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Understanding of Antioxidants Mechanism in Clinical Nursing Practice

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Abstract : The aim of this study is to provide fundamental knowledge for the efficient use of antioxidants in nursing intervention by identifying cellular damage by Reactive Oxygen Species (ROS), antioxidant defense mechanism, and a broad range of antioxidant use. This study investigated the known mechanisms and clinical applications of antioxidants through published literature reviews. The state of nursing research using antioxidants between the period 1966 and 2011 was reviewed using analysis criteria. The collection of literatures in this study was performed through a biomedical database, Pubmed, Korean research information service system, Riss4U, a science and technical database, ScienceDirect and Internet. Acute and chronic diseases are associated with the production of ROS in the human body, and the use of many antioxidants is being considered in order to reduce the pathological damage caused by ROS. Providing effective nursing intervention reducing oxidative stress will prevent various diseases and improve the status of health. To enhance the quality of clinical nursing practice, nurses need to understand the accurate mechanism of antioxidants, identify the risk factors affecting the process of ROS production, and monitor the cellular balance in oxidation-reduction.

Key words : Reactive oxygen species (ROS), Antioxidant, Literature reviews, Nursing practice

1. Introduction

1.1. Background and Justification of the Study

Antioxidants are substances that reduce the production and activity of oxygen radicals as well as reactive oxygen species (ROS) and repair damaged tissues. They include vitamin A, vitamin C, vitamin E, β-carotene, selenium, probucol, and Co-enzyme Q10. Also, they are used to reduce free radicals and oxidative stress by effectively establishing or enhancing cellular defense mechanisms such as promoting other antioxidants' effects.

Oxidative stress causes toxicity to a target cell when the effect of antioxidant system, which removes ROS from the human body, is insufficient or excessive ROS is produced (Karbownik & Lewinski, 2003). Stress such as immobility and isolation reduces the activity of antioxidant enzymes (Bar-Shai, Caemedi, Ljubuncic, & Reznick, 2008), and stimulates radical reactions. Thus, it causes chronic diseases such as cancer, dementia, and atherosclerosis and other problems in the human body, such as compromised immunity, asthma, allergy, and aging. Free radicals and antioxidants draw attention as a contributing factor to the development and treatment of diseases since many studies have reported that acute and chronic diseases are associated with the imbalance of free radicals and antioxidants.

Therefore, nurses need to understand about the process for free radicals to develop diseases through damage to the human body and the effects of antioxidants, which respond to the damage, in order to provide an intervention for people who are exposed to various diseases. This article is written not only to understand cellular damage caused by ROS and antioxidant defense mechanism but also to suggest the effects of antioxidants in nursing interventions by

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identifying an extensive range of antioxidant application, and develop a systemic and evidence-based nursing research based on this.

1.2. Study purpose

The purpose of this study is to provide fundamental knowledge for the efficient use of antioxidants in nursing intervention by identifying cellular damage by ROS, antioxidant defense mechanism, and a broad range of antioxidant use.

2. Study method

2.1. Study subjects and investigational method

This study investigated the known mechanisms and clinical applications of antioxidants through internet searching as well as literature review. A comprehensive search was performed by electronical searching of databases. Databases of Pubmed, Korean research information service system, Riss4U, a science and technical database, ScienceDirect and Internet were searched using keywords, “antioxidants” and “reactive oxygen species”. There was no limitation of research and the last research was performed on November. 2011.

2.2. Systematic Review of antioxidants in nursing research

In order to identify the state of nursing research using antioxidants, web searching was performed using the keyword, “antioxidant(s)” from 1966, when the first research on antioxidant was performed in Korea, to September, 2011, on the websites of Korea Education and Research Information Service (KERIS) (http://www.riss.kr), and Korean Studies Information Service (KSIS) (http://kiss.kstudy.com), DBpia (http://www.dbpia.co.kr).

3. Literature review

3.1. Comprehension about reactive oxygen species (ROS)

Reactive oxygen species (ROS) are oxygen free radicals and oxygen compounds derived from them. They include superoxide anion (O_2-), which plays a pivotal role in oxidative toxicity, hydroxyl radical (HO), hydrogen peroxide (H_2O_2), and singlet oxygen ($1O_2$).

