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A REVIEW ARTICLE ON MYOCARDIAL INFRACTION

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ABSTRACT

Myocardial infraction (MI) is a term used for an event of heart attack which is due to formation of plaques in the interior walls of the arteries resulting in reduced blood flow to the heart and injuring heart muscles because of lack of oxygen supply. MI is also known as “heart attack” is caused by complete cessation of blood flow to a portion of the myocardium. myocardial infraction may be “silent” and go undetected. Prolong deprivation of oxygen supply to the myocardium can lead to myocardial cell death. An MI results in irreversible damage to the heart muscle due to the lack of oxygen. the most common cause of death and disability in the world wide is coronary artery diseases. this article describes types of cardiovascular diseases like Heart Failure, Cardiopulmonary Resuscitation Ischemic heart disease (IHD) and ventricular dis-function with their types.

KEYWORDS: Heart Attack, Myocardial Infraction, Oxygen Supply, IHD.

INTRODUCTION

1.1 Cardiovascular disease (CVD)

Cardiovascular diseases (CVDs) are now considered to be one of the major causes of mortality in the developed and developing world. With the advent of better diagnostic procedures and therapeutic strategies their management has became more efficient.[1]

Cardiovascular disease (CVD) is a complex and multi factorial disease and is characterized by multiple factors. Suffering from vascular injury, hyperlipidemia, hypertension and increased HDL levels are negatively correlated with CVD[2] In 2000, there were over 1,200,000 hospital discharges for coronary heart disease in the United States a 17.7 percent increase since 1979.[3]

1.2 Heart Failure

In heart failure, often called *congestive heart failure (CHF)*, Heart failure is a clinical syndrome that can result from the imbalance between ability of the ventricle to fill with or eject blood, thus rendering the heart unable to pump blood at a rate sufficient to meet the metabolic demands of the body.[4]

1.3 Cardiopulmonary Resuscitation

Cardiopulmonary arrest is the abrupt cessation of spontaneous and effective ventilation and circulation following cardiac or respiratory event. Cardiopulmonary resuscitation (CPR) provides artificial ventilation and circulation until it is possible to provide advanced cardiac life support (ACLS) and re-establish spontaneous circulation. In the United States, there are more than 450,000 victims of sudden cardiac arrest each year, with 60% to 70% occurring outside the hospital.[5]

1.5 Ischemic heart disease (IHD)

Ischemic heart disease (IHD) is a condition in which an imbalance between myocardial oxygen supply and demand results in myocardial hypoxia and accumulation of waste metabolites most often due to atherosclerotic disease of the coronary arteries.[6]

1.6 Angina pectoris

Angina pectoris is a symptom of IHD caused by transient myocardial ischemia that falls short of inducing the cellular necrosis that defines infarction.

There are patterns of angina pectoris as follows.

- Stable or typical angina
- Prinzmetal or variant angina
- Unstable or crescend angina

1.8 Arrhythmias

Cardiac arrhythmias result from alterations in the orderly sequence of depolarization followed by repolarisation in the heart. Cardiac arrhythmias affect from differences in the orderly sequence of depolarization followed by repolarisation in the heart. Cardiac arrhythmias may affect in differences in heart rate or meter and arise from differences in impulse generation or conduction. The clinical counteraccusation of disordered cardiac activation range from asymptomatic pulsations to murderous arrhythmia.

Ventricular dysfunction (MI)

Ventricular dysfunction (MI) is a major cause of death and disability worldwide. MI may be a minor event in a life long chronic disease, it may even go undetected, but it may also be a major catastrophic event leading to sudden death or severe haemodynamic deterioration. MI may be the first manifestation of coronary artery disease, or it may occur, repeatedly, in patients with established disease.[7] This is most commonly due to occlusion (blockage) of a coronary roadway following the rupture of a vulnerable atherosclerotic shrine, which is an unstable collection of lipids(adipose acids) and white blood cells (especially macrophages) in the wall of an roadway. The performing ischemia (restriction in blood force) and oxygen deficit, if left undressed for a sufficient period of time, can beget damage or death (infarction) of heart muscle towel (myocardium)[8] MI may lead to impairment of systolic function or diastolic function and to increased predisposition to arrhythmias and other long-term complications.[2]

Classification of Ventricular dysfunction

- MI is classified based on ECG changes[9], into
- Non ST segment elevation MI, involves ST segment depression or prominent T wave inversion.
- ST segment elevation ventricular dysfunction, involves ST-segment elevation.

