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Antioxidant therapy to ameliorate chronic kidney disease induced by oxidative stress; an updated mini-review

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Abstract

Chronic renal failure is believed to be a serious and common problem which negatively affects the human health and longevity worldwide. Oxidative stress is known to be a pathogenic mechanism in induction of chronic kidney disease. Oxidative stress is developed from an imbalance between free radical production and the antioxidant defense reduction. Antioxidants, therefore, are effective to ameliorate chronic renal failure caused by oxidative stress.

Introduction

The kidney is susceptible to damage induced by reactive oxygen species. One of the influential functions of kidney is to filter waste products from the blood stream (1). Chronic renal failure is gradual, resulting to end-stage kidney disease (2,3). These patients have a high risk of death derived from stroke or heart attack too (3,4). Oxidative stress is referred as an imbalance between generation of reactive oxygen species and natural antioxidant potential (5,6). The main reactive oxygen species include superoxide (O_2^-), the hydroxyl radical (OH^-) and hydrogen peroxide (H_2O_2) (7,8). Notably, reactive oxygen species react with all biomolecules in the cells through inactivating cellular components and oxidizing the nucleic acids (9). Thus, oxidative stress caused several diseases including cancer, atherosclerosis, cardiovascular disease, chronic kidney disease and diabetes (10,11). Hence, it is worthwhile to apply modalities to reduce kidney diseases induced by oxidative stress. One of the most efficient and useful strategies to alleviate the detrimental effect of oxidative stress on kidney health is antioxidant administration (12-15).

Since kidney diseases induced by oxidative stress have been characterized by many studies, a little information is available on antioxidant therapy and its mechanism on kidney health. Hence, the aim of this mini-review article is to assess the effect of antioxidant therapy on chronic kidney disease induced by oxidative stress.

Core tip

Oxidative stress is known to be a pathogenic mechanism in induction of chronic kidney disease. Oxidative stress is resulted from an imbalance between free radical production and the antioxidant defense reduction. Antioxidants, therefore, are effective to ameliorate chronic renal failure caused by oxidative stress.

Materials and Methods

For this mini-review we searched PubMed, EBSCO, directory of open access journals (DOAJ), Google Scholar, and Web of Science with key words as chronic kidney disease, antioxidant, oxidative stress, cardiovascular disease, reactive oxygen species, diabetic nephropathy and herbal medicine.

Sources of reactive oxygen species

Oxygen is crucial to produce energy in humans. In this case, electrons are transferred from the reducing agents to O_2 and finally forming H_2O in mitochondria (16,17). Consequently, energy is conserved to synthesis ATP in electron transport chain (18,19). Thus as the result of intracellular formation of reactive oxygen species (ROS) by various parameters such as heavy metals (20,21), drugs (12,22-25), and toxins (26,27), the kidney will damage. For example

paracetamol is a substance induced oxidative stress which plays an important role in the pathogenesis of renal injury (28,29).

The effects of oxidative stress on kidney health

There are several factors contributing to cardiovascular disease in patients with chronic renal failure including lipid disorders, oxidative stress, inflammation, endothelial function (30,31). Annuk et al (32) reviewed the relationship between oxidative stress and cardiovascular disease in 37 patients with chronic renal failure. They detected that lipid hydroperoxide was increased in subjects with chronic renal failure, compared to control group.

Chronic kidney disease is related to micro-inflammation, morbidity and death (33). Oxidative stress by inducing apoptosis may result to chronic renal failure accordingly (34-36).

Negane et al (37) studied 30 patients with chronic renal failure undergoing hemodialysis. They detected that pre-hemodialytic individuals exposed a rise in serum lipid peroxidation comparing with control subjects. In addition, serum superoxide dismutase and serum nitric oxide were shown to be decreased in pre-hemodialytic subjects when compared to controls. The increased oxidation of lipids, proteins and nucleic acids particularly in the vascular wall, is known to serve important roles in the early stage of atherogenesis in uremia patients (38). Hacisevki (39) studied 64 hemodialysis patients due to chronic renal failure. They found that patients with chronic renal failure showed higher serum superoxide dismutase and lower glutathione peroxidase activities as compared to those of controls. Besides the decreased antioxidants level, serum malondialdehyde content in hemodialysis patients were higher in comparison to that of control group.

Romeu et al (40) studied the oxidative stress-induced by patients with chronic renal insufficiency. They found significant changes in the enzymatic antioxidant systems and non-enzymatic antioxidant systems as compared to controls. Masoomikarimi et al (41) studied the effects of cadmium chloride on renal injury in 30 male mice. They observed that cadmium chloride increased serum malondialdehyde and glutathione concentrations and also superoxide dismutase activity in male mice as compared to controls.

