A REVIEW ON MANAGEMENT PRINCIPLES AND MEDICATION OF MYOCARDIAL INFARCTION

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Abstract

Myocardial infarction is the most common public health issue and a major cause of death including disorders of heart and blood vessels. Among all heart problems, ventricular fibrillation is the major cause that occurs soon after the onset of ischemia. As the patient reaches hospital major aim is to decrease the size of the infarct. The control and management of MI depend on the pathophysiological conditions and the time course of irreversible myocardial injury. The fundamental goals of managing acute MI include: (i) Duration of exposure of myocardium to ischemia should be minimized. (ii) Rapid reperfusion (iii) Preventing recurrent ischemia and re-occlusion. (iv) Managing cardiac arrhythmia and other mechanical complications. Management of MI requires prompt diagnosis and therapy including Fibrinolytic therapy, Antithrombin agents, Antihypertensive, and currently discovered many kinds of drugs including LCZ696 and new FDA- Approved treatment and therapies.

INTRODUCTION

Myocardial infarction is a medical emergency and the most common cause of death. Patients in which ventricular fibrillation develops, the majority of them die before they obtain medical attention. Due to this in order to reduce deaths, it is important to take measures to educate common people about symptoms and signs of acute myocardial infarction so that patients can get CPR and local management as soon as possible. Once the patient comes out of danger and sudden death is prevented, then it is important to reduce the size of infarct by early hospitalization and then drug therapy plays the major role.

ETIOLOGY

Acute myocardial infarction usually results from an imbalance in oxygen supply and demand which is most often caused by complete occlusion of a coronary artery with atherosclerotic plaque (thrombus). The thrombus ruptured at the site of plaque, exposing its inner core and thus promoting thrombus formation.

OBJECTIVES OF TREATMENT

The treatment objective is to reduce the extent of myocardial damage. As the myocardium is damaged by a less oxygen supply due to the obstructed coronary artery, infarct size can be reduced in two ways:

i) Restoration of coronary blood flow by dissolving thrombus.

ii) By decreasing myocardial oxygen supply.

Restoration of blood flow

Restoration of blood flow becomes the important objective of treatment as it reduces the ST-elevation ECG also known as the left bundle branch block. it allows medical practitioners to know that relative therapies are needed or not. Fibrinolytic therapy should not be given to the patient without checking ECG. Flow is normally restored using drug therapy – fibrinolytic agents eg. Streptokinase, tissue plasminogen activator, an antiplatelet drug such as aspirin and antithrombins such as heparin. Recently, coronary angioplasty has been used to restore flow mechanically. The flow should be restored at good speed because for every hour of delay the effect of therapy got diminished and mortality increased.

Decreasing myocardial oxygen supply

As compare to restoration therapy, decreasing myocardial oxygen consumption is considerably less beneficial. A decrease in oxygen consumption is achieved by lowering blood pressure, heart rate and cardiac filling pressures. Drugs that possibly work in a good way to it are beta blockers, glyceryl trinitrate and possibly ACE inhibitors.

MANAGEMENT PRINCIPLES

The basic principles that underlie management of myocardial infarction are based on the pathophysiology of condition and the time course of irreversible myocardial injury.

PRE- HOSPITAL MANAGEMENT

Basic challenges in the early management of MI need recognition by patient that the symptoms advantages emergency evaluation, and then actions that lead to prompt presentation to emergency medical systems. Some patients experience prodromal unstable angina followed

by increase in infarction with or without complete coronary occlusion. Many patients fail to acknowledge the symptoms of MI and may delay presentation because of atypical symptoms, or scared and contradicted that they are experiencing a heart attack.

EMERGENCY CARE

Patients with acute chest pain are required to undergo a rapid diagnosis and early risk stratification to identify patient in whom early interventions can improve outcome. On other side if the diagnosis of acute myocardial infarction has been ruled out, then one must focused on detecting other cardiac or non cardiac causes of presenting symptoms.

A diagnosis report of myocardial infarction must be made first. Diagnosis usually depends on history of severe chest pain lasting for 20 mins or more, that is not responding to GTN.In regards of the disease the major clues are previous history of coronary artery disease, and emerge of pain lower jaw, neck, or left arm. In elderly people most common symptoms are fatigue, dyspnoea, faintness or syncope, pain may not be severe. In most of the patients no individual physical signs of diagnostic, but most of them have evidence of autonomic nervous system activation (pallor, sweating) and sometimes hypotension or a narrow pulse pressure, also including irregularities of pulse, bradycardia or tachycardia and a third heart sound and basal rales.

A rapid electrocardiogram should be obtained as soon as possible. At early stage, the ECG is quite normal. In case of ST-segment elevations or left bundle branch block, an early treatment and an reperfusion therapy is needed.

A routine blood sampling for serum markers is done in acute phase but should not wait for reports to start treatment (reperfusion therapy). The results of elevated markers of necrosis may sometimes is helpful in deciding to give reperfusion therapy.