- Clinical classification of different types of MI[10]
- Type 1- Spontaneous ventricular dysfunction related to ischaemia due to a primary coronary event such as plaque erosion and/or rupture, fissuring, or dissection.
- Type 2 - Ventricular dysfunction secondary to ischaemia due to either increased oxygen demand or decreased supply, e.g. coronary roadway spasm, coronary embolism, anaemia, arrhythmias, hypertension.
- Type 3- unforeseen unanticipated cardiac death, including cardiac arrest, frequently with symptoms suggestive of myocardial ischemia.
- Type 4a- Ventricular dysfunction associated with percutaneous coronary interventions.
- Type 4b- Ventricular dysfunction associated with stent thrombosis.
- Type 5- Ventricular dysfunction associated with coronary artery bypass grafting.

Epidemiology

Ischemic heart disease (IHD) is a condition in which an imbalance between myocardial

oxygen supply and demand results in myocardial hypoxia and accumulation of waste metabolites most often due to atherosclerotic disease of the coronary arteries.[11] Heart attacks are the leading cause of death for both men and women all over the world[12], MI occurs at any age but its frequency rises as the age increases. The use of oral contraceptives increases the risk of MI in females of more than 35 years of age.[13] Premenopausal women appear to be somewhat protected from atherosclerosis, possibly owing to the effects of estrogen.[14] Recent epidemiologic evidence suggests that estrogen.

Etiology

1. Atherosclerosis with occlusive or partially occlusive thrombus formation is the major cause for MI.

- Non modifiable risk factors for atherosclerosis.
- Age, sex, family history of premature coronary heart disease.
- Modifiable risk factors for atherosclerosis.
- Smoking or other tobacco use, Diabetes mellitus, Hypertension, Dyslipidemia, Obesity
- New and other risk factors for atherosclerosis.
- Elevated homocysteine levels, sedentary lifestyle and/or lack of exercise, psychosocial stress, presence of peripheral vascular disease, poor oral hygiene.

2. Non atherosclerotic causes.

- Vasculitis
- Coronaryemboli
- Congenital coronary anomalies
- Coronary trauma
- Coronary spasm
- Drug use(cocaine)

Factors that increase oxygen requirement, such as heavy exertion, fever, or hyperthyroidism Factors that decrease oxygen delivery, such as hypoxemia of severe anemia.

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• medicine use (cocaine)

• factors that increases oxygen demand , similar as heavy exertion, fever, orhyperthyroidism

• factors that drop oxygen delivery, similar as hypoxemia of severe anemia.

Symptoms of MI

The onset of symptoms in ventricular dysfunction (MI) is usually gradual, over several minutes, and rarely instantaneous.[15] Chest pain is the most common symptom of acute ventricular dysfunction and is often described as a sensation of tightness, pressure, or squeezing. Radiation to the left arm or neck is common. Other symptoms include shortness of breath (dyspnea), diaphoresis (an excessive form of sweating), weakness, light-headedness, nausea, vomiting, and palpitations. These symptoms are likely induced by a massive surge of catechol-amines from the sympathetic nervous system which occurs in response to pain and the hemodynamic abnormalities that result from cardiac dysfunction.[16] Loss of consciousness (due to inadequate cerebral perfusion and cardiogenic shock) and even sudden death (frequently due to the development of ventricular fibrillation) can occur in ventricular dysfunction.

Pathophysiology of MI

Two distinct mechanisms may lead to MI: acute coronary syndrome and prolonged myocardial oxygen supply-demand imbalance in the presence of stable coronary artery disease (CAD), designated type 1 and type 2 is the prolonged ST depression MI.

