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Exploring how lifestyle choices influence the management of chronic diseases-role of healthcare providers: Review article

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***Abstract*---Background**: Chronic diseases are increasingly prevalent worldwide, with lifestyle choices playing a significant role in their management. Free radicals and oxidative stress have been implicated in various chronic conditions, including cardiovascular diseases, cancer, and neurodegenerative disorders. These conditions arise from an imbalance between reactive oxygen species (ROS) production and the body's antioxidant defenses. **Aim**: This review aims to explore how lifestyle choices influence oxidative stress and chronic disease management, with a focus on the role of healthcare providers in guiding lifestyle modifications to mitigate oxidative stress and improve health outcomes. **Methods**: A comprehensive review of the literature was conducted, focusing on the mechanisms of oxidative stress and its impact on chronic diseases. Studies on the effects of lifestyle factors such as diet, exercise, smoking, and alcohol consumption on oxidative stress were analyzed. The role of antioxidants in counteracting oxidative damage and their implications for chronic disease management were also examined. **Results**: The review highlights that lifestyle factors significantly affect oxidative stress levels. Moderate exercise enhances antioxidant defenses, while excessive physical activity, smoking, and alcohol consumption exacerbate oxidative stress. A diet rich in antioxidants helps mitigate oxidative damage. ROS play a critical role in the pathogenesis of chronic diseases, including cardiovascular conditions, cancer, and neurodegenerative disorders. Healthcare providers play a crucial role in advising patients on lifestyle modifications to manage oxidative stress and improve health outcomes. **Conclusion**: Effective management of chronic diseases requires addressing lifestyle factors that influence oxidative stress. Healthcare providers should emphasize the importance of balanced exercise, a diet rich in antioxidants, and the reduction of harmful habits such as smoking and excessive alcohol consumption. By guiding patients towards healthier lifestyle

choices, healthcare providers can help mitigate oxidative stress and improve disease management.

***Keywords*---**Oxidative Stress, Chronic Diseases, Lifestyle Choices, Antioxidants, Healthcare Providers, Cardiovascular Diseases, Cancer, Neurodegenerative Disorders.

Introduction

Numerous physiological processes in the human body, including respiration, digestion, alcohol and drug metabolism, and the conversion of fats into energy, generate potentially detrimental byproducts known as free radicals. These free radicals are typically neutralized by the body's intrinsic antioxidant defense systems. However, if these systems are overwhelmed, free radicals can initiate a cascade of adverse reactions, potentially leading to damage of cellular membranes, inhibition of essential enzymatic functions, disruption of critical cellular processes, interference with normal cell division, degradation of deoxyribonucleic acid (DNA), and impairment of energy production (Kurutas, 2015). Oxidative stress is linked to the onset of various metabolic disorders, chronic diseases, and cancers (Finkel and Holbrook, 2000; Reuter et al., 2010; Aminjan et al., 2019). Although the free radical theory of oxygen has been established for over half a century, its implications for disease development and the beneficial effects of antioxidants have only been extensively explored in recent decades (Liu, 2019). Free radicals are integral to several biological functions, some of which are essential for life, such as the intracellular eradication of pathogens by phagocytes, particularly granulocytes and macrophages. They are also implicated in cellular signaling processes known as redox signaling (Finkel and Holbrook, 2000). At low to moderate levels, reactive oxygen species (ROS) are advantageous in maintaining homeostasis and supporting various cellular functions (Finkel and Holbrook, 2000; Bhattacharyya et al., 2014).

Excessive ROS production can cause structural modifications to cellular proteins and disrupt their functions, leading to cellular dysfunction and the impairment of vital cellular processes (Finkel and Holbrook, 2000; Kaminski et al., 2002). High levels of ROS can inflict damage on lipids, proteins, and DNA. Specifically, ROS can compromise lipid membranes, increasing their fluidity and permeability, while protein damage includes site-specific amino acid modifications, peptide chain fragmentation, aggregation of cross-linked reaction products, alteration of electric charge, enzymatic inactivation, and increased susceptibility to proteolysis (Ayala et al., 2014). ROS can also damage DNA by oxidizing deoxyribose, inducing strand breaks, removing nucleotides, modifying bases, and crosslinking DNA-protein complexes (Sharma et al., 2012; Cadet and Wagner, 2013; Cadet et al., 2017; Liang et al., 2020). Primary oxygen free radicals, such as superoxide and hydroxyl radicals, arise from molecular oxygen under chemical reduction conditions. Excessive quantities of these radicals can cause cellular damage and apoptosis, contributing to numerous diseases, including cancer, stroke (Tsatsakis A. et al., 2019), myocardial infarction, diabetes, and other significant conditions (Padureanu et al., 2019). Many cancers are believed to result from the interaction

between free radicals and DNA, leading to mutations that disrupt the cell cycle and contribute to neoplasia (Reuter et al., 2010).

