Review Article

A REVIEW ON CARDIOPROTECTIVE EFFECT OF AN ANTIOXIDANT, VITAMIN-E AGAINST MYOCARDIAL INFARCTION.

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ARTICLE INFO

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Received:
April 2018
Accepted for publication:
May 2018

Keywords:

Vitamin E
Antioxidants
Myocardial infarction,
Cardioprotective

ABSTRACT

Vitamin E (Vit E), an antioxidant, is a compound that has an important role in maintaining health because it can capture free radical molecules that inhibit oxidative reactions in the body, is considered to prolong survival in patients and animals. Myocardial infarction (MI), known as a heart attack, is the formation of a necrosis in heart muscle cells following inadequate blood supply. This study tested the hypothesis that early treatment with Vit E reduces mortality because of its protective effects against myocardial infarction by arresting free radical molecules and reactive oxygen species that cause degenerative diseases. Miocardial Infarction is one of the clinical manifestations of coronary heart disease, which is a major cause of morbidity and mortality worldwide. Early mortality rate of 30 days in acute MI patients is 30% with more than half deaths before the patient reaches the hospital.

INTRODUCTION

Myocardial infarction is the damage or death of an area of the heart muscle (myocardium) resulting from a blocked blood supply to the area, causing the death of heart tissue [1]. Myocardial infarction (MI) usually results from an imbalance in oxygen supply and demand, which is most often caused by plaque rupture with thrombus formation in a coronary artery [2]. This is a complicated event which not only affects mechanical and electrical properties of myocardium but also its structural and biochemical properties [3].

The rates of death from MI have diminished in most high income countries, despite 1 in 3 of all deaths in the USA in 2008 was due to cardiovascular disease [4].

Inspite it is accepted that cardiovascular disease is a common cause of death in the developing world. For example, ischemic heart disease had become the leading cause of death by 2004 accounting for 1.46 million deaths in India (14% of total deaths) and the same were expected to double during next decade [5].

The general assumption is that adequate intake of nutrients like fruits, grains and vegetables and moderate degree of exercise can help prevent coronary heart disease of the populations in advanced and 'near – advanced' countries [6].

Some antioxidants like ascorbate, tocopherols, tocotrienols, flavonoids, other phenols and carotenoids (found in plants) are taken up by humans. The important food antioxidant can significantly reduces the side effects of reactive species, which are involved in chronic diseases and can protect myocardium [7 & 8]. There are documentation about the oxidative damage contributes to the pathology of atherosclerosis and Reactive oxygen or nitrogen species play an integral role in myocardial injury [9].

MYOCARDIAL INFARCTION

Myocardial infarction, known as a heart attack, is the formation of a necrosis in myocardial muscle cells due to inadequate blood supply to an area initiated with ischemic [2]. Transmural and Subendocardial

are the two basic types of acute myocardial infarction [10].

Clinically, myocardial infarction can be subclassified into a ST elevation MI (STEMI) versus a non-ST elevation MI (non-STEMI) based on ECG changes [11]. A coronary occlusion occurs when there a thrombus covers on a uncerated or unstable plaque, which results in break down in the supply of myocardial oxygen and nutrients [12]. Job stress show a minor role computing for only about 3% of cases of myocardial disease, while Smoking appears to be 36% of cardivascular disease, obesity 20% and lack of exercise 7-12% [13].

Myocardial ischemia is a consequence of reduced blood flow in coronary arteries, due to a combination of fixed vessel narrowing following gradual buildup of cholesterol and fibrous tissue in plaques in the wall of arteries and abnormal vascular tone as a result of atherosclerosis and endothelial dysfunction. This blood column irregularities can be visible on angiography for long period of time [14, 15].

Several factors affect the hemodynamic significance of a stenotic myocardial lesion such as length of the lesion and more importantly the degree of vessel narrowing, amount of compensatory vasodilatation that smaller, distal resistance vessels are able to achieve and Myocardial oxygen demand. Distal vessels are affected more when there is long term occlusion of vessels [16]. The report from different studies say that tissue damage in myocardial infarction is due to apoptosis which is also called cell death [17].

Oxidative stress in cardiovascular diseases

Normal mediators in cell signaling are very important for regulating the functions of vessels, which is done by Reactive oxygen species (ROS) [18]. ROS are produced in endothelium, smooth muscle and adventitia of the vessel wall [19]. Under pathophysiological conditions, these free radicals play important role in various conditions, including atherosclerosis, ischemic heart diseases, arrhythmias, cardiomyopathy and congestive heart failure [20].