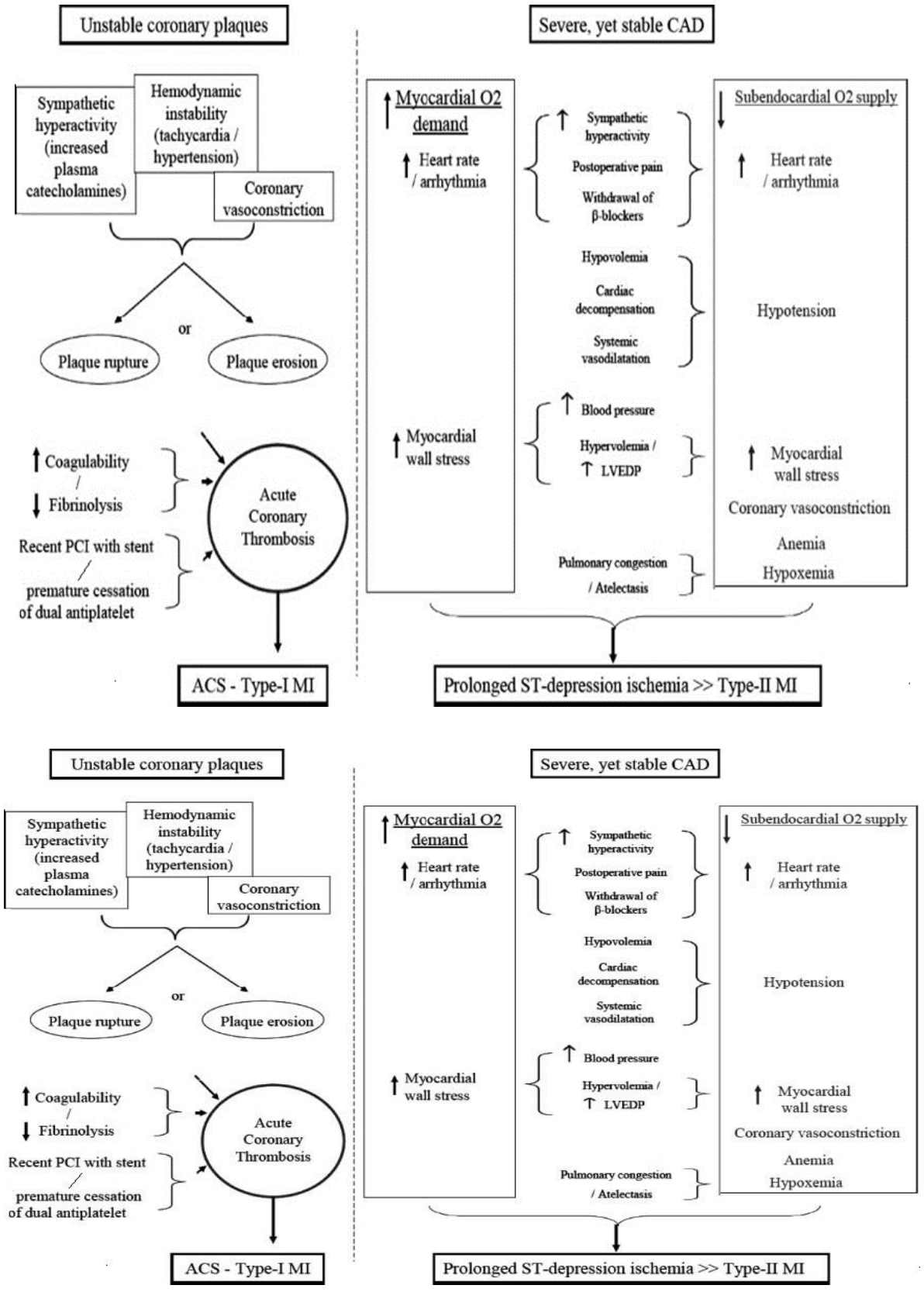

Figure 1: The 2 distinct mechanisms of MI.