Given that free radicals are essential for life, the body employs various enzymatic mechanisms to minimize damage and counteract excessive free radical production. Antioxidants play a crucial role in these protective mechanisms. In healthy individuals, a balance between oxidants and antioxidants is maintained to protect against oxidative damage. Continuous free radical production in aerobic organisms must be matched by a corresponding rate of antioxidant consumption. Antioxidants, whether enzymatic or non-enzymatic, prevent the formation of free radicals and neutralize or repair the damage they cause (Clark et al., 1985). Protection against oxidative damage and chronic diseases is supported by a range of endogenous and exogenous antioxidants (Cadet et al., 2012). Antioxidant systems present in both plants (Sharma et al., 2012) and the human body (Birben et al., 2012) maintain ROS homeostasis. While ROS production through the mitochondrial respiratory chain can be metabolically beneficial, it can also be harmful under certain conditions (Hsu et al., 2000; Poli et al., 2004; Valko et al., 2006). Conversely, pathological or stress conditions can overwhelm antioxidant systems, leading to an imbalance that results in oxidative stress and irreversible changes in cellular components, including proteins, carbohydrates, and lipids, as well as disruptions in normal cellular signaling mechanisms (Birben et al., 2012; Zal et al., 2014; Salehi et al., 2018; Sharifi-Rad et al., 2018).

In autoimmune diseases, free radicals can alter the expression of self-antigen-type proteins, enhancing immune responses or modifying their antigenic profiles. External antioxidants, such as allergens, can also influence immune responses in susceptible individuals. For example, pollen from certain plants contains nicotinamide adenine dinucleotide phosphate oxidase (NADPH oxidase), which induces airway inflammation with specific symptoms due to infiltration by proinflammatory cytokines, including TNF-alpha and interleukins from epithelial cells. The long-term accumulation of intracellular prooxidant factors can alter the immune response by modifying the structure and function of proteins or enzymes such as interferon-gamma (IFN-γ), cluster of differentiation antigen 14 (CD14), and tumor necrosis factor-alpha (TNF-α) (Tsoukalas et al., 2019c). In cancers, alterations in purine or pyrimidine structures within cellular DNA, associated with oxidative reactions that produce oxides and free radicals, may contribute to neoplasms. When intracellular mechanisms for repairing oxidative damage are insufficient or disrupted by oxidative factors, it results in gene mutations or modifications that affect apoptotic mechanisms, leading to tumor cell formation (Buj and Aird, 2018).

Over time, these changes can perpetuate autoimmune responses and the accumulation of local proinflammatory factors such as TNF-alpha, proteases, and kinases. These factors promote tissue necrosis and accelerate tissue growth, leading to the appearance of new modified cells that sustain the immune response and propagate initial genetic defects, resulting in chaotic and extensive cell proliferation. Additionally, oxidative stress causes structural changes in cell membranes, reducing adhesion and facilitating the migration of altered tumor cells to neighboring tissues or distant sites via blood and lymph (Forni et al., 2019). Two primary theories regarding cellular aging are currently accepted: the

mitochondrial theory and the free radical theory. Both propose that increased levels of intracellular free radicals impact mitochondrial function, reducing cellular regenerative capacity. Additionally, the progressive accumulation of intracellular oxidizing factors that surpass antioxidant capacity leads to biological decline and reduced stress adaptation. Regardless of the mechanism—whether mitochondrial DNA damage or direct involvement of prooxidant factors—the cellular response to stress results in the overexpression of proinflammatory genes and elevated prooxidant factors (Liguori et al., 2018).

Oxidative stress also stimulates immune responses and contributes to allergic diseases such as asthma, allergic rhinitis, atopic dermatitis, and food allergies. Patients with allergic diseases often have outdated antioxidant protection systems compared to healthy individuals (Sackesen et al., 2008). Antioxidant supplementation might help alleviate inflammatory and oxidative stress processes in asthma patients. However, Murr et al. (2005) demonstrated that excessive antioxidant supplementation could increase susceptibility to allergic diseases and asthma by decreasing the Th1-type immune response and enhancing the Th2-type response, leading to increased immunoglobulin synthesis. Modern lifestyles characterized by unhealthy diets, lack of physical activity, and exposure to chemicals from various sources—such as pesticides (Tsatsakis A.M. et al., 2019), heavy metals, food additives, and environmental pollutants—can exacerbate oxidative stress and contribute to the rising prevalence of chronic diseases, as suggested by numerous experimental and human studies (Fenga et al., 2017; Docea et al., 2018; Fountoucidou et al., 2019; Kostoff et al., 2020). This comprehensive review aims to provide compelling evidence that antioxidants may mitigate some chronic-degenerative conditions and promote healthy aging.

