INTRODUCTION
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Ischaemic heart disease is first leading cause of death in western countries. In United States Approximately 1.5 million myocardial infarction cases occur each year. The mortality with acute myocardial infarction is approximately 30 percent with more than half of the deaths occurring before the striken individual reaches the hospital. Several studies have shown that survival following hospitalization has improved over the last two decades. An additional 5-10 percent of survivors die in the first year following myocardial infarction.

Myocardial infarctin generally results from abrupt decrease in coronary blood flow. This generally follows a thrombotic occlusion of a coronary artery previously narrowed by atherosclerosis. The progression of atherosclerotic lesion to the point where thrombus formation occurs is a complex process related to vascular injury. The injury is produced or facilitated by factors such as cigarette smoking, hypertension and lipid accumulation in the majority of cases. Infarction occurs when an atherosclerotic plaque fissures, reuptes or ulcerates and with conditions favouring thrombogenesis (Factors which may be local or systemic). A mural thrombus forms leading to coronary artery occlusion. In rare cases infarction may be due to coronary artery occlusion secondary to coronary
emboli, congenital abnormalities, coronary spasm and wide variety of systemic diseases particularly of inflammatory naturae. Ultimately the amount of myocardial damage caused by the affected vessels, whether or not the vessel becomes totally occluded. Patients at increased risk of developing acute myocardial infarction include those with unstable angina, multiply coronary risk factors and prinzmetal's variant angina. Less common etiological factors includes hypercoagulability, coronary embolcollagen vascular disease and cocain abuse. The acute myocardial infarction can be precipitated by some factors these are physical exercise, emotional stress and medical or surgical illnesses. The onset of myocardial infarction may be at any time being more commonn and earliest symptoms of acute myocardial infarction. The intensity of pain varies with great deal, and although it is severe excruciating and heavy squeezing type. The pain of acute myocardial infarction is more severy and persist longer than the pain of angina pectoris. Pain occurs at centre of chest/epigastrium and is 30 percent cases radiates to the arm, less common sites of radiation of pain include, abdomen, back, lower jaw and neck. The pain is followed by weakness, sweating, nausea, vomiting, giddiness, and anxiety and discomfort at rest. But about 15-20 percent of myocardial infarctions are painless. The incidence of painless infarction is greater in diabetes mellitus and it increases with age. In elderly patients acute myocardial infarction may present as sudden onset of breathlessness which may progress to
pulmonary oedema. Other less common presentations of acute myocardial infarction are sudden loss of consciousness and confusional state. The pain of acute myocardial infarction is similar to the pain of acute pericarditis, pulmonary embolism, acute aortic dissection or costochondritis. In physical findings, the patient is anxious, restless and attempting to relieve the pain by moving about in bed, squirming and stretching. Pallor is common and is often associated with perspiration of substernal chest pain persisting more than 30 minutes and diaphoresis strongly suggests acute myocardial infarction. About 1/4 th patients of anterior infarction have tachycardia and hypertension and upto 1/2 with inferior infarction shows evidence of bradycardia and hypotension. The apex beat is difficult to palpate. Third heart sound (S₃) and fourth heart sound (S₄) are present and the first heart sound (S₁) and second heart sound (S₂) are diminished in intensity. Rarely paradoxical splitting of second heart sound. A transient apical systolic murmur due to mitral regurgitation and dysfunction of papillary muscle is commonly seen during acute infarction. Pericardial friction rub is found in many patients of transmural myocardial infarction. Jugular venous distension occurs commonly in patients with right ventricular infarction, carotid pulse is often decreased in volume, reflecting reduced stroke volve. Temperature upto 38 °C elevated during the first week of acute myocardial infarction. The acute myocardial infarction is diagnosed by:
1. Non specific indices of tissue necrosis and inflammation - A non - specific reaction to myocardial injury is associated with polymorphonuclear leukocytosis and it often reaches levels of 12000 - 15000 leukocytes per ml, the ESR rises more slowly than W. B. C.

2. The electrocardiographic manifestation of acute myocardial infarction - Transmural infarction is often present if ECG shows Q wave or loss of R wave and non transmural infarction may be present if ECG, shows only ST segment and / or T wave changes which persist.

3. Serum enzymes changes - Enzymes are released in large quantities into the blood from necrotic heart muscles following myocardial infarction.

A. Estimation of SGOT and SGPT : The isoenzyme of CK / LDH has the advantage over CK and LDH in that these are not present in significant concentration in extracardias tissues and therefore are more specific.

B. Creatine phosphokinase (CPK) rises withing 8-24 hours and generally returns to normal by 48-72 hours except in large infarction.

C. Lactic dehydrogenase (LDH) rises later (24-48 hours) and remains elevated for as long as 7 to 14 days.
The myocardial specificity of the isoenzyme determined by the use of radioimmunoassay technique or gel electrophoresis technique for LDH. The isoenzyme which predominates in the heart is referred to as LDH₁ other potential sources of total CK elevation are:

a. Muscular disease includes muscular dystrophy, myopathies and polymyositis.

b. Electric cardioversion.

c. Cardiac catheterization.

d. Hypothyroidism.

e. Stroke.

f. Skeletal muscles damage.

Secondary to trauma, convulsions and prolonged immobilization after cardiac surgery, myocarditis and electric cardioversion often result in elevation of serum levels of CPK MB - isoenzyme. The CK and LDH enzymes level generally do not rise in unstable angina.