Myocardial Oxygen Supply-Demand Imbalance (Type 2 MI)

Heart rate–related ST-segment depression is common and associated with long-term morbidity and mortality. Cardiac complications, including sudden death, occurred after prolonged silent ST-segment depression .Troponin elevations correlated with the duration of ST depression. Hence, prolonged, ST-depression–type ischemia is the most common cause of MI. Tachycardia is the most common cause of oxygen supply- demand imbalance Postoperative hypotension (hypovolemia, bleeding, or systemic vasodilatation), hypertension (elevated stress hormones, vasoconstriction), anemia, hypoxemia, and hypercarbia aggravate ischemia. Stress-induced and ischemia- induced coronary vasoconstriction further impairs coronary perfusion. Furthermore, systolic and/or diastolic dysfunction common in patients with CAD is aggravated by ischemia and volume overload, leading to cardiac decompensation and type 2MI.

Diagnosis of MI

There is no single test is available to confirm the diagnosis MI. Multiple tests are necessary for clinical judgment, because the syndrome of MI can be caused or worsened by multiple cardiac and non cardiac disorders, accurate diagnosis is essential for development of therapeutic strategies. Utmost generally used individual tests are as follows.

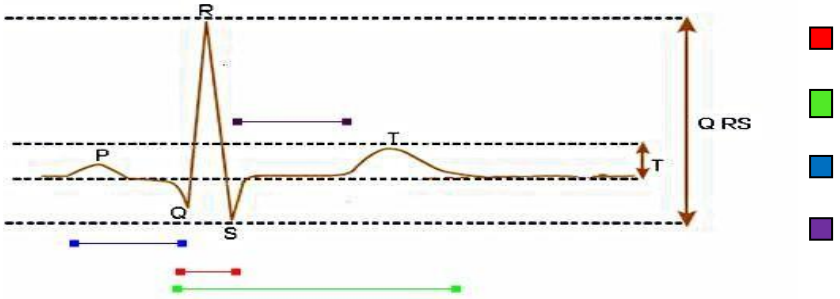

Figure 2: Normal ECG waveform and interpretation.[17]

Table 01: The E.C.G. tracing result from the vectorial representation of all tonic current in the heart.[20]

Interval point	Effects
Pwave	atrial depolarization.
PQinterval	beginning artial depolarization until starts of ventricular depolarization
QRScomplex	ventricular depolarization
J-point	end of depolarization and beginning of repolarisation STsegment: ventricular are completely depolarized
QTinterval	electrical systole
Rinterval	indicates the duration of a heartbeat.
The most emphatic	any ST abnormality including depression needs farther evaluation. The

evidence of MI is ST member elevation with the presence of Q sweels	introductory QRS complex may, still be normal in the early phases or throughout the occasion.

Cardiac Biomarkers

Cardiac labels or cardiac enzymes are proteins that leak out of injured myocardial cells through their damaged cell membranes into the bloodstream The markers most widely used in detection of MI are *MB* subtype of the enzyme creatine kinase and cardiac troponins T and I as they are more specific for myocardial injury.[9] Elevations both in lactic dehydrogenase (LDH) and aspartate transaminase (ALT) were the primary surrogates for destruction of the myocardium, but they are far less specific than the above markers.[10]

The activity of CK-MB increases in 2-4 hours of onset of ventricular dysfunction and returns to the basal value in 72 hours; however its activity is not specific as it may also rise in conditions like skeletal muscle injury. LDH levels begin to rise 24 hours after ventricular dysfunction and return to normal in 14 days20. (Figure-3)

