Introduction
50% of deaths due to Acute Myocardial Infarction (AMI) occur within one hour of symptom onset.\(^1\) Therefore, rapid diagnosis and management is vital to reduce mortality.

Out of Hospital – Sudden Cardiac Arrest
Majority are the result of fatal arrhythmias that can be treated with emergency Cardio-Pulmonary Resuscitation, defibrillation and prompt Advanced Cardiac Life Support. This requires patient education regarding symptoms, availability of trained Emergency medical services and rapid transport to a fully equipped cardiac hospital.\(^2,11\)

Recognition and Management
Most patients seek medical care after 2 hours of symptom onset and even wait 12 hours or more. Pharmacologic therapy beyond 12 hours may offer little benefit.\(^2\) Thus, prompt treatment is essential.

Components of Delay to Treatment and Goals\(^3\)
1. Patient related (failure to recognize problem and delay in seeking help). Goal ≤ 15 minutes.
2. Pre hospital evaluation, treatment and transport time. Goal ≤ 30 minutes.
3. Diagnosis and initiation of treatment in hospital. Goal – door to needle time for thrombolysis ≤ 30 minutes.
4. Time to reperfusion – door to balloon time ≤ 90 minutes.

High Risk Patients
Include those with tachycardia (≥ 100 bpm), hypotension (≤ 100 mmHg), pulmonary edema (rales > one half way up) and shock. They should be managed in a tertiary hospital with early thrombolysis or Percutaneous Coronary Intervention (PCI).\(^4\)

Pre Hospital Thrombolysis
A meta-analysis of trials showed a 17% relative improvement in outcome\(^5\). However, it is administered only if transport time is >90 minutes or if a trained physician is present in the ambulance.\(^11\)
Diagnosis of AMI

1. History of Ischaemic type chest discomfort (lasting >20 minutes): Presentation in 70 to 80% of patients.\(^6\)

2. Changes in serially obtained ECG: ST segment elevation has sensitivity of 46% and specificity of 91% for diagnosing AMI.\(^7\) Mortality increases with number of leads showing ST elevation.

3. Rise and fall of cardiac markers: Elevated cardiac specific troponins cTnI or cTnT identify patients who are at increased risk of death and those who benefit from treatment with GPIIb/IIIa inhibitors.\(^8\) Myoglobin may be detected after two hours of MI. CK-MB2 >1U/L or ratio of CK-MB2 to CK-MB1 of 1.5 has improved accuracy of diagnosing AMI within 1st 6 hours.\(^9\)

Routine Measures – Oxygen

Given to patients with overt pulmonary congestion, desaturation (SaO\(_2\) < 90%) and routinely to all patients with uncomplicated MI during 1st 3 hours.\(^11\) It limits myocardial injury, reduces ST segment elevation and hypoxia due to excess lung water.

Nitroglycerine (NTG)

Given for 1st 24 - 48 hours in patients with AMI + CHF, large anterior MI, persistent ischaemia or hypertension.\(^11\) It should be avoided in patients with hypotension (SBP < 100 mm Hg), bradycardia (<50 bpm), tachycardia or RV infarct.\(^11\) Pre hospital sublingual NTG 5 mg every 5 minutes up to 3 doses. In hospital it is given as an infusion.

Analgesia

IV Morphine 4-8 mg relieves anxiety without causing myocardial depression. It reduces pain induced sympathetic activation which causes vasoconstriction and increased cardiac workload.\(^11\) Alternatively, pentazocine or buprenorphine may be used.

Aspirin

160-325 mg of soluble Aspirin immediately after onset of symptoms. ISIS-2 study showed that Aspirin alone in AMI resulted in 35-day mortality reduction of 23%. When combined with Streptokinase (STK), mortality reduction was 42%.\(^13\) It reduces coronary re-occlusion and recurrent Ischaemic events after fibrinolysis.\(^14\) The tablet may be chewed or swallowed with equal benefit. Aspirin suppositories or intravenous form may be used in patients with severe nausea and vomiting or upper GI disorders.

Other Anti-platelet Agents

Clopidogrel, ticlopidine or dipyridamole are used if patient is allergic to aspirin or has aspirin resistance. Loading dose of 300mg clopidogrel or 500mg ticlopidine is given if PCI is contemplated.

