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Oxidative Stress, Pathophysiology And Antioxidant Properties In Disease.

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Abstract : Oxidative stress (OS) can cause harm to various molecules and cellular structures, which can change how well organs and systems function. The body uses both endogenous and exogenous mechanisms to accumulate OS. A growing body of research indicates that OS plays a role in the physiopathology of several chronic illnesses that need long-term pharmacological intervention. Modifications to systemic OS may be a result of prolonged treatment. In this review, we go over how OS may play a role in the pathogenic mechanisms of certain chronic illnesses, the benefits of pharmaceutical treatments that promote antioxidant activity, and potential adjuvant antioxidant substitutes.

A class of extremely reactive molecules called reactive oxygen species (ROS) is produced during the metabolism of oxygen. Superoxide radicals, hydroxyl radicals, and hydrogen peroxide molecules are examples of ROS that are frequently produced as byproducts of biological reactions or by external stimuli. A wealth of evidence suggests that ROS play a role in the onset of degenerative diseases. Research indicates that certain substances, particularly those derived from natural sources, have the ability to shield cells from free radical damage.

Key words : Disease ,factor affecting, oxidative stress ,pathophysiology ,reactive oxygen stress ,

INTRODUCTION

Oxidative stress

Oxidative stress (OS) has the ability to damage different molecules and cellular structures, altering the correct function of organs and systems. OS accumulates in the body by endogenous and exogenous mechanisms. Increasing evidence points to the involvement of OS in the physiopathology of various chronic diseases that require prolonged periods of pharmacological treatment. Long-term treatments may contribute to changes in systemic OS. In this review, we discuss the involvement of OS in the pathological mechanisms of some chronic diseases, the pro- or antioxidant effects of their pharmacological treatments, and possible adjuvant antioxidant alternatives. Diseases such as high blood pressure, arteriosclerosis, and diabetes mellitus contribute to the increased risk of cardiovascular disease. Antihypertensive, lipid-lowering, and hypoglycemic treatments help reduce the risk with an additional antioxidant benefit. Treatment with methotrexate in autoimmune systemic inflammatory diseases, such as rheumatoid arthritis, has a dual role in stimulating the production of OS and producing mitochondrial dysfunction. However, it can also help indirectly decrease the systemic OS induced by inflammation. Medicaments used to treat neurodegenerative diseases tend to decrease the mechanisms related to the production of reactive oxygen species (ROS) and balance OS. On the other hand, immunosuppressive treatments used in cancer or human immunodeficiency virus infection increase the production of ROS, causing significant oxidative damage in different organs and systems without widely documented exogin troduction in 1985 [1], it has attracted widespread interest and also some critical comments [2], and it is covered in detail in a textbook [3]

"An imbalance between oxidants and antioxidants in favour of the oxidants, leading to a disruption of redox signalling and control and/or molecular damage" is the definition of "oxidative stress" as used globally [4,5].enous antioxidant administration alternatives.

Food allergies, atopic dermatitis, allergic rhinitis, and asthma are examples of allergic diseases that are brought on by oxidative stress, which also boosts the immune system. According to Sackesen et al. (2008), this indicates that patients with allergy diseases have an antiquated antioxidant defence system in comparison to healthy people. Antioxidant supplementation may therefore make up for asthma patients' elevated oxidative stress and inflammatory processes. However, Murr et al. (2005) have demonstrated that by reducing the Th1-type immune response and boosting the Th2-type response with immunoglobulin synthesis, excessive antioxidant supplementation can increase the susceptibility to allergic diseases and consequently asthma.

When a cell's normal redox state is disturbed, peroxides and free radicals are produced, which harm all parts of the cell, including DNA, lipids, and proteins. This can have toxic effects. In addition to base damage, oxidative stress resulting from oxidative metabolism also breaks DNA strands. The reactive oxygen species that are produced, such as the superoxide radical O2 and the hydroxyl and hydrogen peroxide radicals OH and H2O2, primarily cause indirect base damage.[2]

ROS Reactive Oxygen Species

ROS are molecules with high reactivity due to their chemical composition; they can result from the metabolism of nitro Free radicals like superoxide can be present in generation ROS and RNS. O2 radical (hydroxyl radical, or OH, both nitric oxide (NO) and
However, there are also some nonfree radicals, like Peroxynitrite (ONOO-) and hydrogen peroxide (H2O2)] [2].
Enzymatic reactions are produced by ROS in the mitochondria. defined by the oxygen being reduced by the electron chain of tron transport [3]. Furthermore, the endoplasmic reticulum

Additional sources of ROS include lum and peroxisomes [4, 5]. various biological functioning including the phosphorylation of proteins, transcription factor activation, immune response, and apoptosis depending on the ROS level in the cell

