side effects

- Headache
- Flushing
- Dizziness
- Postural hypotension
- Tachycardia
- Overdose rarely precipitates methaemoglobinemia
• Reduced heart rate
• Reduced contractility
• Arterial smooth muscle relaxation
BETABLOCKERS

L.V. PRESSURE

L.V. filling

O2 DEMAND

BLOOD FLOW

O2 SUPPLY

ARTERIAL O₂

L.V. WORKLOAD

Contractile state

Heart rate

Wall tension
Pharmacological properties

- Cardioselective – eg atenolol, metoprolol
- Non selective – eg propranolol
- Intrinsic sympathomimetic (partial agonist) activity – eg celiprolol, pindolol
- Alpha-blocking activity eg carvedilol
- Lipid soluble (eg propranolol) versus water soluble (eg atenolol)
- Up-regulation of receptors – withdrawal syndrome
Indications

- Symptomatic angina
- Hypertension
- Acute coronary syndromes
- Post myocardial infarction
- Stable heart failure
- Arrhythmias
- Thyrotoxicosis/Benign essential tremor
Dose

- Rational choice - long-acting cardioselective beta blocker od or bd
- Anti-anginal effects are dose related
- Titrate to resting heart rate 50-60 bpm
Side effects

- Beta-1 effects – Bradycardia, heart block, heart failure
- Beta-2 effects – bronchospasm, worsening PVD, Raynaud’s phenomenon
- Fatigue, depression, nightmares, impotence
- May mask hypoglycaemia and worsen glycaemic control in IDDM
Cautions/Contraindications

- C/I in asthma
- Uncontrolled heart failure
- Bradycardia
- Heart block
- Phaeochromocytoma without prior alpha blockade
- Caution coronary spasm/COPD/PVD
- Avoid abrupt withdrawal
Important Interaction

- Verapamil and beta blockers → precipitate heart block ± asystole
- Must NOT give IV verapamil to beta blocked patients
- Extreme caution combined orally
Calcium antagonists
CALCIUM CHANNEL BLOCKERS

- Contractile state
- Heart rate
- Wall tension
- L.V. filling
- L.V. PRESSURE
- L.V. WORKLOAD
- O2 DEMAND
- O2 SUPPLY
- BLOOD FLOW
- ARTERIAL O₂
Pharmacological properties

- 3 classes
- Phenylalkylamines eg verapamil
  - relatively cardioselective
  - -ve chronotropic and inotropic
- Dihydropyridines eg nifedipine amlodipine
  - relatively smooth muscle selective
  - potent vasodilator
- Benzothiazepines eg diltiazem
  - intermediate
Indications

- Symptomatic control of angina
- Coronary spasm
- Hypertension
- Arrhythmias
- Subarachnoid haemorrhage (nimodipine)
Side effects

- Peripheral vasodilation
  - flushing, headache, ankle oedema
- Cardiac effects
  - AV block, heart failure
- Constipation
- Short-acting dihydropyridines may ↑ mortality in MI
Potassium channel activators
Potassium channel activators - nicorandil

- Activates K ATP channel
- NO donor effects
- Arterial and venodilator
- S/E Flushing, dizziness, headache
- Usually 3rd or 4th line agent
Vasculoprotective agents

- Aspirin: 20-25%
- Statins: 25-30%
Vasculoprotective agents

- LDL cholesterol reduction to 1.6-1.8 mmol/L

- ACE-Inhibitors in patients with hypertension, particularly those with:
  - Diabetes
  - Hypertension
  - LV hypertrophy and dysfunction
  - history of myocardial infarction,
  - impaired renal function
Revascularisation therapy

Re-establish vascular patency

Percutaneous (i.e., balloon angioplasty & stenting)
• coronary-artery bypass surgery (CABG)

No benefits in patients with chronic stable angina

Indications
1. Angina not controlled with optimal/ maximal therapy
2. Patients with high risk of future myocardial infarction
Bare-metal stents may be narrowed or obstructed by ingrowth of tissue. With drug-eluting stents, this process is inhibited, but since the struts remain uncovered, they may be prone to thrombosis after antiplatelet therapy is discontinued.
• In chronic stable angina Class II due to single vessel disease patients early recanalisation does not offer benefit over vasculo-protective therapy.
PUTTING IT TOGETHER