Chronic Diseases Influenced by ROS: Mechanisms of Action

Sources of ROS: Reactive oxygen species (ROS) are primarily generated through external factors, such as environmental pollutants and cigarette smoke, or internally due to metabolic processes when antioxidant defenses are overwhelmed.

Exogenous ROS: External sources contributing to increased ROS production include exposure to cigarette smoke, ultraviolet (UV) radiation, heavy metal ions, ozone, allergens, drugs, toxins, pollutants, pesticides, and insecticides (Antunes dos Santos et al., 2018; Mahajan et al., 2018; Oke et al., 2019). Ionizing radiation generates hydroxyl radicals, super oxides, and organic radicals, which convert into organic hydroperoxides and hydrogen peroxide. These peroxides subsequently interact with metal ions such as Fe and Cu through redox reactions, exacerbating oxidative stress (Spitz et al., 2004; Spitz and Hauer-Jensen, 2014). UV radiation, particularly UVA, triggers oxidative stress by activating riboflavin, porphyrins, and NADPH-oxidase, resulting in the production of 8-oxo-guanine and a temporary decrease in intracellular glutathione levels (Marchitti et al., 2011). Heavy metals like iron, copper, cadmium, nickel, arsenic, and lead contribute to ROS formation via Fenton or Haber-Weiss reactions and by directly reacting with cellular components, leading to lipid peroxidation and DNA damage (Ściskalska et al., 2014; Jan et al., 2015). Ozone exposure can exacerbate

lung inflammation even in healthy individuals by increasing inflammatory cell infiltration in the respiratory epithelium (Wu X. et al., 2019).

Endogenous ROS Production:

Endogenous ROS and reactive nitrogen species (RNS) are primarily produced in the mitochondrial electron transport chain (ETC), endoplasmic reticulum (ER), peroxisomes, membrane-bound NADPH oxidase (NOX) isoforms, dual oxidases (Duox) complexes, and nitric oxide synthases (NOS) (Rodriguez and Redman, 2005). The mitochondrial ETC, particularly complexes I and III, is a significant source of superoxide anions (Rodriguez and Redman, 2005). Other internal sources of ROS include microsomes and peroxisomes, and immune cells like macrophages and neutrophils produce ROS through mechanisms involving NOX2 isoform (Curi et al., 2016). Dysregulated ROS signaling is linked to various diseases associated with oxidative stress (Finkel, 2011).

Mitochondria are both major producers and receptors of ROS. The inefficiency of oxidative phosphorylation results in 0.2–5% of electrons escaping the ETC and forming superoxide radicals (Hamanaka et al., 2013). Superoxide radicals are also generated by NADPH oxidases and other metabolic enzymes, including cyclooxygenase (COX) 1/2, lipoxygenase, xanthine oxidoreductase (XOR), and cytochrome P450 (Finkel, 2003). Superoxide radicals are reduced to hydrogen peroxide and hydroxyl radicals, and further reactions produce peroxyl and alkoxyl radicals, as well as hypochlorite ions (Bartosz, 2009; Valko et al., 2007). ROS can significantly damage cellular components, including lipids, proteins, and DNA, leading to cell death through apoptosis or necrosis (Valko et al., 2007). Studies have shown that cells can regulate ROS production to manage cell survival and proliferation, serving as a defense mechanism against pathogens (Bartosz, 2009; Sena and Chandel, 2012). Specific enzymatic systems, such as the NOX family, are dedicated to producing superoxide radicals for physiological signaling (Bedard and Krause, 2007). In typical conditions, mitochondria transfer electrons through the ETC for oxygen reduction, with 1–3% of electrons escaping to produce superoxide (Ramsay, 2019). Additionally, ROS are generated through oxidative bursts by phagocytes during pathogen elimination and through various metabolic processes (Birben et al., 2012).