ROS are produced not only by inner factors such as respiration in mitochondria, the effects of enzymes such as nicotinamide adenine dinucleotide phosphate (NADPH oxidase), bacterial reactions, and emotional stress (Muqbil, Azmi, & Banu, 2006), but outer factors such as polluted air, increased metabolic rate, smoking, carcinogens, UV light, heat, and radiation (Bar-Shai et al., 2008). Also, ROS are constantly expelled within cells as long as a living organism is alive.

A free radical, which is one of the ROS, has unpaired electrons in the outermost orbit, and is characterized by great reactivity with surrounding chemicals in order to gain or lose electrons in order to change to a stable status. When excessive ROS are produced, a switch protein called oxyal separates normal proteins from modified proteins. Free radicals that are not removed by a defense mechanism rapidly react with biomolecules and cause oxidative stress by inducing protein modification or peroxidation of phospholipid cellular membrane. When lipid is peroxidized, destruction of membranes, loss of functions of cellular organelles, deactivation of receptors in the membranes, and problems with a transport system occur. A lipid peroxidation product diffusing into the cell or transferring through blood stream stimulates another radical reaction, and thus causes chronic diseases such as cancer, dementia, and atherosclerosis and promotes aging. Moreover, ROS induce inflammation by stimulating inflammatory cells and activating NF-kB (nuclear factor kappa B), which leads to the increased production of inflammatory cytokines.

As addressed above, ROS cause cellular damage by readily interacting with adjacent molecules such as lipids, proteins, and carbohydrates in a human body. They also expose a human body to aging, acute or chronic diseases by stimulating radical reactions.

On the other hand, ROS produce free radicals in order for neutrophils to attack and destroy pathogens. They cause chronic diseases, aging and inflamma-

tion, but they are also used for detoxification in the liver as a defense mechanism. That is, ROS are contributed not only to chronic diseases, aging, and inflammation, but to wound healing and immune reactions since they can cause cellular growth, division, development and gene expression. Therefore, it is necessary to understand the mechanism to suppress the disease development of ROS and to activate human body defense system, and develop nursing interventions based on accurate understanding.

3.2. Measurement of oxidative stress

3.2.1 Measurement of antioxidants

What is clinical evidence of oxidative stress in fatal diseases?

There is no standardized method to measure oxidative stress, and thus it is not used in clinical diagnosis. Measurement is challenging given that ROS have a very short half-life. Instead, we can measure various products, such as TBARS, which contain damages made by oxidative stress (Pryor, 1991). Another way to measure oxidative stress is to measure the missing incidents of oxidative suppressants such as á-tocopherol because most á-tocopherol is found in plasma lipid, and this decreases in diseases. The measurement of a certain plasma tocopherol needs to be an indicator of total cholesterol in the population of fatal illnesses (Howitt, Harvey, & Dahm, 1972).

Acute phase response is related to oxidative stress even if the patient is not hospitalized. Boosalis, Snowdon, Tully, & Gross (1996) studied the association between acute phase response and the concentration of antioxidants in 85 nuns aged 77 to 99. Among them, 10 (11%) showed acute phase response, which was found to be due to increased plasma concentration of c-reactive proteins (≥ 143 nmol/L). The existence of acute phase response has a significant and negative association with the concentration of plasma licopene (p<.05), â-carotene (p<.05), β-carotene (p<.05), and total carotenoid (p<.01). The concentrations of lutein, zeaxanthin, cryptoxanthin, and α-tocopherol are not significantly associated with acute

Table 1. Increase in Oxidative Stress Produced in a Human Body: Selection between the Indicator to Measure the Degree of Dependence of Nature (A) and the Sites in which ROS are Produced (B)

A. Which indicator of oxidative stress needs to be measured?
Total antioxidant capacity of plasma
Consumption of antioxidant synthesis (albumin, vitamin E, vitamin C, uric acid, bilirubin)
Consumption of cofactors of antioxidant enzymes (selenium, copper)
Activation of antioxidant enzymes (SOD, glutathione peroxidase)
ROS (by electronic spin resonance whether spin capping or not)
Myeloperoxidase (mostly neutrophils, found by activated phagocytes)
Compounds induced by the reactions with ROS
Nitrate or chloroprotein(chloramine) or lipid(chlorohydrin)
Oxidized protein (carbonyl compounds, oxidized thiol)
Oxidized lipid (oxidized lipids, dien complexes, aldehyde, isoprostane, TBARs)
Oxidized thiol (sulfoxide)
B. Where does the oxidative stress need to be measured?
Plasma
Lungs : BAL bronchoalveolar lavage, epithelial lining fluids
Brain : blood from jugular vein and cerebral spinal fluid
Heart : blood from coronary sinus
Peritoneum: peritoneal fluid
Kidney: urine
Pleural fluid, lymph
Body fluid drainage

BAL, Bronchoalveolar lavage; ROS, reactive oxygen species; SOD, superoxide dismutase; TBAR, thiobarbituric acid reactant (malondialdehyde)

phase response. This study suggested that a mild inflammatory disease such as acute phase response has a negative effect in antioxidative phase (Boosalis et. al, 1996).