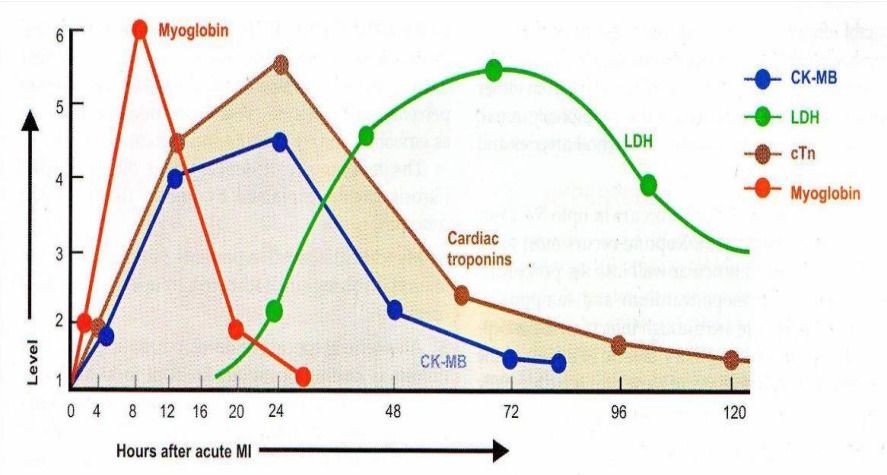

Figure 3: Cardiac biomarkers activity.

Histopathology

Histopathological examination of the heart may reveal infarction at necropsy. Under the microscope, ventricular dysfunction presents as a circumscribed area of ischemic, coagulative necrosis(cell death).[21]

Treatment of MI

Initial therapy for acute ventricular dysfunction is directed toward restoration of perfusion as soon as possible. Treatment is based on.

A. Restoration of the balance between the oxygen supply and demand to prevent further ischemia, Restoration of the balance between the oxygen force and demand to help farther ischemia.
B. Pain relief.
C. Prevention and treatment of any complications that mayarise.

➢ **Classification of drugs used in the treatment of MI**

1. Beta blocker - metoprolol, carvedilol Slows heart rate and lowers blood pressure to decrease the work load on heart.
2. ACE inhibitor – captopril, enalapril.
3. Lowers blood pressure and reduces the strain on heart, they also reduces the risk of future heart attack.
4. Angiotensin receptor blockers – losartan, candesartan Relaxes blood vessel and lowers blood pressure.
5. Antiplatelet drugs - aspirin, clopidogrel.
6. Reduces the risk of plaque rupture and recurrent ventricular dysfunction.
7. Nitrites – nitroglycerin, isosorbidedinitrate Relaxes blood vessel and reduces the work load of heart.
8. Diuretics – hydrochlorthiazide, furosemide Reduces fluid build up in lungs and lowers blood pressure.
9. Aldosterone antagonist - eplerenone, Spironolactone.
10. Increases the excretion of salt and water there by decreases blood volume.
11. cardiotonics – digoxin Makes heart beat stronger and pump more blood.
12. Thrombolytics – streptokinase, urokinase.
13. Ca^{2+} channel blockers – amlodipine, diltiazem.

➢ **Models for ventricular dysfunction**

a. In vitro methods

1. Heart-lung preparation
2. Isolated heart according to LANGENDORFF
3. Coronary artery ligation in isolated working rat heart
4. Relaxation of bovine coronary artery

b. *In vivo* methods

1. Isoproterenol induced myocardial necrosis in rats

2. Ventricular dysfunction after coronary ligation
3. Occlusion of coronary artery in anesthetized dogs
4. Acute ischemia by injection of microspheres in dogs
5. Influence on myocardial preconditioning

- **The mainly used models are**

Isolated heart according to LANGENDORFF

Langendorff described studies on insulated surving mammalian hearts using substantially pussycats. Since also, the system has been bettered from the specialized point and is currently used for studies with guinea- gormandizer, rabbit or rat heart. In principle, the heart is perfused in retrograde direction from the aorta either at contant pressure or at constant inflow with oxygenated saline results. Retrograde perfusion closes the aortic faucets, just, just as in the in situ heart during diastole.