Oxidative stress and atherosclerosis

Free radical induced oxidative stress that influences the occurrence of degenerative diseases such as heart disease causes atherogenic process and its steps of pathogenic consequences [21]. The collective confirmation that oxidative modification of low density lipoprotein (LDL) plays an important role in the pathogenesis of atherosclerosis [22].

Management of myocardial infarction

Myocardial infarction can be diagnosed by assessing the chief complaints of the patients and physical examination. Some investigations like canhges in ECG and coronary angiogram and increase in levels of the cardio-markers guide us to establish the diagnosis. The main aspect of ECG is to let us know the site of infarction (heart muscle damage), while coronary angiogram locates the exact site of narrowing or obstructions in coronary vessels [23].

In myocardial infarction, the cardiac enzymes those raised are aspartate transaminase (AST), alanine transaminase (ALT) and lactate dehydrogenase (LDH) and one cardiac marker is very important is Troponin T [24]. Creatine kinase (CK) is an enzyme that has been measured for the detection of MI, is used confidently since old age. CK is increased not only in myocardial injury and but also in other tissues like muscle injury. After a heart attack, rise in CK occurs 4 to 9 hours after the onset of chest pain, peaks at 24 hours, and returns to baseline at 48 to 72 hours [25].

Cardiac troponins I and troponin T is now been popular for their speficity and accuracy for myocardial damage and has beed used for the diagnosis. These parameters are routinely used in hospitals for diagnostic purposes. [26]. After a myocardial infarction, both troponins starts increasing in serum within 4 to 9 hours, goes to peak at 12 to 24 hours, and remain elevated for up to 14 days [27].

Nowadays the occurance of myocardial infarction can decreased by restricting and managing some of the risk factors like control of blood pressure, lifestyle modificaton, cessation of smoking, regular exercise, a balanced healthy diet for cardiact problems, and limitation of alcohol intake [28]. Among the drug therapy Beta blocker such as metoprolol or carvedilol is used to reduce the risk of MI [29]. Some high-risk patients particularly MI with left ventricular dysfunction or continuing cardiac ischaemia shows great benefit from risk factors modification [30].

ANTIOXIDANTS

Free radical is an atom or molecule having an unpaired electron. Free radicals are considered to be harmful because they become highly reactive in the effort to get their electron pairs, as well as new free radicals from the atoms or molecules whose electrons are donated to pair with previous free radicals. The free radicals usually come from oxygen, nitrogen and sulfur molecules [31]. Reactive oxygen species (ROS) and reactive nitrogen species (RNS) are described free radicals and other non-radical reactive derivatives. For example, ROS includes free radicals such as superoxide anion ($O2^{-\bullet}$), perhydroxyl radical ($HO2\bullet$), hydroxyl radical ($\cdot OH$), nitric oxide (NO), and other species such as hydrogen peroxide ($H2O2$), singlet oxygen ($1O2$), hypochlorous acid (HOCl) and peroxynitrite ($ONOO^-$) [31].

The development of natural antioxidants has received great attention over the last few years. Natural antioxidants in addition to protecting the

body from free radicals can also slow the occurrence of chronic diseases caused by reduced reactive oxygen species (ROS), especially hydroxyl radicals and radical superoxide. [32].

Antioxidant is a compound inhibit that have an important role in protecting health due to it can absorb free radical molecules and inhibit oxidative reaction which cause any kinds of diseases [33]. Anti-oxidants delay or inhibit oxidative damage to a target molecule. At a time one antioxidant molecule can react with single free radicals and are capable to neutralize free radicals by donating one of their own electrons, ending the carbon-stealing reaction [34].

Fruits and vegetables are loaded with key antioxidants such as vitamin A, C, E, betacarotene that can play important roles as cellular antioxidants [35]. The sources of the natural antioxidants are also spices, grains, and herbs such as ginseng, curcuma, ginkgo, rosemary, green tea, grape, ginger and garlic. The main antioxidant compounds that these foods contain are phenol, polyphenols, flavonoids, carotenoids, steroids and thiols [36].

Overproduction of the free radicals can responsible for tissue injury. Cell membranes are made of unsaturated lipids and these unsaturated lipid molecules of cell membranes are particularly susceptible to free radicals. Oxidative damage can direct to a breakdown or even hardening of lipids, the main component of all cell walls. Breakdown or hardening is due to lipid peroxidation leads to death of cell or it becomes unfeasible for the cell to properly get its nutrients or get signals to achieve another. [37]. These antioxidant enzymes such as xanthine oxidase (XO), superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX) provide a crucial fence against free radicals [38].