3.2.2 Bio-indicator measurement of oxidative stress

An ideal method is to measure ROS, but it is unstable (even when they are not free radicals) and its extraction is difficult. Especially, free radicals have a very short half-life. They are measured only by ESR, and mostly they pair as spin trapping in order to increase their life span and the sensitivity of their classification.

3.2.3 Bioindicators of oxidative stress in the intensive care unit (ICU)

The measurement of a bio-indicator of oxidative stress is the level of ROS (e.g. malondialdehyde, F2-isoprostane, 8-isoprostane, and 8-hydroxydeoxyguanosine) and trace elements. A bioindicator cannot provide information about the tissue region of oxidative stress. The types of damages caused by ROS vary depending on the site of onset and a type of ROS. However, ROS impair blood vessels and produce more ROS in the plasma, and thus the measurement of antioxidants in the plasma is associated with considerably acute diseases given that cellular membranes become more permeable in acute diseases.

Antioxidants in most patients with acute diseases are measured in the plasma, but oxidation occurs within a cell. However, it is difficult to calculate ROS as it does not have a clear target and its half-life is short. The limit of calculating oxidative stress is that some bioindicators measured in the plasma reflect differently in tissues (Arguelles, Garcia, Maldonado, Machado, & Ayala, 2004). For example, the level of H2O2 in an ARDS patient with a mechanical ventilator is high in breath condensate but not in the plasma (Goodyear-Bruch & Pier, 2002).

3.2.4 Calculation of antioxidants in acute illness patients

ROS is a molecule or a part of molecule and contains one or more unpaired electrons in the outer orbit, in which the reaction increases. Fundamental oxidants produced during excessive sepsis and infection are not peroxynitrite, singlet oxygen, hypochlorous acid, and transition metal but superoxide anions, hydroxyl radicals, and hydrogen peroxide. The only technique to directly protect against ROS is the electron spin resonance (ESR). However, this method is still not sensitive to shield ROS, which has a very short half-life like superoxide anions and hydroxyl radicals in a new biological system. Therefore, the only stable oxygen such as ascorbyl oxygen can be directly protected by ESR. Courderot-Masuyer, Lahet, Verges, Brun, & Rochette (2000) suggested that ascorbyl free radical (AFR)/vitamin C ratio can be a method of calculation of oxidative stress. By using electron paramagnetic resonance (EPR) to measure the AFR release, an inverse correlation between plasma vitamin C and AFR/vitamin C ratios was noted in type 2 diabetic patients, whereas no significant change of AFR was found in patients with cardiac surgery. However, for ESR spectroscopy, sample analysis can be applied with the addition of the spin trapping method, which rapidly reacts with a more stable and fundamental additive form of ROS. In this sense, increased oxidative stress was shown in type 1 diabetic patients (Davison et al., 2002) and coronary artery bypass surgery patients with cardiopulmonary bypass (Wu et al., 2001). Methodological results of ROS deficiency is usually calculated by an indirect method.

3.3. Comprehension about the defense system of antioxidants

The defense mechanism of antioxidants is to remove ROS and get involved in tissue repair as well as new growth, and thus maintain the balance of the human body (Muller, Lustgarten. Jang, Richardson, & Van Remmen, 2007). Oxidant stress is produced when the balance between the production of ROS and defense mechanism of antioxidants, and this causes oxidative toxicity to a cell (Karbownik & Lewinski, 2003).

The human body uses an antioxidant system consisting of antioxidant vitamins, non-enzymatic antioxidant substance and antioxidant enzymes in order

to prevent tissue damage by neutralizing ROS. This antioxidant system plays a unique role and works complementarily. Antioxidant vitamins directly remove oxygen free radicals, and antioxidants such as glutathione and other thiol compounds play a significant role in maintaining cellular oxidation-reduction status. Antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT) and GSH peroxidase (GPX) prevent the attack of ROS by preventing the production of ROS and removing reactive metabolites. They also prevent a dioxide from being converted to a more destructive form of ROS such as hydroxyl radicals, expedite the repair in case of the attack of ROS, and stimulate the electronic reduction reaction of ROS by providing the environment for other antioxidants to play an effective function.

