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Oxidative stress and its complications in human health

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ABSTRACT

Under normal physiological conditions, a homeostatic balance exists between the formation of oxgyen radicals (ROS) and their removal by endogenous scavenging antioxidants. An imbalance between oxidants and antioxidants that is in favor of the oxidants potentially leading to damage is termed "oxidative stress". Mitochondria are a major producer of ROS, which mainly consists of superoxide anion, hydrogen peroxide, and hydroxyl radical. Especially, during systemic inflammatory response syndrome, sepsis, septic shock, there is an overproduction of ROS while the natural antioxidant mechanisms are weakened, mainly because of endothelial cell damage. General anesthesia can impair the immunological defense mechanisms while inducing an inflammatory reaction in alveolar macrophages. In chronic diseases and high mortality situations like sepsis, oxidative/anti-oxidative equilibrium shifts to the direction of oxidative stress. When elderly patients with chronic diseases and patients with sepsis undergo surgical operations, anesthesia and anesthetic agents used increases the oxidative stress in addition to the surgical trauma. Thence many studies are ongoing on the antioxidant drugs and enzymes. We must never forget to take the oxidative stress of our patients into account while planning their treatments.

Keywords: Oxidative Stress; Release Oxygen Radicals; Anti-Oxidative Defense; Choric Diseases

1. INTRODUCTION

Molecular oxygen is reduced to water. The intermediate steps of oxygen reduction are the formation of the superoxide anion radical, hydrogen peroxide and the hydroxyl radical, corresponding to the steps of reduction by one, two, and three elections, respectively. Further, ground-state molecular oxygen, a diradical can be electronically excited to singlet molecular oxygen. Oxygen radicals (ROS) can occur as alkyl or peroxyl radicals in lipids [1]. Mitochondrion is a main producer of ROS, which mainly consist of superoxide anion, hydrogen peroxide, and hydroxyl radical. Under normal physiological conditions a homeostatic balance exists between the formation of ROS and their removal by endogenous scavenging antioxidants [2]. Antioxidant is any substance that when present at low concentrations compared with that of an oxidizable substrate significantly delays or inhibits oxidation of the substrate. An imbalance between oxidants and antioxidants in favor of the oxidants leading to potential damage is termed "oxidative stress" [3]. Being able to react to any deficit or excess in energy and regulating ATP production, mitochondria play an important role in this equilibrium. Mitochondrial oxidative phosphorylation is responsible for 90% of total oxygen consumption and ATP generation [4].

ROS are known as the major signaling molecules in the modulation of cellular processes. Immoderate generation of ROS may result in the attack of many diseases and harm to most intracellular and extracellular biomolecules in a living organism [1]. The main source of ROS in most cell types is possibly the electron leakage from mitochondrial electron transport chain that diminishes molecular oxygen to the superoxide anion. Superoxide dismutase (SOD) will convert superoxide anion to hydrogen peroxide and then produce hydroxyl radical [1]. Cells contain multiple antioxidant systems to protect the injury induced by increased intracellular ROS. Among, than glutathione (GSH) and SOD are an antioxidant that defends cells from ROS induced apoptosis. Many studies have reported that GHS depletion is a major factor on chromosomal DNA fragmentation and apoptosis or necrosis in oxidative stress-induced cell death [3].

An increasing attention has been paid to oxidative stress blaming it as an important causative factor for complications. Several diseases are known to generate reactive species that may trigger oxidative stress when not properly scavenged by the antioxidant defenses and result in tissue damage. Increased reactive oxygen species resulting from an external trigger such as hyperglycemia, hypertension or dyslipidemia in conditions of oxidative stress could lead to enhanced mitochondrial biogenesis. Mitochondria are often thought as an important therapeutic target (in aging and pathologies such as

diabetes mellitus, neurodegeneration, cancer and cardiovascular disease) in part because they are considered to be the main source of ROS in the cells [5]. Hypertension is a common disease of the elderly. Both aging and hypertension have a critical role in cardiovascular and cerebrovascular complications. Although aging and hypertension, either independently or collectively, impair the endothelial function, aging and hypertension may have similar cascades for the pathogenesis and development of endothelial dysfunction. An imbalance of increased production of reactive oxygen species mainly superoxide, may promote endothelial dysfunction. Endothelial cell senescence is also involved in aging-related endothelial dysfunction [5,6].