VITAMIN E

The natural forms of vitamin E include α-tocopherol, β -tocopherol, γ-tocopherol, and δ-tocopherol as well as the tocotrienol forms of each of these. The α-tocopherol and γ-tocopherol isoforms. The tocotrienols from vitamin are alpha-, beta-, gamma-, and delta-tocotrienols. The human body maintains effectively alpha-tocopherol, the only form of vitamin E; therefore, this form of vitamin E found in the largest quantities in blood and tissues [39].

Vitamin E may exert their activity by several mechanisms, like by suppressing the production of active species by reducing hydroperoxides and H2O2, by sequestering metal ions, termination of chain reaction by scavenging active free radicals and also caused repairing and/or clearing damage of cell, thus stop cancer and cardiovascular disease. The effect of protection of vitamin E supplements against oxidative stress in humans protects other fat-soluble vitamins from destruction[40].

Human body enriched with vitamin E as antioxidants can prevent the onset as well as treat diseases caused and/or fostered due to free-radical mediated oxidative stress and anti-inflammatory processes. This can also inhibit platelet aggregation and can cause immune enhancement [41].

Atherosclerosis and Vitamin E

Of all the antioxidants, vitamin E can easily be assimilate into low density lipoprotein (LDL) molecule and ultimately can protect against LDL oxidation which is the initial stage of atherosclerosis [42]. There is an evident relationship between dosage and effectiveness of vitamin E. The higher the dose taken for vitamin E the higher is the chance of safeguard against oxidative damage to LDL cholesterol. From the previous explanation we can see Vitamin E can reduce may LDL cholesterol peroxidation and increase plasma LDL breakdown. This signifies the prevention activity of cardiovascular disease by inhibiting excessive platelet aggregation and increase in fibrinolytic process [42].

FREE RADICALS AND CARDIOVASCULAR DISEASES

A free radical may be defined as a molecule or molecular fragments containing one or more unpaired electrons in its outermost atomic or molecular orbital [43]. This radical is likely to have a chain reaction which occurs in the body can cause continuous damage. The number of free radicals can increase due to stress, radiation, cigarette smoke and environmental pollution causing an inadequate body defense system thus result in several chronic disease such as cardiovascular diseases, neurological diseases, cancer [44].

Recent researches have shown that the antioxidants of plant origin with free-radical scavenging properties could have great importance as therapeutic agents in several diseases caused due to oxidative stress which is a common mechanism of molecular and cellular damage. Plant extracts and phytoconstituents found effective as radical scavengers and inhibitors of lipid peroxidation [45].

Free radicals are always produced in our body system by various mechanisms and physiological processes. These include mitochondrial respiration, nicotinamide adenine dinucleotide phosphate (NADPH) oxidases, xanthine oxidoreductase and uncoupled nitric oxide (NO) synthases [46].

There are several theories about the mitochondrial production of ROS. One of popular theory says about the electron transport where about five percent electron is escaped and reacts with oxygen, which results in formation of ROS. Another theory about the generation of ROS is Mitochondrial superoxide production, which occurs during normal cellular activity [47].

Redox potential maintains the electron balance between oxidants and antioxidants which ultimately guard the mitochondrial permeability to electrons which is also described in chemiosmotic theory. Diseases occur due to any imbalance between coupling and coupling of electrons and generation of ROS [48]. The vascular process of atherosclerosis and LDL cholesterol disease is closely related to ROS/NO abnormal production [49].

ROS and cardiovascular diseases

Among the long list of heart disease risk factors endothelial dysfunction is important, as it is the source of atherosclerosis. The theory around how the cardiovascular disease starts is mainly through the endothelial dysfunction where coronary walls become more vulnerable to atherosclerosis and coronary heart disease [50].

Early atherosclerosis is due mainly to mitochondrial overproduction of ROS and uneven distribution of antioxidants and oxidants. When there is endothelial damage of the coronary vascular wall, there is multiple cell populations resulted from abnormal ROS signaling [51]. A number of process that occurs during over production of free radical that leads to bizarre oxidation of LDL which ultimately causes vascular endothelial damage. Then the pathogenesis of atherosclerosis starts and myocardial infarction occurs [52].

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