3.4. Use of antioxidants

3.4.1 Vitamin

A precursor of vitamin A, â-carotene, works as the most effective antioxidant under low oxygen pressure like biological oxygen pressure and thus complement vitamin E effect under high oxygen pressure (Schmidt et al., 2002). The higher the blood concentration of carotenoid is, the lower the blood sugar is. Also, the blood concentration of carotenoid is inversely associated with type 2 diabetes mellitus and impaired glucose tolerance, and thus its use is considered in diabetes mellitus.

Vitamin C is an antioxidant that directly removes ROS with its capacity to reduce other substances and reproduce the oxidized form of á-tocopherol. It also deactivates singlet oxygen or hydrogen peroxide outside of the cells (whole blood and plasma) filled with extracellular fluid, removes hydroxyl radicals in a neutral solution (Duarte & Lunec, 2005), and is contributed to the protection of a cell membrane by blocking the production of hydroperoxide (Cook et al., 2007). With high plasma concentration of vitamin C, systolic and diastolic blood pressure considerably decreases, and cardiovascular diseases can be prevented through antioxidants preventing lipid peroxidation. Vitamin C also prevents the oxidative mechanism of diabetes mellitus and is effective in the prevention of glycation, in which glucose non-enzymatically combines with proteins, given that it is similar in structure to glucose and thus replaces glucose in chemical reactions. Vitamin C is involved in the protection and synthesis of collagens as it reduces capillary leak and fluid demand in patients with burns over more than 30% of the total body surface area (Tanaka et al., 2000), synthesizes procollagen by stimulating fibroblasts, and acts as a co-factor to strengthen collagens by progressing the formation of cross-links of triple helix hydroxyproline. Thus, its effect is taken into consideration for the prevention of aging as well as diseases such as cardiovascular disease, dyslipidemia, diabetes mellitus, and a burn.

Vitamin E is an antioxidant, located in the mitochondrial membrane, blocks the chain reaction of free radicals and suppresses oxidative stress, which is a cause of aging and illnesses, by preventing tissue damage through the reaction with free radicals for the oxidative impairment of phospholipid cell membrane (Ratnam, Ankola, Bhardwaj, Sahana, & Kumar, 2006). It also stops lipid peroxidation by blocking free radical chain reactions as it oxidizes itself in lieu of polyunsaturated fatty acid, which is readily oxidized by ROS in cell membranes, and is ultimately contributed to the prevention of diabetes mellitus by removing ROS. Moreover, vitamin E reduces oxidative stress and thus improves liver function (Manning et al., 2004). In combination with vitamin C during pregnancy, it can prevent preeclampsia and premature rupture of membranes by affecting the tissue integrity of villous membranes (Yang et al., 2009).

β-carotene, vitamin C, and vitamin E are used as antioxidants affecting villous membranes and aging as well as diseases such as hypertension, cardiovascular diseases, diabetes mellitus, and a burn. However, it is known that high dose β-carotene increases osteoporosis and fetal malformation; while, vitamin C increases abdominal bloating, diarrhea, anemia, and arrhythmia. Also, overdose of vitamin E is known to cause hemorrhagic stroke (Song, 2010), and thus it is necessary to provide accurate suggestions and audit for the permitted dose.

3.4.2 Co-enzyme Q10 (Co-Q10)

Co-enzyme Q10 (Co-Q10), a molecule produced naturally, is an antioxidant found in 1957, acts as a reduced form and plays a significant role in the production of ATP by getting involved in aerobic cellular respiration (Tempestini et al., 2003). Co-enzyme Q10 suppresses cellular apoptosis (Tempestini et al., 2003), and has a cardioprotection effect through a mitochondrial function after cardiac ischemia-reperfusion (Crestanello et al., 2002). Also, it improves cardiovascular diseases such as hypertension, coronary sinus disease, myocardial infarction, congestive heart failure, and cardiomyopathy by stimulating oxygen supply to all tissues (Belardinelli et al., 2006), and has effects such as anticancer, immune system enhancement, delaying aging, alleviating asthma and allergy, and maintaining blood pressure. Kojima et al. (2007) suggested the applicability of co-enzyme Q10 in various diseases by reporting that co-enzyme helps to lower the incidence and progression of senile glaucoma.