2D-echocardiography and perfusion scintigraphy has also been used successfully and helpful to rule out acute myocardial infarction.

When the history, ECG and serum markers do not allow us to diagnose acute myocardial infarction then the patient can proceed safely to stress testing for investigation of underlying heart disease.

SUDDEN CARDIAC DEATH AND RESUSCITATION

Most commonly acute myocardial infarction leads to prehospital cardiac arrest and sudden deaths. Resuscitation success is critically time dependent as after each minute of ventricular fibrillation survival reduces 7% to 10%.Epidemiological studies reveals that 60% to 73% of deaths associated with ST elevation occurs out of hospital within 1-2 hrs after attack leads to early death as a result of cardiac arrest caused by ventricular fibrillation. So to address this deficiency many communities are focusing on new initiatives eg. Survival campaigns chain, which boost the availability of trained individuals to initiate cardiopulmonary resuscitation (CPR),a standard CPR increases survival by approximately 30% and who knows how to use automatic external defibrillators are designated to reduce prehospital mortality caused by cardiac arrest.

POST-HOSPITAL MANAGEMENT

As soon as patient is in hospital the emergency management of patient with suspected MI is initiated with rapid diagnosis and swift restoration of flow in the culprit artery. Critical concepts in emergency management of MI includes emergency medical service response times within <10min,transfer to percutaneous coronary intervention capable center <30 min, first medical contact to reperfusion <90 min.

RAPID REPERFUSION

Delay to reperfusion is minimized in patients with STEMI is critical to retrieve ischemic myocardium, to restrict residual injury, to reduce the risk of following heart failure, and to improve survival. The effect of time is not linear, the most effective salvage of myocardium is achieved with reperfusion within 60-90 minutes of onset of ischemia. First 60 mins are known as "golden hour" because this is the best time in which myocardial function can be best restored. Administration of a fibrinolytic agent was basis of reperfusion therapy before the development of primary percutaneous coronary intervention (PCI), and still constitutes major therapy in settings where primary PCI is not available or not available promptly. The oldest fibrinolytics streptokinase and urokinase are still widely used in some parts of the world because of its cost effectiveness. Future evolution of fibrinolytic therapy has focused to improve ease and rapidity of administration as well as create a balance between fibrinolytic efficacy and bleeding. After streptokinase the new generation fibrinolytics includes alteplase, reteplase, and tenecteplase and they all have magnified effects at the sites of thrombus formation.

PATHWAYS OF CARE (ST-ELEVATION MI)

Pathway of care for patients with STEMI are focused at reducing the duration of ischemia and sorting of patients to the favorable environment for management of the complications of MI. PCI primarily and timely preferred whenever it is present and provided by experienced STEMI teams, and has become the presiding approach to reperfusion therapy in most countries. Condemnatory elements of pathways of care for STEMI include instant recognition by the patient of the need to call emergency medical systems ,rapid dispatch and arrival of emergency

providers (<10 minutes),in-ambulance diagnosis of doubted STEMI, administration of antithrombotic agents and analgesics, quick transfer to a PCI capable center (<30 minutes).

PATHWAYS OF CARE (NON-ST ELEVATION MI)

The clinical presentation or NSTEMI is more sneaked than that of STEMI and may be preceded by new onset exertional angina, deteriorating angina or no previous symptoms. Not like STEMI, autonomic features do not usually accompany the onset of NSTEMI. Because of the onset pattern the patient may misunderstood the symptoms as gastrointestinal or musculoskeletal in nature, and presentation is frequently to nonemergency medical services. The diagnosis depends on the clinical syndrome plus ECG findings of ischemia, but without persistent ST-elevation and sensitive biomarkers of necrosis.

MEDICATION

INITIAL TREATMENT

ANALGESICS: Relieving pain is important to relieve distress but also to avoid the results of sympathetic stimulation on the heart, including increases in afterload and arrhythmogenesis. Opoid analgesia that is administered through intravenous route is most commonly used therapy and should be carefully titrated, and is often administered with antiemetics. For eg. To relieve pain a dose of 2-8 mg morphine sulphate intravenously is administered repeated at intervals of 5 to 15 min has been recommended, until the pain is relieved or side effects like hypotension, depression of respiration, or severe vomiting has emerged. A successful analgesia diminishes the patient's restlessness, reduces anxiety and the activity of the autonomic nervous system and consequently reduces the heart's metabolic demands.

NITRATES: In acute MI nitrates are most commonly given drug that may relieve vasospasm and reduces pain. Sublingual nitrates have been recommended for the initial treatment of patients with MI by the virtue of their ability to increase coronary blood flow by coronary vasodilatation and to decrease ventricular preload by increasing venous capacitance. At present, sublingual nitrates should not be given to the patients with STEMI and those with suspected right ventricular infraction, especially if accompanied by bradycardia. After treatment improvement in patient's symptoms or a change in hemodynamics should be observed. A sudden hypotension and bradycardia can be produced even at small doses that can usually be reversed with intravenous atropine. In early course of STEMI long acting oral nitrates preparation should be avoided. In patients with a prolonged period of waxing and waning chest pain, nitroglycerine i.v injection may help to control symptoms and correct ischemia, simultaneously requires monitoring of blood pressure.