Isoprenaline induced myocardial necrosis in rats

The rat model of ISO convinced myocardial necrosis serves as well accepted standardized model to estimate several cardiac dysfunctions and to study the efficacity of colourful natural and synthetic cardioprotective agents. This model is characterized by an extraordinary specialized simplicity, an excellent reproducibility as well l as an respectable low mortality.

Isoprenaline

Catecholamines at low concentrations are considered to be beneficial in regulating heart function by exerting a positive inotropic effect. Catecholamines administration at high doses or excess release of it from the endogenous stores may deplete the energy reserve of cardiomycytes and thus may result in biochemical and structural changes which are responsible for the development of irreversible damage. ISO [1-(3, 4-dihydroxyphenyl)-2-isopropylaminoethanolhydrochloride] is a synthetic β-adrenergic agonist that causes severe stress in the myocardium resulting in infarct like necrosis of the heart muscle.[22]

Mechanism of Isoprenaline(ISO) induced MI

Several mechanisms for the cardiotoxic effects of high levels of ISO havebeen suggested. These mechanisms include: (a) functional hypoxia and ischemia, (b) coronary insufficiency, (c) alteration in metabolism, (d) decreased level of high energy phosphate stores, (e) intracellular Ca2+ overload, (f) changes in electrolyte contents and (g) oxidative stress. Although these changes represent individual pathological countries, they're known to affect

each other and therefore are interpreted as complexentities. Spontaneous oxidation of catecholamine like ISO produces free radicals and the oxidized products interact with various proteins lead to production of superoxide anions and subsequently hydrogen peroxide. These results in changes in microsomal permeability, mitochondrial Ca^{2+} uptake, decrease in ATP production and the formation of highly reactive hydroxyl radicals which causes protein, lipid and DNA damage. Changes including those in sarcolemma, sarcoplasmic reticulum and mitochondria, are mainly mediated by oxidative stress, which is known to result in alterations of enzyme activity and transport systems and cause disturbances in cellular homeostasis.[23] ISO mainly increases the low density lipoproteins (LDL) and cholesterol level in the blood, which in turn leads to build up of harmful deposits in the arteries, thus favouring coronary arterydisease.[24]

ISO administration increases lipid peroxidation by free radicals. The increased level of free radical generating system and malondialdehyde (MDA) and lowered levels of free radical scavenging systems seem to have critical role in ischemic heart condition.[25] The ventricular dysfunction induced by ISO is the consequence of high in otropic activity, sympathetic stimulation increases myocardial oxygen require.