3.4.3 N-acetylcystein

N-acetylcystein is an antioxidant existing outside living organisms and a precursor of GSH synthesis. In animal studies, it is shown that it increases phagocytic activities of neutrophils in systemic inflammatory response syndrome (SIRS) or sepsis, and it has anti-inflammatory and anti-hypersensitivity in asthma (Lee et al., 2004). It also affects the treatment for adult respiratory distress syndrome (ARDS) by increasing GSH concentration in the plasma and red blood cells, oxygen delivery and lung compliance, and reduces oxidative stress in human immunodeficiency syndrome as well as chronic obstructive pulmonary disease (COPD).

Moreover, it is considered to prevent the peritoneal membrane damage during dialysis in the patients with chronic renal failure as it delay peritoneal fibrosis by suppressing ROS production by peritoneal dialysis fluid, and suppresses upward adjustment of vascular endothelial growth factor (VEGF) increasing peritoneal permeability fibrosis-inducing transforming growth factor-β1 (TGF-β1)(Song, 2003).

However, research on the antioxidant effect of N-acetylcystein is limited on animal studies, and a large clinical research has not proven a distinctive effect (Kim, 2010). Thus, the verification of biological safety of N-acetylcystein dose and treatment has to precede its treatment.

3.4.4 Probucol

Probucol decreases the formation of neointima by suppressing the malfunction of endothelial cells and low dense lipoprotein peroxidation, and affects the remodeling of blood vessels. It also affects the remodeling of extracellular fluids by suppressing IL-1 secreted by phagocytes and metalloprotease secreted by smooth muscle cells. This mechanism of probucol is used in coronary angioplasty as it prevents the restenosis of coronary sinus by affecting the remodeling of blood vessels in patients with coronary artery stents (Lee et al., 2002).

Moreover, it is expected to prevent chronic complications as well as oxidative damage caused by diabetes mellitus as it suppresses the production of peroxidized lipids in blood plasma, liver, kidneys, and heart in diabetes mellitus. It also would be used in the treatment for diabetes mellitus and hyperlipidemia as it has been reported that it prolongs the LDL oxidation time increased in Raynaud's diseases and decreases plasma TG concentration and the degree of LDL oxidation in hyperlipidemia (El-Swefy et al., 2000).

Concerning that there are 38 studies about probucol in Korea but there is no nursing research among them, it is essential to pay attention to probucol in nursing research in order to prevent and treat coronary artery diseases, diabetes mellitus and hyperlipidemia. Furthermore, it is necessary to accurately comprehend the mechanism of probucol in the human body as well as its safety through repeated human-subject research since most of the research related to diabetes mellitus and hyperlipidemia are animal studies.

3.4.5. Selenium

Selenium is an essential trace mineral distributed to liver, kidneys, heart, spleen, and blood plasma, and an

essential antioxidant in glutathione oxidation. Selenium removes free radicals, delays aging by suppressing the accumulation of lipid peroxides, reduces the incidence of cancer and diabetes mellitus by affecting cellular growth and death (Rayman & Rayman, 2002), and prevents fatty acid oxidation and its complications, blood coagulation and endothelial damages.

Chronic deficiency of selenium affects the level of iron and hematogenous functions by stimulating lipid peroxidation of the membranes of red blood cells and causing red blood cell lysis. Also, it increases the incidence of arterial sclerosis, cancer, diabetes mellitus, hypertension, anemia, cardiovascular diseases, and aging through the induction of platelet hypercoagulation, stimulation of lipid peroxidation and suppression of prostacyclin synthesis (Burk, 2002). Systemic inflammatory response syndrome (SIRS) and sepsis are conditions in which the activity of glutathione peroxidase is reduced. With selenium supplement, the activity of glutathione peroxidase is restored, and diabetes mellitus as well as its secondary complications can be prevented by increasing antioxidant activities in â-cells of pancreas, which is susceptible to the attack of ROS due to low activity of antioxidant enzymes (Nam, 2007). However, Stranges et al. (2007) have reported that long-term selenium supplement has a negative effect on glucose metabolism. Chung et al. (2006) have reported that overdose of selenium results in a functional loss of proteins consisting of mitochondria, which mediates cell death by inducing direct oxidation of proteins.

Therefore, it is considered that proper standard for the selenium dose, duration and the blood concentration of selenium as an antioxidant is needed through repeated research (Lee et al 2010). Also, it is expected that comprehension about the mechanism of selenium would be effectively used for nursing interventions related to the prevention and treatment of diseases including diabetes mellitus, cancer, arterial sclerosis, and anemia.