Urolithiasis

Urolithiasis is one of the most widespread diseases in urinary tract. There is an association between urolithiasis and free radical (42). In this case, an increase in oxidative stress led to stone forming conditions (43).

Diabetic nephropathy

Diabetes related-kidney disease is a causal agent of end-stage kidney disease. Two agents promote diabetic nephropathy including high blood sugar level and blood pressure (44-46). Interestingly, high blood sugar level elevates formation of oxidative stress (47). Thus, the increased in oxidative stress induced diabetes consequently affecting kidney negatively (48,49). High blood pressure derives from oxidative stress is the main cause of renal failure too (50,51).

Natural antioxidants

There are several endogenous antioxidants enzymes including superoxide dismutase, catalase, glutathione peroxidase (52) and non-enzymatic defenses such as glutathione, melatonin, N-acetyl cysteine, urate, and plasma protein thiols (53,54). Studies have demonstrated that oxidative damage mainly occurs from the decreased endogenous antioxidants levels rather than the increased reactive oxygen species production (55). Superoxide dismutase converts O_2^- to H_2O_2 and then H_2O_2 is decomposed to O_2 via catalase and glutathione peroxidase (56).

N-acetyl cysteine

One of essential precursor for endogenous antioxidants is N-acetyl cysteine interfere with the decomposition of peroxides (57). N-acetyl cysteine mitigated oxidative stress via amending intracellular glutathione stores (58). However, the results of N-acetyl cysteine supplement in kidney disease are variable depending on the type and cause of kidney injury as well as the time of treatment (59).

Vitamins E and C

Priya and Vasudha (60) reviewed the effect of administration of antioxidant vitamins on 40 patients with renal failure. They detected that antioxidant vitamin levels were reduced in patients with chronic kidney disease in comparison with control subjects. Thus, supplementation with antioxidant vitamins is effective to prevent lipid peroxidation and to depress chronic renal failure in patients. Vitamin E contains eight lipid soluble tocopherols and tocotrienols scavenging free radicals through incorporating into the plasma membrane and also stopping lipid peroxidation (61). It was observed that patients with chronic renal failure showed the lowest serum α-tocopherol levels which reflect the increased α-tocopherol requirement in chronic renal failure (62). In this case, it decreased the risk of resultant cardiovascular disease and increased natural antioxidant levels (63). Administration of vitamin E is known to display the potential to decrease proximal tubular damage and to increase glutathione level and catalase activity (64). In addition, vitamin C supplementation ameliorated the oxidative stress and renal damage (65).

Selenium

Selenium is believed to be an important co-factor of antioxidant enzymes comprising glutathione peroxidase and thioredoxin (66). In this case, Dzobo and Naik (67) investigated the effect of selenium on cadmium-induced oxidative stress in rat kidneys. They observed that selenium intake enhanced catalase and superoxide dismutase activities in the kidney of rats exposed to cadmium.

Dietary herbal medicines

Bioactive component existed in herbal medicines possessing antioxidant activity because of the presence of hydroxyl group on their structures (68-70). Mohamed et al (71) investigated the efficacy of citrus peel extract on castration-induced oxidative stress in rat kidneys. They found that citrus peel extract protected kidney through decreasing the oxidative stress by promoting the antioxidant defense system in rats. In vitro studies also showed, silymarin keeps kidney against oxidative stress induced by paracetamol, cisplatin and CCl4 (26,27) and also by mycotoxins (72). Administration of medicinal plant antioxidants is considered to mitigate the pathology of oxidative stress induced by kidney damage (64). Mansouri et al (73) studied the effect of grape seed extract on oxidative stress induced by diabetes in rat kidney. They found a rise in lipid peroxidation content and the declines in catalase, superoxide dismutase and glutathione peroxidase activities in rat kidney. Furthermore, supplementation of grape seed extract reduced lipid peroxidation and increased the antioxidant enzyme activities in rat kidney. Similarly, Cecen et al (74) showed that silymarin protects doxorubicin-induced oxidative stress in rat kidney. Furthermore, Mahmoud et al (75) studied the effects of curcumin on gentamicin-induced nephrotoxicity in rats. They observed that administration of curcumin could attenuate the detrimental effects of gentamicin on nephrotoxicity induction through protecting glutathione level and increasing antioxidant enzyme activities.

Conclusion

Overall, the results of studies indicated that the presence of antioxidants in the cell or administration of herbal medicines having antioxidant property could ameliorate oxidative stress induce kidney injury.

Author's contribution

HN was the single author of the manuscript.

Conflicts of interest

The author declared no competing interests.

Ethical considerations

The author of this manuscript declares that he has followed the ethical requirements for this communication. Also, Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the author.

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