**CARDIAC IMAGING**

Acute infarct scintigraphy (Hot spot) imaging is carried out with an infarct imaging agent such as (99m Tc). Stannous pyrophosphate. Scans are usually positive 2-5 days after infarction particularly in patients of
transmural infarction. Myocardial perfusion imaging with thallium - 20/- or technetium 99 M Sesta-mibi which are distributed in proportion to myocardial blood flow and concentrated by viable myocardium reveals a defect (Cold spot) in most patients during the first few hours after development of transmural infarct. The wall motion abnormality determined by two dimensional echocardiography. It is also useful in diagnosis of right ventricular infarction, ventricular aneurysm, pericardial effusion and left ventricular thrombus, while Doppler echocardiography is useful in detection of VSD, MR and complication of acute myocardial infarction.

THROMBOLYTIC THERAPY IN ACUTE MYOCARDIAL INFARCTION

1. Intracoronary Infusion

   With catheterization intracoronary infusion of streptokinase is given within 3-4 hours of onset of symptoms have been shown to restore the patency of thrombosed artery in about 60 percent cases. In some patients immediate relief from angina is achieved and reversal of ST segment occurs and abnormal ECG towards normal ECG.

2. Intravenous Therapy

   (A) Streptokinase

   The streptokinase complexes with plasminogen which then converts circulating and fibrin fixed plasminogen to plasmin which lyses fibrin.
This streptokinase plasminogen complex results in circulation plasmin which causes systemic fibrinolysies with consumption of prothrombin factors V an VIII, Fibrinogen plasminogen and fibrin degradation products, it is antigenic.

(B). **Tissue plasminogen Activator rt PA**

Unlike streptokinase tpa is relatively thrombus specific there are two form of rtPA.

(A) - Alteplase (Single chain form)

(B) - Duteplase (Double chainin form)

(C). **Anistreptoplase or APSAC (An isolated plasminogen Streptokinase Activator Complex)**

This agent is a complex of streptokinase and lysoplasminogen with a P-anisoyl group placed in the catalytic centre of molecule in the intact stat. APSAC in an inactive complex but when injected into the blood hydrolysis of anisoyl group occurs. Producing the active streptokinase plasminogen complexes, this produces fibrinolysis with a half of streptokinase that is 15-20 minutes and ultrashort half life of 5 minutes of tPA.
(D). **Urokinase**

(a). Urokinase acts on plasminogen coverting it to plasmin directly.

(b) Pro-urokinase : It is a single chain urokinase type plasminogen activator (SCU-PA) urokinase is not antigenic but it is not yet proved for use in acute myocardial infarction.

The reduction in the mortality was inversely related to the time after onset of symptoms when streptokinase was given.

(i) Under 1 hour there was 50% reduction in the mortality rate.

(ii) Under 3 hours there was 25% reduction.

(iii) 3-6 hours 10% reduction in mortality rate and after 6 hours there was no any benefit GISSI trial (Grouppo Italiano, 1987) at 21 days rate was 1.7% in treated group and 13% in control group.

**INDICATIONS FOR THROMBOLYTIC THERAPY**

1. If ischemic symptoms persist more than 30 minutes that are associated with new ST segment elevation of at least 0.1 MV in at least two leads in the inferior, anterior or lateral location or ST segment depression in the anterior leads.

2. The thrombolytic therapy also indicated with different dose variations. These are:

(i) Obstructive peripheral arteriopathies.
(peripheral arterial thromboembolisms).

(ii) Deep vein thrombosis and pulmonary embolism.

(iii) Ocular pathology -

3. a. Retinal vein thromboembolism.
   b. Haemophthalmia.
   c. Hyphaema.

CONTRAINDICATIONS OF THROMBOLYTIC THERAPY

A. **Absolute Contraindications**

1. Recent (within 2 weeks) invasive or surgical procedure or prolonged cardiopulmonary resuscitation.

2. Marked hypertension, if more than 180/100 mm Hg.

3. History of cerebrovascular haemorrhage.

4. Suspected Aortic dissection or pericarditis.

5. Haemorrhagic ophthalmic conditions such as diabetic haemorrhagic retinopathy.

6. Known allergy to streptokinase or APSAC (can be use tPA or urokinase).
B. **Relative Contraindications**

1. Head trauma or surgery of more than 2 weeks duration.
2. Recent severe hypertension with or without treatment.
3. Active peptic ulcer.
4. History of cerebrovascular accident.
5. History of bleeding diathesis or current use of anticoagulants.
6. Significant hepatic dysfunction.
7. Use of streptokinase or APSAC 6 months before
   
   (does not apply to use of tPA or urokinase)

**DOSES OF THROMBOLYTIC AGENTS**

a. **Urokinase**: 2 millions IU I/V over 60 minutes.

b. **Streptokinase**: 1.5 million IU I/V over 60 minutes. Heparin can be started I/V 4 hours after streptokinase and maintain for 48 hours.

c. **Anistreplase (APSAC)**: 30 mg I/V over 5 minutes (2-5 minutes).

d. **tPA**: 10 mg bolus I/V then 50 mg in 1st hour, 20 mg in 2nd and 3rd hours. Rapid or front loading - 15 mg bolus I/V 0.75 mg/kg over 30 minutes.

50 mg over 60 minutes in both of these schedules the total does in 100 mg, heparin can be started I/V immediately after tPA and maintain for 48 hours.
e. tPA + SK: tPA 1 mg/kg over 60 minutes 10% as a bolus (total dose 90 mg and SK 1 million units over 1 hour, start heparin after thrombolysis and maintain for 48 hours.)
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1. Usual doses

2. C/A selectivity

3. Patenty of intact related

4. Time depending

5. Reoccussion

6. Improvement of LL

7. Improvement of Survival

8. Hypotension

9. Halt life

10. Allergic reaction

11. Rhino gonodysitis

12. Intracrania bleeding

13. Repeat dosing possible

14. Cost

OVERALL COMPARISON OF VARIOUS THROMBOTIC AGENTS.