Diabetes Mellitus, obesity and obstructive sleep apnea play a role in the epidemiology of cardiovascular/cerebrovascular diseases independent of age and sex factor. There is a positive correlation between the rates of these diseases. According to few theories, the factor that affects the prognosis of these diseases is the response the body gives to the sympatic activation, oxidative stress and inflammation that develops following the endothelial dysfunction. This response consists of mainly the balancing of antioxidant/anti-inflammatory equilibrium and treatments (statins, Vitamin C, E, selenium, zinc and omega 3) focusing on expediting this balance are recommended [5,7].

In the active period of diseases where the balance is impaired with the increasing oxidative stress, nutrition of the patients becomes essential. The production of ATP by the body to meet its energy need is closely related to the nutrients it consumes. Many studies show that hypocaloric feeding during the diseases increases the complications and mortality. Just as hypercaloric feeding, hypocaloric feeding increases the inflammation, the duration and the magnitude of the oxidative stress, causing a deficiency in the functions of immune system that leads to metabolic syndrome. Overfeeding increases glucose levels, incidence of infection, and the duration of mechanical ventilation and hospital stay. The hypocaloric diets used by the obese patients in order to lose weight are very dangerous. Besides it should not be forgotten that many diseases accompany the obesity as well. A number of studies have demonstrated that many proteins and lipids that cause oxidative stress increase in endothelial cells of the patients with chronic diseases [4-8].

Today, life expectancy has risen hence many patients with the mentioned chronic diseases may have to go under surgery during the acute phases of their sicknesses and/or need a follow-up in the intensive care units.

Many critically ill diseases states (such as sepsis, septic shock, burns, ischemia-reperfusion injury, acute lung injury, acute respiratory distress syndrome) lead to excessive lipid peroxidation and oxidative stress induced by increasing ROS is believed to adversely affect the state of normal human health [2]. Especially, during systemic inflammatory response syndrome, sepsis, septic shock, there is an overproduction of ROS while the natural antioxidant mechanisms are weakened, mainly because of endothelial cell damage. The ROS which includes malon dialdehyde (MDA) hydrogen peroxide and hydroxyl radicals cause oxidative stress. In the critically ill patient, failure of the mitochondrial function not only causes impairment in the oxygen and nutrient supply, and in the substrates with adequate coupling efficiency of oxidative phosphorylation but also, causes limitation in the hormonal maintenance of mitochondrial gene transcription [6-9].

On the other hand, nitro oxide (NO) has an important role in regulation of vascular tonus. An imbalance of decreased production of NO or increased production of ROS mainly superoxide dismutase, may promote endothelial dysfunction. One of the possible mechanisms by which the critically ill diseases are arisen could be oxidative stress. Endothelial cells senescence is also involved in patient-related endothelial dysfunction [5].

Appropriate anesthesia methods should be used for the patients who have increased inflammation and oxidative stress related to chronic diseases. General anesthesia can impair immunological defense mechanisms while inducing an inflammatory reaction in alveolar macrophages. Inflammation was initiated in general anesthesia following endotracheal intubation and enhanced by the addition of inhalation agents (sevoflurane, desflurane, halothane and isoflurane). Generalized inflammatory reactions inducing the production of leucocytes release inflammatory mediators and ROS. Damage to membrane lipids by ROS is implied by the appearance of lipid peroxidation products (e.g. MDA) during general anesthesia [10,11]. The diets in the postoperative care period of patients with increased oxidative stress should be monitored closely and hypo and hypo-caloric diets should be avoided. A normocaloric diet rich of proteins should be preferred. In addition early mobilization prevents the developing of many complications [4,9].

2. CONCLUSIONS

Today, although life expectancy increased, rate of chronic diseases has raised parallel with the increasing age. In chronic diseases and high mortality situations like sepsis, oxidative/anti-oxidative equilibrium shifts to the direction of oxidative stress. When elderly patients with chronic diseases and patients with sepsis undergo surgical operations, anesthesia and anesthetic agents used increase the oxidative stress in addition to the surgical trauma. Thence many studies are ongoing on the antioxidant drugs and enzymes.

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We must never forget to take the oxidative stress of our patients into account when planning their treatments.

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