Atropine

Recommended in patients with: 1) sinus bradycardia with low cardiac output and peripheral hypoperfusion. 2) acute inferior MI with type 1 second or third degree A-V block with hypotension, ischaemic discomfort or ventricular arrhythmia. 3) sustained bradycardia and hypotension after NTG. 4) ventricular asystole. Dose: 0.5 to 1mg I.V repeated every 3-5 minutes up to 2.5mg (0.04mg/kg).\(^11\)

Beta-blocker

Analysis of 28 trials reveals absolute mortality reduction at 7 days from 4.3% to 3.7%\(^15\). It should be used in setting of tachycardia (without CHF), hypertension or pain unresponsive to opioids or NTG.\(^11\)

ACE Inhibitors

Given to patients with CHF or impaired LVEF in early phase. GISSI-3\(^16\) and ISIS-4\(^17\) have shown that it reduces mortality at 4-6 weeks.
An overview of 9 trials have shown an 18% proportional reduction in 35-day mortality with thrombolytic therapy (9.6% fibrinolysis v/s 11.5% control). Comparing Thrombolytic Efficacy

The GISSI-2 and ISIS-3 studies showed that mortality rates at 4 to 5 weeks were similar. GISSI-2: tissue plasminogen activator (tPA) 8.9% and STK 8.5%. ISIS-3: alteplase 10.3%, STK 10.6% and anistreplase 10.5%.

Limitations of Thrombolysis

1) Reduced efficacy: GUSTO-1 study showed that TIMI grade 3 ow is seen in 32% with STK and 54% with tPA with corresponding mortality of 7.4% and 6.3%. 2) Reocclusion: Ohman et al in the TAMI study showed post fibrinolysis re-occlusion rate of 12.4%. 3) Re-infarction: occurs in 3-5%. 4) Recurrent ischaemia: in upto 34%. 5) No Tissue ow: occurs in about 30%. Thus, effective tissue ow is achieved in only about 25% of patients.

Adjunctive Anti-thrombotic Therapy

Heparin: Does not improve clot lysis but enhances coronary patency after rtPA.

Low molecular weight heparin: In the ASSENT-3 trial, enoxaparin(30mg i.v bolus and 1mg/kg every 12 hours) for 7 days plus tenecteplase reduced in-hospital re-infarction or refractory ischaemia compared to heparin.

Direct thrombin inhibitors: Hirudin, bivalirudin and argatroban have not shown clear benefit over heparin following fibrinolysis.

Combination therapy: fibrinolysis + GpIIb/IIIa Inhibitors

Pooled analysis of TIMI-14, SPEED and INRO-AMI trials showed an improvement in TIMI Grade 3 ow from 56% with lytic therapy to 64% in patients with combination therapy (8% improvement with 0.4% mortality reduction).

Percutaneous Coronary Interventions (PCI)

Includes primary PCI, PCI + Pharmacologic reperfusion therapy-Facilitated PCI and Rescue PCI after failed thrombolysis.

Primary PCI

The DANAMI-2 investigators found that routine transfer to a tertiary care hospital for primary PCI
is superior to in-hospital thrombolysis. A significant reduction in combined end point of death, re-infarction and stroke at 30 days was seen in primary PCI group (14.2% to 8.5%, p< 0.002). Primary PCI results in higher patency, less re-occlusion, improved LVEF and better clinical outcome. It is indicated in patients ineligible for fibrinolytic therapy and treatment of choice in cardiogenic shock.

Facilitated PCI
The SPEED trial\textsuperscript{31} showed that PCI after combination therapy increased rate of TIMI 3 ow from 47% to 87%. In TIMI-14\textsuperscript{32} study, those who received half dose alteplase and abciximab and early PCI had greater ST segment resolution compared to those with only combination therapy (57% v/s 24%) or with only fibrinolysis + PCI (54% v/s 8%).

Rescue PCI
Trials have shown clinical benefit if infarct related artery is recanalized by PTCA after failed thrombolysis\textsuperscript{33}

Role of IABP
Used in patients with hemodynamic instability, persistent ischaemia or refractory arrhythmia often in conjunction with PCI.

CABG
It is performed when Angiography reveals unfavourable anatomy for PCI, failed PTCA or mechanical complications like VSD, papillary muscle rupture with MR or cardiac rupture.\textsuperscript{30}

Conclusion
Successful management of AMI during the first 3 hours depends on early diagnosis, rapid triage and optimum combination of pharmacologic reperfusion and PCI.

References

Acute Myocardial Infarction · Management in First 3 Hours 23
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