ROS affect cellular processes by altering phosphatase activity, enhancing protein tyrosine phosphatase (PTP) phosphorylation, and influencing signal transduction pathways. They can disrupt nuclear factor-κB (NF-κB) activation and translocation, with oxidative modifications reducing NF-κB's DNA binding potential (Kabe et al., 2005). Cyclopentenones, which are anti-inflammatory prostaglandins, conjugate with ROS-modified peptides and proteins, reducing ROS-mediated NF-κB signaling (Homem de Bittencourt and Curi, 2001). Oxidative stress from endogenous sources can alter gene expression and DNA stability, leading to DNA damage and mutations, which are associated with various diseases including cancer (De Bont and van Larebeke, 2004). Non-enzymatic ROS sources include the mitochondrial respiratory chain, NADPH oxidase, XOR, uncoupled endothelial NOS, cytochrome P450 enzymes, lipoxygenase, and COX (Sena and Chandel, 2012; Battelli et al., 2014a). ROS and organic peroxides are by-products of cellular mitochondrial electron transport and metal-catalyzed

oxidation of metabolites (Forman and Torres, 2002; Hussain et al., 2016). Nitric oxide produced under hypoxic conditions and RNS can trigger the formation of reactive aldehydes and malondialdehyde (MDA), contributing to cellular damage (Hussain et al., 2016). Imbalances in ROS production and antioxidant defenses can result in damage to DNA, proteins, and lipids, leading to cell death (Bhattacharyya et al., 2014; Hussain et al., 2016). Initially observed in phagocytes, ROS production is now recognized in various cells, where it plays a role in physiological signaling (Di Meo et al., 2016).

Role of Lifestyle in Oxidative Stress Response:

- **Exercise and Oxidative Stress:**
  - Moderate exercise has been found to enhance the body's antioxidant defenses and promote beneficial oxidative signaling processes. This contrasts with exhaustive or prolonged physical activity, which can lead to a significant increase in reactive oxygen species (ROS). Such excessive ROS production is associated with oxidative stress, contributing to muscle fatigue and potentially leading to overtraining syndrome if recovery is inadequate (Pingitore et al., 2015; Antonioni et al., 2019).
- **Smoking and Alcohol Consumption:**
  - Smoking introduces a variety of oxidants and free radicals into the body, which increase local oxidative stress and inflammation in the lungs. This contributes to chronic respiratory issues and exacerbates oxidative damage (Valavanidis et al., 2009). Similarly, alcohol consumption can increase ROS production and diminish the body's antioxidant capacity, leading to oxidative stress and associated health problems (Salehi et al., 2018).
- **Diet:**
  - A diet rich in antioxidants helps mitigate oxidative stress and supports cellular health by neutralizing ROS. Conversely, a poor diet lacking in antioxidants can fail to adequately counteract ROS, leading to greater oxidative damage and increased risk of chronic diseases (Chen et al., 2012; Gandhi and Abramov, 2012).

Biochemical/Molecular Targets and Chronic Diseases:

- **Cardiovascular Diseases:**
  - Oxidative stress plays a critical role in the development and progression of cardiovascular diseases. It contributes to endothelial dysfunction, atherosclerosis, and damage from myocardial ischemia and reperfusion. Elevated ROS levels can lead to oxidative modifications of low-density lipoprotein (LDL), promoting endothelial dysfunction and increasing the risk of thrombosis and cardiovascular events (Li et al., 2014; Singh et al., 2002; Esper et al., 2006). Additionally, in conditions like myocardial ischemia, ROS cause mitochondrial damage, further exacerbating cardiac injury (Elahi et al., 2009; Wattanapitayakul and Bauer, 2001).

- **Cancer:**
    - Oxidative damage to DNA is a key factor in the initiation and progression of cancer. This damage includes the formation of genetic mutations and chromosomal defects, which can lead to cancerous transformations (Smith et al., 2016; Li et al., 2015). High levels of ROS in cancer cells contribute to various aspects of tumor growth, including increased cell proliferation, metastatic potential, and resistance to apoptosis. Cancer cells often activate protective mechanisms, such as NRF2, to counteract ROS-induced damage and support continued growth (Pizzino et al., 2014; Jaramillo and Zhang, 2013).

Mechanistic Insights:

- **ROS Production Sources:**
    - ROS are generated through normal cellular processes, including mitochondrial respiration, NOX activity, and other metabolic pathways. Both endogenous sources (such as mitochondria and NOX) and exogenous sources (such as pollution and UV radiation) contribute to ROS levels (Reid, 2001; Chen et al., 2018; Sage et al., 2012).
- **Impact on Cells:**
    - At physiological levels, ROS function as signaling molecules involved in cell processes like proliferation and apoptosis. However, excessive ROS can cause oxidative damage to DNA, proteins, and lipids, which plays a significant role in the development of various diseases and cellular dysfunction (Salehi et al., 2018; Pizzino et al., 2014).
- **Autophagy and Cardiovascular Health:**
    - Autophagy, a process involved in recycling cellular components, is important for cardiovascular health. Regular exercise induces autophagy, which helps in adapting to physical stress and mitigating oxidative damage, thus supporting cardiovascular function (Wu N. N. et al., 2019).
- **Cancer and ROS:**
    - In cancer cells, ROS accumulation contributes to disease progression by affecting signaling pathways that regulate cell growth and survival. ROS enable cancer cells to evade apoptosis and continue proliferating, despite the high mutagenic potential associated with ROS (Jaramillo and Zhang, 2013).