- ASPIRIN / CLOPIDOGREL in low doses
- A CARDIOSELECTIVE BETABLOCKER (UNLESS ASTHMA / PVD / OTHER C.I.) OR
- CALCIUM CHANNEL BLOCKER
- ACE-I, STATIN
- AGGRESSIVE LIFESTYLE CHANGES
- TREAT LIPID /BP/ DIABETES
- CONSIDER INVASIVE PROCEDURES
TOTAL OCCLUSION (M.I.)
“I had my plumber install new pipes. I got tired of fretting about my cholesterol!”
Mortality post MI: the importance of evidence based intervention!
A  Before myocardial infarction

No symptoms

Normal electrocardiogram

B  During myocardial infarction

Acute onset of chest pain

Elevation of ST segment

Occlusive thrombus

Plaque

Plaque
Immediate treatment

- Oxygen
- Intravenous morphine 2.5-10mg + antiemetic cyclizine 50mg
- Aspirin 150-300mg chewed/dispersible
- Clopidogrel 150-300 mg
- Nitrates GTN 0.4mg sublingual +/- IV
- Beta blockers
- Transfer to Coronary care Unit
- ACE-I within 36 hours
Restoring patency

Maintaining patency

Balloon angioplasty with stenting

Anti-platelet therapy
tissue plasminogen activator
Others
The most appropriate reperfusion therapy

- 90% recanalisation
- 1% fall in benefit over fibrinolysis with every 10 minutes passed
- 0% fall in benefit over fibrinolysis

Presence of complicated MI and cardiogenic shock are exceptions to this rule.

Patients with high risk for bleeding complications have better outcomes with angioplasty.
The most appropriate reperfusion therapy

Lab and personnel

Cardiogenic shock
Pulmonary oedema

High risk for haemorrhagic complications

Time <90 min

Angioplasty

Delay to invasive strategy (upto 24 hrs)
Maintaining patency

- Abciximab as early as possible before primary PCI.
- Low molecular weight heparin
- Un-fractionated heparin if renal failure is present
• Maintain normal
  – glucose,
  – K+
  – Mg levels
Fibrinolysis

Primary PCI not available

Thrombolysis

50-60% recanalisation

Door to needle time <30mins
Effective up to 12 hours
Fibrinolysis Mode of action

- Activate plasminogen to form plasmin which degrades fibrin breaking up thrombi
  - Streptokinase, alteplase, reteplase, tenecteplase
  - Streptokinase – antibodies within 4 days
  - Alteplase, reteplase followed by heparin for 48 hours
Indications

- Acute ST elevation myocardial infarction
- Acute pulmonary embolism
- Acute ischaemic stroke
Contraindications

- Recent haemorrhage trauma or surgery
- Recent dental extraction
- Coagulation defects; bleeding disorders
- Aortic dissection
- History of cerebrovascular disease
- Active peptic ulceration
- Severe menorrhagia
- Severe hypertension
- Active cavitating lung disease
- Acute pancreatitis
- Severe liver disease
- Oesophageal varices
- Previous reaction to streptokinase (Streptokinase)
Relative contraindications

- Venepuncture
- Recent invasive procedure
- External chest compressions
- Pregnancy
- Abdominal aortic aneurysm
- Diabetic retinopathy
- Anticoagulant therapy
Side effects

- Nausea and vomiting
- Bleeding
- Reperfusion arrhythmias
- Hypotension
- Back pain
- Allergic reactions (esp streptokinase)
Unstable angina/NSTEMI

- Oxygen
- Nitrates GTN 0.4mg sublingual +/- IV
- Intravenous morphine 2.5-10mg + antiemetic
- Aspirin 150-300mg chewed/dispersible
- Heparin eg enoxaparin 1mg/kg 12 hourly
- Beta-blocker atenolol 5mg over 5 mins repeated after 10-15 mins
- Clopidogrel if undergoing PCI
- Glycoprotein IIb/IIIa inhibitors (abciximab) if undergoing PCI
- ACE inhibitor if indicated
- Tight glycaemic control
- Optimise potassium and magnesium
Reading/Website list

- British national formulary BNF
- www.uptodate.com
- American heart association guidelines