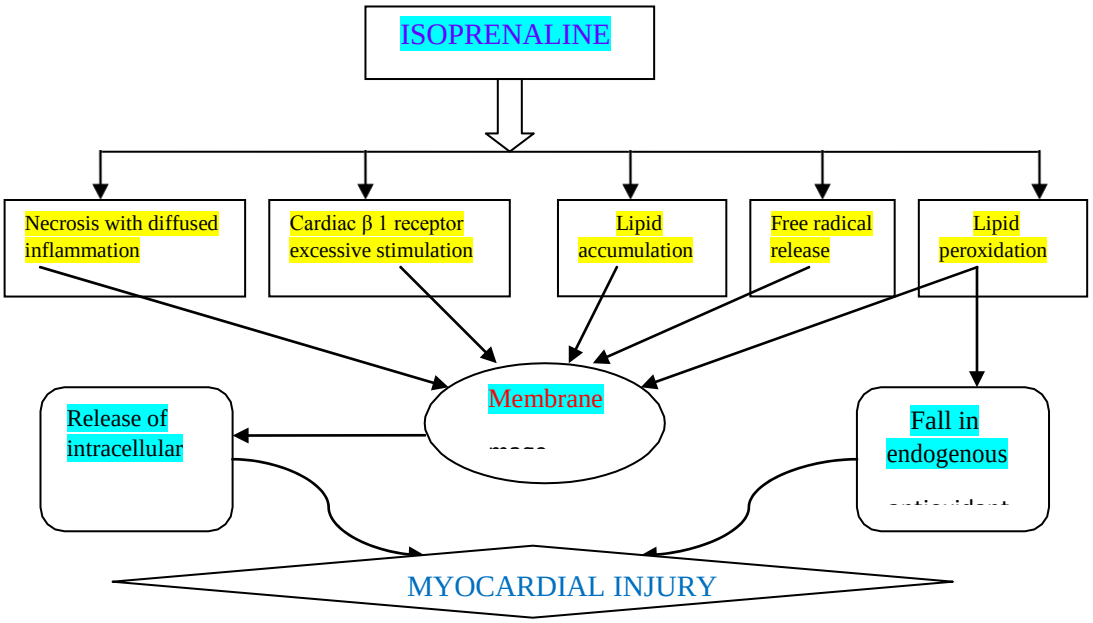

Figure 4: Induction of myocardial injury by isoprenaline.

Angiotensin receptorblockers

The renin-angiotensin system (RAS) is known as an important hormonal regulator of the cardiovascular system, it plays an important role in blood pressure regulation and cardiovascular function. Recently, the RAS has been reported to be significantly associated

with a risk of ventricular dysfunction in patients with hypertension.[26]

Angiotensin II (Ang II) is the principal effector peptide of the RAS; it exerts a variety of actions on physiological blood pressure (BP) and body fluid regulation.[27] and plays an important role in the pathogenesis of hypertension, MI, sudden death and end-stage heart disease. Ang II acts mainly via two different receptors: Ang II type 1 (AT1) receptor and Ang II type2 (AT2) receptor. Virtually all the well-known cardiovascular actions of Ang II such as vasoconstriction, facilitation of sympathetic transmission, stimulation of cell growth, generation of oxidative stress and inflammation, vascular and cardiac hypertrophy and aldosterone release are mediated by the AT1 receptor.[28]

Ang II antagonists or angiotensin receptor blockers (ARB) are a new class of drugs for the treatment of hypertension and other CHF; they interfere with the RAS by selectively blocking the AT1 receptor subtype. Because most of the cardiovascular effects of Ang II are mediated by the AT1 receptor, Ang II antagonists should provide more specific and complete blockade of the RAS.

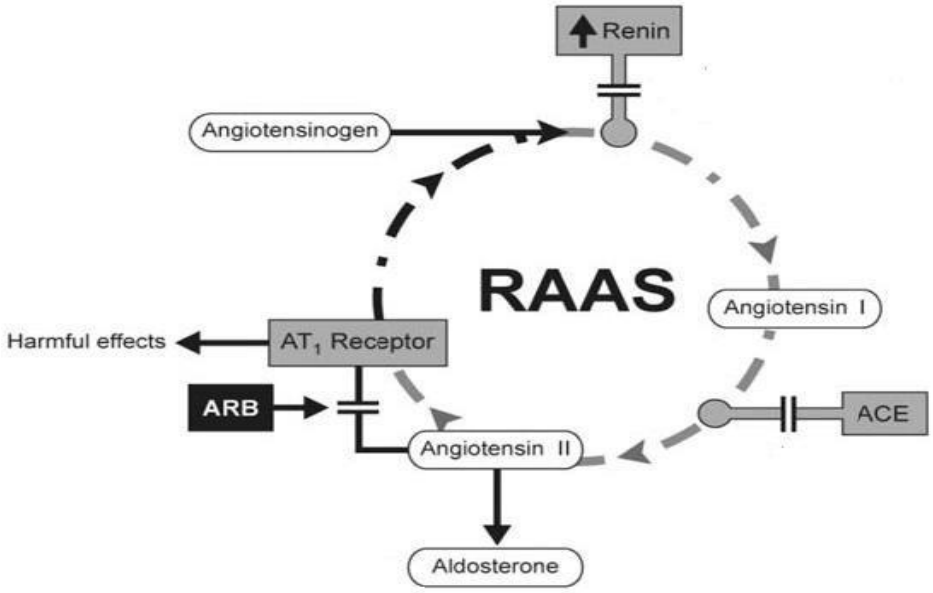

Figure 5: Mechanism of action of ARB.

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