ROS and Neurodegenerative Disorders

- **Neuron Sensitivity to Oxidative Stress:**
    - Neurons with longer axons and multiple synapses are particularly susceptible to oxidative stress due to their high energy demands for axonal transport and plasticity. This increased demand, coupled with mitochondrial dysfunction, makes these neurons more vulnerable to degeneration (Salehi et al., 2019c; Tsatsakis A. et al., 2019). Dopaminergic neurons, for instance, experience

additional oxidative stress from dopamine metabolism, which generates hydrogen peroxide (H2O2) and superoxide through dopamine autoxidation (Delcambre et al., 2016; Buga et al., 2019).

- **Common Neurodegenerative Disorders:**
  - Alzheimer's, Parkinson's, Huntington's disease, amyotrophic lateral sclerosis (ALS), and Friedreich's ataxia are prevalent neurodegenerative disorders (Reddy, 2009; Nussbaum et al., 2017; Salehi et al., 2020a). Aging accelerates neurodegeneration through the accumulation of mitochondrial DNA mutations, calcium dysregulation, and decreased electron transport chain (ETC) function. These factors collectively contribute to neurodegeneration (Payne and Chinnery, 2015). Post-mortem brain tissue from patients with these disorders often shows oxidative damage to DNA, proteins, and lipids, highlighting the role of oxidative stress (Sharifi-Rad M. et al., 2020).
- **Alzheimer's Disease and Metal Dysregulation:**
  - In Alzheimer's disease, amyloid beta (Aβ) protein, which is typically a natural antioxidant, becomes harmful when aggregated into plaques. These plaques, found in brain areas controlling cognitive functions, accumulate high levels of copper, zinc, and iron. The modified form of Aβ (Aβ42) fails to bind metals properly and promotes oxidative processes. This results in neurons producing more antioxidants, including Aβ42, which paradoxically exacerbates oxidative stress (Danielson and Andersen, 2008; Li et al., 2013; Riederer et al., 1989).
- **Superoxide Dismutase 1 (SOD1) and ALS:**
  - Mutations in SOD1 are linked to familial ALS, a disease affecting motor neurons. Normally, SOD1 acts as an antioxidant, preventing the formation of harmful peroxide anions. Mutant SOD1 forms bind fewer metals and lead to excess peroxynitrite formation, which damages motor neurons and causes severe motor dysfunction (Huai and Zhang, 2019; Saccon et al., 2013; Pasinelli et al., 2004).
- **Glucose Utilization and ROS Production:**
  - The brain's high glucose utilization makes it particularly prone to oxidative stress, with the mitochondrial ETC being a major source of ROS. Complexes I and III of the ETC generate superoxide ions, contributing to oxidative damage (Cobley et al., 2018; Andreyev et al., 2005). Additionally, monoamine oxidase (MAO) in Parkinson's disease contributes significantly to ROS production. Major mitochondrial targets of ROS include the mitochondrial permeability transition pore (MPTP), poly (ADP-ribose) polymerase (PARP), and mtDNA (Gandhi and Abramov, 2012).
- **Other ROS Sources and Pathogenesis:**
  - NADPH oxidase in astrocytes, microglia, and neurons also contributes to oxidative stress, and inhibition of nitric oxide synthase (NOS) has shown neuroprotective effects (Abramov et al., 2005). Neurodegenerative diseases are characterized by protein misfolding, aggregation, abnormal kinase signaling, neuronal calcium dysregulation, and impaired synaptic transmission. Aggregated proteins, disrupted metal ion homeostasis, and

oxidative stress are closely linked to these conditions (Gandhi and Abramov, 2012; Chen et al., 2012). ROS modify proteins, leading to their aggregation and subsequent inhibition of proteasomes, creating a cycle of oxidative damage (Blokhuis et al., 2013; Takalo et al., 2013).