Superoxide dismutase (SOD), catalase (Cat), and glutathione peroxidase (GPx) are the three primary endogenous antioxidant enzymes that neutralise reactive oxygen species (ROS) [6]. SOD is a member of a class of metalloenzymes that converts H2O2 and O2 -- into oxygen [7]. Mammals are known to produce three different forms of SOD: extracellular SOD (SOD3), mitochondrial SOD (SOD2), and cytoplasmic SOD (SOD1) [8]. Other nonenzymatic substances with the ability to scavenge free radicals, such as vitamins, melatonin, and glutathione (GSH), can neutralize ROS [9] when ROS are not adequately neutralised by antioxidant defences,

Longer-lasting in the body, ROS oxidize sensitive biomolecules [10]. Overabundance of reactive oxygen species (ROS) can harm nucleic acids, membrane lipids, and cellular proteins, impairing normal cellular function [10]. An endothelium-dependent mediator of vascular vasorelaxation is the NO radical. The nitric oxide synthase (NOS) enzyme normally produces NO [11]Under OS conditions, NO and the radical O2- combine to produce ONOO-, which damages endothelium [12].

Pathophysiology

The process of lipoperoxidation (LPO) is one way that OS damages lipids. The presence of carbon-carbon double bonds, particularly in polyunsaturated fatty acids, is a defining characteristic of LPO. Hydroperoxides, including propanal, hexanal, 4-hydroxynonenal, and malondialdehyde (MDA), are the principal LPO products [13]. Isoprostanes from the nonenzymatic oxidation of essential fatty acids are another type of LPO.Arachidonic acid, for example [14]. In addition, when ROS interact with guanine bases, they can cause structural damage to DNA. 8-hydroxy-2′-deoxyguanosine (8-OHdG) or 8-oxo-7,8-dihydro-2′-deoxyguanosine (8-oxodG) are frequently formed by guanine oxidation [15]. Under typical circumstances, these metabolites are restored by the oxoguanine glycosylase (hOGG1) enzyme and are collectively referred to as OS biomarkers [16]. Many chronic illnesses include OS, which may accelerate the disease's development [17]. Some autoimmune diseases, like rheumatoid arthritis, cause tissue damage due to their close relationship between OS and the inflammatory process [18]. Hyperglycemia and the advancement of type 2 diabetes mellitus (DM) are associated with OS [19]. The primary reasons for OS's involvement in cardiovascular disease are its effects on hypertension and theAtheroma leaf-let formation [20, 21]. Increased ROS production is linked to the pathological development of other chronic diseases, including cancer [24], HIV infection [25], and neurodegenerative diseases [22, 23]. However, the production of ROS can be changed by exogenous factors, such as the prescribed pharmaceutical treatments for specific chronic pathologies [2]. This brief review aims to outline the part that OS plays in various pathological processes, including cancer, HIV, DM, rheumatoid arthritis, high blood pressure, and some neurodegenerative diseases. Some pharmacological management options' prooxidant or antioxidant effects will be briefly discussed

Factor responsible for oxidative stress

1.Sex

We found no explanation for the significantly higher lipid peroxidation among women in this study, which was unexpected. We speculate that one possible contributing factor could be women's higher body fat percentage. However, we were unable to measure body fat more precisely and the sex effect persisted even after controlling the data for body mass index. This result is especially noteworthy because studies have shown that women who are exposed to comparable levels of cigarette smoke have a higher risk of developing lung cancer than men (24). Our findings concur with those of Coudray et al. (37) who discovered that women had greater levels of lipid peroxidation than men.

2. Smooking

To the best of our knowledge, this is the only study on oxidative damage markers in smokers and passive smokers where the use of vitamin supplements at the time of the study was strictly regulated and smoking status was classified based on both plasma cotinine level and self-report. Unlike MDA, the two lipid peroxidation biomarkers showed different relationships with smoking status. Specifically, plasma Iso-P did not positively correlate with smoking. Numerous research studies have reported elevated Iso-P excretion in smokers (26,27), and elevated Iso-P levels in individuals with a range of medical conditions (28,29). Few research, nevertheless, have looked at plasma Iso-P in smokers and non-smokers (30).

3. Ascorbic acid

In our multivariate analyses, the only factor that significantly inversely correlated with both MDA and Iso-P was the plasma ascorbic acid level . There has been little cross-sectional population research on ascorbic acid and oxidative damage (31), despite the fact that many other investigators have reported an inverse relationship between smoking and plasma ascorbic acid (32)

4. Reactive protein

In bivariate analyses, the inflammatory marker C-reactive protein was linked to significant increases in both lipid peroxidation biomarkers and MDA in the multivariate model. Smoking increases the recruitment and activation of phagocytes, which raises smokers' levels of free radicals (33). Research has demonstrated that C-reactive protein is an effective indicator of the risk of cardiovascular disease (34, 35). We think that this is the first study to look at oxidative damage markers in conjunction with smoking status and the inflammatory/immune response that comes with it.