3.4.6. Other antioxidants

An essential amino acid, glutamine, is a precursor of glutathione, which is significant in amino acid delivery and protein synthesis. In case that it is intravenously injected with alanine in critical care patients, inflammatory adverse effects decrease (Dechelotte et al., 2006). Melatonin secreted by the pineal gland removes free radicals and thus is considered to be a potential antioxidant. Flavonoid is a potent scavenger of oxygen radicals, and has a protective effect for lipid peroxidation as a metal chelator (Kim, 2004). Urate, which has high concentration in the blood plasma of human beings, protects vitamin C from getting oxidized by copper or iron ions and maintains the level in the blood. It is also used as an antioxidant as it mutually interacts with singlet oxygen as well as hydroxyl radicals, and protects the peroxidative damage and lysis of red blood cells. However, the mechanism related to arthritis or gout has not been identified.

3.4.7 The state of nursing research using antioxidants

The state of nursing research using antioxidants between the period 1966 and 2011 was reviewed using analysis criteria. As a result, 717 journal articles and 1298 theses were identified, and they were a total of 1920 articles except redundancy. Antioxidants-related research in Korea was being performed in various studies such as medicine, athletics, nutrition, food science and technology, and biological sciences. Korean nursing research among these was 17 in total (10 journal articles and 7 theses). However, 2 journal articles and 5 theses among 17 articles were about the status of vitamin intake without insights into the mechanism of antioxidants, and thus antioxidant-related nursing studies were 10 in total (8 journal articles and 2 theses).

There were three studies about stroke and coronary artery diseases, as the most common Korean nursing research related to antioxidant effects, two studies about liver cancer, and 1 study about diabetes mellitus, skin, stress and immune system for each. Most of them were to verify the effects after the intake of vitamins or soya beans. In terms of study subjects, 8 studies were from whitepaper and 2 were from human subjects (diabetes mellitus and coronary artery diseases).

International nursing research was searched on

Pubmed (http://www.ncbi.nlm.nih.gov/pubmed) using the keyword, antioxidant(s), and 352,514 articles were found. Nursing studies among these were 692 articles, and 561 articles were found from the search using the keywords of English and human beings from 1965 to 2011. As a result of the analysis of 121 articles based on re-searching articles published from 2007, 32 articles, as the greatest volume of the articles, were published in 2007and more than 20 articles were published annually. Based on age, 32 articles were about the middle-aged adults, the most common, and the elderly (25 articles), adults (22 articles) and neonates (17 articles) in order. The most common subjects of articles were related nursing given that 11 articles including pressure ulcer (2 articles) and diabetic foot management (1 article), and others were related to cardiovascular diseases (11 articles), neuropathy (2 articles), neurological diseases including Parkinson's disease (2 articles), liver diseases (7 articles), and Alzheimer's disease/urology/nutrition (5 articles for each). In addition to these, articles about psychiatric diseases such as anxiety, depression, and autism, muscular skeletal diseases such as arthritis, gout, peritoneal dialysis, aging and AIDS were being published, indicating that research on antioxidants was flourishing. Thus, it is essential to pay more attention to antioxidants in the study of nursing in Korea through the comprehension of antioxidant mechanism, and to develop actual nursing interventions based on this.

4. Conclusion and Suggestion

In this study, an extensive range of application of antioxidants as well as cell damage by ROS and the defense mechanism of antioxidants were discussed for the effective use of antioxidants in nursing intervention. As a result of reviewing antioxidant-related studies, it has been found that acute and chronic diseases are associated with the production of ROS in the human body, and the use of many antioxidants is being considered in order to reduce the pathological damage caused by ROS. However, for some antioxidants, their mechanisms and effects have been identified through animal studies or the biological safety about accurate mechanism, dose, and treatment duration are being discussed. There is a little interest in the application of antioxidants as there are only 10 articles related to antioxidants in the study of nursing in Korea. Therefore, it is suggested that further research in nursing need to understand the molecular change and mechanism in order to prevent diseases and improve the status of patients. It is also essential to identify effective nursing interventions providing balance within cells and develop practical nursing interventions to reduce oxidative stress through continuous research and audit for the factors affecting the process of ROS production, excessive production, knowledge about ROS in relation with the balance in cellular oxidation-reduction, and antioxidant defense mechanism.

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