ROS, Diabetes, and Metabolic Syndrome

- **Oxidative Stress in Type 2 Diabetes:**
  - Type 2 diabetes is associated with oxidative stress, where insulin resistance and compensatory hyperinsulinemia are key features. ROS can disrupt insulin signaling mechanisms, contributing to insulin resistance (Chen X.F. et al., 2018). Diabetes itself exacerbates oxidative stress through hyperglycemia, which generates superoxide ions at the mitochondrial level. This results in decoupled electron transfer and oxidative phosphorylation, producing superoxide anions and inefficient ATP synthesis (Aroor et al., 2012).
- **Effects of Hyperglycemia and Free Fatty Acids:**
  - Hyperglycemia and elevated free fatty acids contribute to oxidative stress by initiating free radical formation in various cell types, including muscles and adipocytes. This oxidative stress leads to mitochondrial dysfunction and damage (Karam et al., 2017). In diabetes, mitochondrial abnormalities, such as smaller, rounder mitochondria with increased superoxide production, are observed (Cobley et al., 2018). Lipoperoxidation and decreased antioxidant mechanisms further contribute to the condition (Zhou et al., 2018).
- **Cardiovascular Complications:**
  - Diabetes-related cardiovascular complications arise from impaired cardiac microvascular function and are influenced by factors such as hypertension and dyslipidemia. Antidiabetic drugs, such as sodium-glucose co-transporter-2 (SGLT2) inhibitors, have been shown to reduce cardiovascular risk by alleviating oxidative stress and improving cardiac microvascular health (Karam et al., 2017; Zhou et al., 2018). Aminoguanidine has also been found to mitigate diabetes-induced cardiac abnormalities by inhibiting endoplasmic reticulum stress and promoting autophagy (Pei et al., 2018).
- **Metabolic Syndrome and Oxidative Stress:**
  - Metabolic syndrome is characterized by oxidative stress, involving an imbalance between ROS production and antioxidant defense. Factors like insulin resistance, abdominal obesity, dyslipidemia, endothelial dysfunction, and chronic stress contribute to this condition (Karam et al., 2017). Lenalidomide has been shown to reduce oxidative cardiovascular damage in obesity by inhibiting tumor necrosis factor (Zhu et al., 2014).

ROS and Aging:
Free Radical Theory of Aging:

The "free radical theory of aging," proposed over 60 years ago, suggests that reactive oxygen species (ROS) cause damage accumulation in cellular components and connective tissues, leading to aging and age-related degenerative diseases (Tsoukalas et al., 2019a). Aging results from both genetic and external factors, including poor diet, inadequate exercise, chronic drug use, unresolved inflammation, smoking, and alcohol abuse.

Theories of Aging and Oxidative Stress:

Despite the evolution of various aging theories, oxidative stress remains a central concept in many of them (Finkel and Holbrook, 2000; Payne and Chinnery, 2015). Mitochondria and NADPH oxidase (NOX) are key contributors to excessive oxidative stress in cells. NOX, a family of membrane-associated enzymes found in many cell types, is linked to age-associated diseases due to its increased activity and/or expression (Bedard and Krause, 2007; Zhang et al., 2004; Park et al., 2008; Egea et al., 2017).

Protein Aggregates in Aging:

Aging is characterized by the accumulation of high-molecular-weight protein aggregates in cells, primarily composed of oxidized or modified proteins and some lipids (Davalli et al., 2016; Barrera, 2012; Takalo et al., 2013; Tsoukalas et al., 2019b). These aggregates disrupt protein homeostasis and emphasize the need for effective degradation mechanisms.

Proteasome Function and Aging:

The proteasome is crucial for degrading damaged proteins, specifically targeting unfolded proteins (Saez and Vilchez, 2014). Inhibiting the proteasome prevents the breakdown of newly formed oxidized proteins, leading to increased protein aggregation (Takalo et al., 2013; Saez and Vilchez, 2014). Proteasome dysfunction correlates with aging and protein aggregation, while proteasome activation has been shown to slow aging and enhance longevity (Chondrogianni et al., 2014). Overexpression of proteasomal subunits or treatment with specific compounds can positively affect proteasome activity in various models (Saez and Vilchez, 2014).

Antioxidant Supplements:

The rise of antioxidant supplements was inspired by the free radical theory of aging. However, recent studies indicate that antioxidant supplementation does not significantly reduce the incidence of age-related diseases (Conti et al., 2016; Schottker et al., 2015).