5 . Alcohol

In order to eliminate high alcohol consumption as a source of lipid peroxidation, we excluded from this study individuals who reported regularly consuming more than two alcoholic drinks per day. We also found no

evidence of peroxidative effects associated with alcohol consumption within the low range of intake allowed. According to one study, having two alcoholic drinks a day increased urinary Iso-P levels nonsignificantly but significantly higher doses were needed to increase urinary F isoprostane levels statistically.[36]

Oxidative stress and Disease relationship

1..Oxidative Stress in Cardiovascular Diseases:

Nicotinamide-adenine dinucleotide phosphate (NADPH) is one of the oxidase enzymes that produces reactive oxygen species (ROS[38]). uncoupled endothelial NO syn- oxidase, xanthine oxidase, and glucose oxidase, lipo-, cyclooxygenase, and eNOS shows mitochondrial electron transport and oxygenase. Low levels of ROS production are equivalent to their detoxification under physiological conditions and are crucial for cellular signaling and function [38]. The specific and reversible oxidation/reduction modification of cellular signaling components that can control gene expression, excitation–contraction coupling, or cell growth, migration, differentiation, and death is known as redox signaling [39,40].

Redox signaling involves multiple kinases. For example, H2O2 may activate p38 mitogen-activated protein kinase (p38 MAPK) and c-Jun N-terminal kinase (JNKs), which would inhibit insulin production, or Ca/calmodulin-dependent kinase II (CAMKII), which would result in excitation–contraction coupling [40] .transduction of signal. Oxidation of its cAMP-induced protein kinase A (PKA) also causes it to become active regulatory subunit R1α and moved from the cytoplasm to the membrane, where PKA controls heart's excitation-contraction coupling and blood vessels' vasodilation [40]. NO has a vasodilator action and is a cytoprotective molecule under physiological conditions.

NO has protective effects against ischemia reperfusion and heart failure by inhibiting the activation and adhesion of platelets and neutrophils [41,42]. NO may function biologically through binding to soluble guanylate cyclase, which generates cyclic guanosine monophosphate and activates protein kinase G (PKG) [43] or through S-nitrosylation. This latter alteration may regulate the activity of multiple proteins, including tropomyosin, myosin heavy chain, pro-caspase 3, peroxiredoxins, and ryanodine receptor (RyR). PKA and CAMKII, which are redox-regulated themselves, phosphorylate RyR, which mediates Ca2+ release from the sarcoplasmic reticulum [40]. In addition, PKG controls hypertrophy or contraction of cardiomyocytes and vascular tone through oxidation that occurs independently of NO [40].

2.Oxidative stress in diabetes

Hyperglycemia's Part in Microvascular Problems In general, the causes of diabetic microvascular complications are extended contact with elevated glucose levels .

The degree of tissue damage caused by diabetes is also influenced by genetic factors that determine a person's susceptibility and, similar to athero-sclerosis due to the existence of such separate accelerating such as dyslipidemia and hypertension. The function of hyper-Glycemia has been demonstrated through extensive prospective research on diabetes type 1 and type 2, the DCCT/EDIC[The UKPDS, the Diabetes Control and Complications Trial, [44] and (Personal Diabetes Study, UK).[45] Analogous data have been as stated in the Steno-2 research[.46]. However, additional examination of Despite the fact that intensive therapy decreased, the DCCT data the risk of progressive sustained retinopathy by 73% in comparison to standared treatment. Hemoglobin (Hb)A1c and the duration of diabetes (glycemic exposure) explained only approximately 11% of the variation in retinopathy risk for the entire study population when combined with standard treatment. Population, indicating that 89% of the variation that remains in Risk is most likely explained by characteristics of glycemia that taken in by Is there a reason why hyperglycemia damages some cell types more than others when diabetes patients' bodies are subjected to abnormally high glucose concentrations[47] Generalized hyperglycemia targets particular cell types because these cells are unable to decrease their uptake of glucose in response to elevated extracellular glucose concentrations. Extracellular glucose concentrations and glucose transport have an inverse relationship in cells that are not directly susceptible to hyperglycemic injury. On the other hand, when glucose concentration is raised, vascular endothelial cells—which are major targets of hyperglycemic damage—show no discernible change in glucose transport rate, leading to intracellular hyperglycemia[48]

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