OXYGEN: All the hospitalized patients with MI are commonly treated with oxygen for atleast 24 to 48 hrs on the basis of an assumption that the inspired air may protect hypoxia and ischemic myocardium. Although there are very less examples and evidences to support its use in patients with heart failure or hypoxia. Patients with hypoxia can be treated by oxygen level below 94% delivered using a face mask and for those with hypoxia associated with heart failure; ventilation and circulation support may be required.

ANTIPLATLET DRUGS: Aspirin is a powerful antiplatlet drug, with a speedy effect, which reduces mortality by 20%. All the suspected patients with myocardial infarction should be given aspirin. A correct dose of 150-300 mg should be given as soon as possible. Patients suffering from MI should advise to take aspirin by the medical practioners as there is no need to wait for ECG.

FIBRINOLYTIC THERAPY: This therapy plays an important role given to dissolve the thrombus in the artery and restore flow. The two fibrinolytic drugs that is most commonly used in streptokinase and tissue plasminogen activator. Patients with appropriate indications and no contraindication should be given with fibrinolytic therapy. An intravenous infusion of 1.5 million units of streptokinase is given over 30- 60 minutes. If the streptokinase is given rapidly then hypotension may emerge but it can be overcome by slow down the infusion and given fluid.

Tissue plasminogen activator (tPA) specifically binds to thrombus, it produces local fibrinolysis. Systemic effects of tPA are not same as streptokinase. Clot dissolution occurs more spottily with tPA than streptokinase restoring potency at 90 min in 55% of patients. As compare to streptokinase, tPA appears to cause more bleeding and in particular produces a higher incidence of cerebral bleeding. Despite the increased risk of stroke, the total clinical benefit is greater with tPA in nearly all subgroups of patients.

OTHER DRUGS

ANTITHROMBIN AGENTS: Heparin is the major antithrombin agent. It has been given subcutaneously and intravenously and used with both fibrinolytics. Intravenous heparin is given as 5000 unit bolus followed by 1000 units per hour intravenously, adjusted after 24 hrs according to the activated partial thromboplastin time and in case with combination of heparin and tPA adjusted after 6 hrs.

ACE INHIBITORS: ACE inhibitors are the class of medication that is priorly used for the treatment of high blood pressure , heart failure and helpful in reducing the mortality of myocardial infarction that can be seen within intial 30 days. They act by relaxing blood vessel as well as a decrease in blood volume ,which further causes lowering

of blood pressure and leads to reduced oxygen demand from heart. Captopril dose of 6.25 mg or equivalent low doses of another ACE inhibitors, should be used as a first dose and, if tolerated, dose can be increased upto 25 mg twice daily.

BETA BLOCKERS: Beta blockers are the specific class of medication that is majorly responsible for reducing the incidences of arrhythmias, infarct size and mortality. Intravenous beta blockers include atenolol, metoprolol, and timolol. In haemodynamically stable patients with heart rate above 50 beats per minute and systolic blood pressure above 100 mm of hg beta blockers can be given. The standard regimen is atenolol 5 mg intravenously over 5 mins followed 10 mins later by a further 5 mg.

NEWLY DISCOVERED DRUGS AND THERAPIES

LCZ696: LCZ696 is a new drug recommended by US guidelines as a first line treatment for heart failure. This drug is proved to be the better than conventional drugs at reducing cardiac death and hospitalization due to heart failure. This drug also specifically protects heart from cardiac rupture after myocardial infarction.LCZ696 is a novel drug combination of Valsartan, a traditional antihypertensive drug, and Sacubitril an organoprotective drug. Sacubitril inhibits neprilysin which deteriorate hormones secreted majorly from the heart called Atrial Natriuretic Peptide (ANP), and B-type Natriuretic Peptide (BNP). Ann extensive clinical trial of patients who had chronic heart failure with reduced ejection fraction (the percentage of blood exiting the heart at each contraction) described that the number of cardiac deaths and re-hospitalizations due to heart failure was reduced promptly with LCZ696 treatment than with existing ACE inhibitors.

LCZ696 is now used on large scale in Europe and the United States as the first treatment for chronic heart failure.

TherOX: It is a Supersaturated oxygen(SSO_2) therapy for patients who suffers from left anterior decending (LAD) ST-elevation myocardial infarction(MI). This treatment has acquired premarket approval from the Food and Drug Administration(FDA). In this to a specific targeted ischemic region supersaturated oxygen is delivered and perfused by patient's LAD coronary artery immediately following revascularization through percutaneous coronary intervention (PCI) with stenting that has been completed within 6 hours after the onset of anterior acute MI symptoms caused by a LAD artery infarct lesion. SSO delivers a one-time, 60- minute infusion of the superoxygenated blood through a small catheter by using in- hospital oxygen and saline and mixing it with the patient's arterial blood.

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