Antioxidant Defenses

- **Role and Types of Antioxidants:**
  - Antioxidants neutralize radical chain reactions, mitigating oxidative stress-related damage (Da Pozzo et al., 2018). They operate in both hydrophilic and hydrophobic environments, leading to a diverse chemical structure.
  - Antioxidants are classified into enzymatic and non-enzymatic types (Banafsheh and Sirous, 2016). A nutritional perspective divides them into endogenous and exogenous categories:
    - **Endogenous Antioxidants:** Synthesized by cells, including all enzymatic antioxidants and some non-enzymatic ones like thiol antioxidants and coenzyme Q10.
    - **Exogenous Antioxidants:** Must be obtained from the diet as they cannot be synthesized in eukaryotic cells. This class requires attention due to its variability in cellular redox balance.
- **Solubility and Absorption:**
  - **Water-Soluble Antioxidants:** Easily absorbed from water-containing fruits and vegetables but rapidly eliminated through urine. Examples include polyphenols and vitamin C (Lazzarino et al., 2019).
  - **Liposoluble Antioxidants:** Absorbed with dietary fats and can accumulate in the body. Vitamin E is a notable example (Lazzarino et al., 2019).

Discussion

- **Meta-Analysis Overview:**
  - The article reviews meta-analyses on the impact of antioxidants on chronic diseases. Although data from meta-analyses are considered high-level evidence, some criticize their use over individual studies.
- **Antioxidant Efficacy and Balance:**
  - Consuming antioxidants does not necessarily equate to improved health. Free radicals and antioxidants both have roles in the body; the key is maintaining a balance rather than attributing solely negative or positive roles to them.
  - Excessive free radicals can lead to the degradation of cellular components and are associated with diseases like cancer, cardiovascular disease, Alzheimer's, and autoimmune disorders (Poprac et al., 2017).
- **Antioxidants as Prooxidants:**
  - The term "antioxidant" refers to a substance's ability to donate electrons. In some contexts, antioxidants can act as prooxidants depending on their chemical environment (Chen X.F. et al., 2018). Each antioxidant has unique biological properties and mechanisms of action, making it incorrect to assume one can replace another.
- **Food vs. Supplements:**
  - Antioxidants from food are often more effective than supplements due to the synergistic effects of multiple substances in whole foods.

Isolated antioxidants in supplements may not always show beneficial effects, and their bioavailability can be limited (Fernández-García et al., 2012).
    - Foods rich in bioactive substances often activate endogenous antioxidant mechanisms rather than acting directly as antioxidants in isolation (Kurutas, 2015).
- **Research and Future Directions:**
    - The health benefits of antioxidant supplements can vary, with some benefits possibly due to other food components or the unique chemical structure of antioxidants in whole foods versus supplements (Firuzi et al., 2011).
    - Observational studies and small, short-term studies may not provide conclusive evidence of a superfood's effectiveness. More extensive randomized trials are necessary to evaluate the role of antioxidants in disease prevention and treatment.

Concluding Remarks and Perspectives

- **Lifestyle and Diet:**
    - A balanced lifestyle, including proper nutrition, is crucial in managing oxidative stress. Antioxidants play a significant role in combating oxidative stress, which is linked to severe conditions like cancer, diabetes, cardiovascular disease, and neurodegenerative disorders.
- **Phytochemicals and Therapeutic Potential:**
    - Plant-derived bioactive molecules have therapeutic potential for disease prevention and treatment. A diverse intake of phytochemicals may offer chemopreventive benefits, although more research is needed to confirm their effectiveness in clinical settings.
- **Safety and Future Research:**
    - Antioxidants, due to their oxidation-prone nature, require careful consideration in both food and supplement forms. High doses of antioxidants may have detrimental effects. Future research should focus on understanding the chemical components of antioxidants to develop safer and more effective prophylactic and therapeutic agents.
- **Understanding Oxidative Stress:**
    - Studying oxidative stress remains crucial for better managing and understanding various diseases. Continued research in this field will help develop more effective strategies for disease prevention and treatment.

Conclusion

Oxidative stress, resulting from an imbalance between the production of reactive oxygen species (ROS) and the body's antioxidant defenses, plays a pivotal role in the development and progression of chronic diseases. The detrimental effects of excessive ROS are well-documented, contributing to cellular damage and the pathogenesis of conditions such as cardiovascular diseases, cancer, and neurodegenerative disorders. Understanding how lifestyle choices influence

