Drugs in Cardiology

**MEDICATIONS**

**ASPIRIN**
- Prevents Thromboxane A2 formation which is an agonist of platelet aggregation
- **Dose:** >160mg - causes immediate near complete inhibition of TxA2
- **How effective is it?**
  - Decreases mortality by 23%
  - Alone it is as efficacious as Streptokinase given alone.
  - With streptokinase it decreases mortality by 43%
  - In patients with previous AMI or stroke it decreases vascular events by up to 40 events per 1000 patients.
  - Adverse effects are mainly GIT

**Clopidogrel**
- **300-600mg loading dose**
- **GRADE B recommendation**
- **Add to aspirin if having stent**
  - PCI-CURE study Lancet 2001;35:527-533
- **Withhold if likely to undergo CABG**
  - Increased bleeding

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I'm allergic to aspirin. What can I take?

**Adenosine Diphosphate inhibitors**

**CLOPIDOGREL**
- Inhibits platelet aggregation, but its effect is delayed 24-48 hours after given
- New studies since 2000 ECC guidelines
- **ACS**
  - Clopidogrel before PCI reduced adverse ischaemic events
- **STEMI**
  - In <75yo with fibrinolysis, aspirin and heparin, improved coronary patency

Does it cause adverse bleeding?
- Studies show mixed results especially in post hoc analysis - risk benefit ratio analyses have shown no such trend, and certainly not intracranial bleeding.
Clarity Trial- clopidogrel

- Sabatine NEJM 2005
- No difference in death/MI
- Only difference in open artery in cath lab
- WHAT???

Beta blockers

- Antiarrhythmic, anti-ischaemic, antihypertensive.
- Decrease oxygen demand by decreasing HR, BP, contractility.
- Decrease infarct size and mortality in patients who do not receive thrombolytics
- In those that receive fibrinolytics
  - They decrease post infarction ischaemia
  - They decrease non-fatal AMIs
- When to use
  - Use in ED for all ACS unless contraindications
- Dose metoprolol 25-50mg po
- Contraindicated: HR<60, SBP<100, mod-severe LVF, PR>0.24s, 2°/3° block, severe CDAD, asthma, IDDM, severe peripheral vascular disease.

B- blockers

2007
- IV if ACS and SBP >140mmHg
- NNT to prevent death/MI/arrest = 100
2005 Chen Lancet – 45,000 STEMI patients
- Metoprolol 5mg IV x 3 then 50 mg PO
  - 1% decrease in MI/Arrest
  - 1% increase in cardiogenic shock

Who to not give b-blockers to?

- HR >110
  - An indicator for impending cardiogenic shock
  - Associated with low ejection fraction
- SBP > 120mmHg
- Age >70
- CHF
- Airways Disease
- Conduction Blocks
Ca channel blockers

- Do not reduce mortality in AMI but may be harmful.
- **When to use**
  - ongoing ischaemia in patients who cannot tolerate beta blockers
  - rapid AF
- **Contraindicated**: CCF, LV dysfunction, AV block
- Note Verapamil may be detrimental in CCF and bradycardia.

Ace Inhibitors

- Decrease LV dysfunction and dilatation, slow development of CCF during AMI
- There is decrease in mortality when treated with oral ace inhibitor at or soon after AMI.
- **When to use**
  - (a) AMI with ST elevation ≥ 2 anterior praecordial leads
  - (b) Clinical heart failure
  - Its use in unstable angina is not evaluated.
- **Contraindication**: hypotension, renal failure, bilateral renal artery stenosis
- Note: Enalapril IV is not recommended for use in AMI

Nitrates

- **Effect**
  - Decrease preload/afterload, decrease cardiac work and decrease oxygen consumption.
  - Dilate coronary vessels and increase oxygen supply
  - Inhibit platelet aggregation
- **When to use**
  - They reduce infarct size when used in AMI not treated with thrombolytics.
  - Benefit in reducing mortality/morbidity in AMI
  - Use of Nitrates in PCI
  - Use in LV or RA failure in AMI, severe CHF, HT.
  - Adverse effects: hypertension which may lead to tachycardia and increase ischaemia
- **Do not use**
  - In right ventricular infarction as patients are volume-dependent and decreased BP or preload may lead to hypotension
  - Caution in use with STEMI infarct as LVEF may not reflect antemural involvement.

ANTITHROMBINS

- Heparin or Enoxaparin
- Heparin NNT = 30-40
- In PCI
  - Use is GRADE A recommendation
  - Bolus dose on way to cath lab is GRADE D recommendation
- In Fibrinolysis
  - Use with fibrin-specific fibrinolytics
  - GRADE A recommendation
**Medications: Antithrombins**

**HEPARIN**
- Combines with ATIII and inactivates thrombin and X
- Decreases the risk of AMI and death during the acute phase of unstable angina.
- Aspirin and Heparin:
  - Reduced short term risk of death or MI by 54% of aspirin alone.
  - Higher heparin is needed to achieve anticoagulation.
- Low molecular weight heparin:
  - Safer in elderly and renal function.

**Aspirin and Fibrinolytics**
- No benefit in adding heparin—risk of major/major bleeding.

**Use**
- In STEMI with fibrinolysis give 60U/kg (max 4000) and infusion of 12U/kg/hr
- UA/NSTEMI—Enoxaparin beneficial over UFH when used with aspirin
- STEMI—LMWH superior to UFH in reducing ischaemic complications and a 14% reduction in mortality rates.
- No difference in PCI

**RISKS**
- Increasing incidence of stroke with age
- Reduces its relative benefit
- Small but definite increased risk of haemorrhagic stroke
- Risk of stroke greatest in:
  - >= 65yo
  - <70kg
  - Initial BP > 180/110
  - tPA

**FIBRINOLYTIC THERAPY**
- Act on coronary thrombus. They are plasminogen activators which bind to thrombus and form a complex with fibrin in the thrombus promoting fibrinolysis.
- For STEMI with:
  - onset of symptoms <=12hrs
  - Creatinine >1.5
- Benefits of therapy:
  - Early therapy critical
  - 30% reductions in death at 30 days
  - 19% reduction in 90 day mortality
  - Not recommended in 4-12 hrs post symptom onset
  - Less impressive for inferior MI except when associated with RV infarct
  - NOT for patients presenting >48 hours after symptom onset, or in SS depression

**LOW MOLECULAR WEIGHT HEPARIN**
- Greater bioavailability, more reliable anticoagulant effect.