oxidative stress is essential for effective chronic disease management. Lifestyle factors, including diet, physical activity, smoking, and alcohol consumption, significantly impact oxidative stress levels. Moderate exercise has been shown to enhance the body's antioxidant defenses, whereas excessive physical activity can increase ROS production, leading to oxidative stress. Smoking and alcohol consumption introduce additional oxidants and free radicals into the body, exacerbating oxidative damage and inflammation. In contrast, a diet rich in antioxidants can neutralize ROS and mitigate oxidative stress, thereby reducing the risk of chronic diseases. Healthcare providers are crucial in managing chronic diseases influenced by oxidative stress. They have the opportunity to guide patients in adopting healthier lifestyle choices that can reduce oxidative damage. This includes promoting regular, moderate exercise, recommending antioxidant-rich diets, and advising against smoking and excessive alcohol consumption. By integrating lifestyle modifications into chronic disease management plans, healthcare providers can enhance patient outcomes and contribute to overall public health improvements. In summary, lifestyle choices have a profound impact on oxidative stress and chronic disease management. Healthcare providers play a key role in advising and supporting patients to make beneficial lifestyle changes. Addressing oxidative stress through lifestyle modifications can improve disease management and potentially prevent the onset of chronic conditions. Future research should continue to explore the complex interactions between lifestyle factors, oxidative stress, and chronic diseases to further refine prevention and management strategies.

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استكشاف كيفية تأثير اختيارات نمط الحياة على إدارة الأمراض المزمنة - دور مقدمي الرعاية الصحية: مقال مراجعة

الملخص:

الخلفية :الأمراض المزمنة أصبحت شائعة بشكل متزايد في جميع أنحاء العالم، حيث تلعب اختيارات نمط الحياة دورًا كبيرًا في إدارتها. تم الإشارة إلى الجذور الحرة والإجهاد التأكسدي في العديد من الحالات المزمنة، بما في ذلك الأمراض القلبية الوعائية، السرطان، والاضطرابات العصبية التنكسية. تنشأ هذه الحالات من عدم التوازن بين إنتاج أنواع الأكسجين التفاعلية (ROS) والدفاعات المضادة للأكسدة في الجسم.

الهدف :يهدف هذا الاستعراض إلى استكشاف كيفية تأثير اختيارات نمط الحياة على الإجهاد التأكسدي وإدارة الأمراض المزمنة، مع التركيز على دور مقدمي الرعاية الصحية في توجيه التعديلات في نمط الحياة لتقليل الإجهاد التأكسدي وتحسين نتائج الصحة.

الطرق :تم إجراء مراجعة شاملة للأدبيات، مع التركيز على آليات الإجهاد التأكسدي وتأثيره على الأمراض المزمنة. تم تحليل الدراسات المتعلقة بتأثيرات عوامل نمط الحياة مثل النظام الغذائي، التمارين الرياضية، التدخين، واستهلاك الكحول على الإجهاد التأكسدي. كما تم دراسة دور مضادات الأكسدة في مكافحة الأضرار التأكسدية وتداعياتها على إدارة الأمراض المزمنة.

النتائج :يبرز الاستعراض أن عوامل نمط الحياة تؤثر بشكل كبير على مستويات الإجهاد التأكسدي. تعزز التمارين المعتدلة الدفاعات المضادة للأكسدة، في حين أن النشاط البدني المفرط، والتدخين، واستهلاك الكحول يفاقمون الإجهاد التأكسدي. يساعد النظام الغذائي الغني بمضادات الأكسدة في تقليل الأضرار التأكسدية. تلعب أنواع الأكسجين التفاعلية دورًا حاسمًا في تطور الأمراض المزمنة، بما في ذلك الحالات القلبية الوعائية، السرطان، والاضطرابات العصبية التنكسية. يلعب مقدمو الرعاية الصحية دورًا حيويًا في نصح المرضى بالتعديلات في نمط الحياة لإدارة الإجهاد التأكسدي وتحسين نتائج الصحة.

الاستنتاج :تتطلب إدارة الأمراض المزمنة الفعالة معالجة عوامل نمط الحياة التي تؤثر على الإجهاد التأكسدي. يجب على مقدمي الرعاية الصحية التأكيد على أهمية التمارين المتوازنة، نظام غذائي غني بمضادات الأكسدة، وتقليل العادات الضارة مثل التدخين واستهلاك الكحول بشكل مفرط. من خلال توجيه المرضى نحو اختيارات نمط حياة أكثر صحة، يمكن لمقدمي الرعاية الصحية المساعدة في تقليل الإجهاد التأكسدي وتحسين إدارة الأمراض.

الكلمات المفتاحية :الإجهاد التأكسدي، الأمراض المزمنة، اختيارات نمط الحياة، مضادات الأكسدة، مقدمو الرعاية الصحية، الأمراض القلبية الوعائية، السرطان، الاضطرابات العصبية التنكسية.