Open Access Review

Journal of Renal Endocrinology

J Renal Endocrinol 2017;3:e01.
DOI: 10.15171/jre.2017.01
http://www.jrenendo.com

Nickan Research Institute

Oxidative stress in chronic kidney disease; an updated review on current concepts

Sara Beigrezaei[1], Hamid Nasri[2*]

Abstract

Chronic renal failure is associated with enhanced oxidative stress. Oxidative stress has been implicated in various pathological systems that are prevalent in both chronic kidney disease (CKD) and cardiovascular disease, most importantly are inflammation and fibrosis. Chronic inflammation is provoked by oxidative stress and chronic degenerative diseases. The inflammatory cells are source of free radicals in the forms of reactive oxygen (O2) and nitrogen species, while reactive oxygen species (ROS) are considered as the most responsible factor in CKD. ROS are able to be harmful in a variety of functional and structures pathways in cells. Oxidative stress rises free radicals are general product of normal aerobic cellular metabolism. While, O2 is vital for life, imbalanced metabolism and excess ROS generation lead into a range of disorders such as CKD. The purpose of this review is to provide an overview of development of oxidative stress, biomarkers, the involvement of mitochondrial dysfunction and the molecular pathways of oxidative stress in CKD.

Keywords: Oxidative stress, Chronic kidney disease, Chronic inflammation, Free radicals, Reactive oxygen species

Citation: Beigrezaei S, Nasri H. Oxidative stress in chronic kidney disease; an updated review on current concepts. J Renal Endocrinol. 2017;3:e01. DOI: 10.15171/jre.2017.01.

Introduction

In recent decades numerous experimental and clinical investigations have been inscribed for detection of signs of oxidative stress in renal failure patients. One of the kidney functions is to filter waste products that are made in the blood and tissues. Kidney insufficiency defines that waste products are not cleared sufficiently or completely. The development of kidney failure is slow and subtle, with ensuing chronic renal failure. It is frequently many years existed before obvious loss of kidney function happens. People with chronic renal failure have a high mortality from heart attack, or stroke. Chronic renal failure is also able to progress to total and permanent kidney failure. The structural characteristics of chronic renal failure consist of glomerulosclerosis, interstitial fibrosis, increased tubular atrophy, kidney vasculopathy, and lessened kidney regenerative ability. These features can be attributable to, the gradual loss of kidney energy by development of mitochondrial perturbation and resultant, rising of oxidative stress (1,2).

Materials and Methods

For this review, we used a diversity of sources by searching through EMBASE, Web of Science, EBSCO, PubMed/ Medline, Scopus and directory of open access journals (DOAJ). The search was conducted using combination of the following keywords and or their equivalents; antioxidant, chronic kidney disease, reactive oxygen species and hydroxyl radicals. Titles and abstracts of review articles, case-control studies, clinical trials, cohort studies, and reports that held relevance to the intended topic were studied too.

Oxidative stress in chronic kidney disease

Oxidative stress is attributable to the presence of free radicals or radical generating mediators in concentrations that overwhelm natural scavenging mechanisms or radical blocking. The antioxidant protection system initiates and increases the processes of pathogenesis of many diseases. Oxidation of biomolecules can play a role in vulnerability to many diseases. On the other hand, there are few great scale survey describing oxidative injury that occurs in humans and population, while, nutritional or physical factors may also be associated with oxidative stress (3). Oxidative stress determines an imbalance between the formation of reactive oxygen species (ROS) and antioxidant protection that determines the tissue damage. It results from an unbalance between an extreme generation of oxidant compounds and insufficient antioxidant defense mechanisms. Production of oxidative compounds is physiologically essential as part of a protection mechanism (4). However, oxidative stress

Received: 28 October 2016, Accepted: 4 December 2016, ePublished: 26 December 2016

[1]School of Nutrition & Food Science, Isfahan University of Medical Sciences, Isfahan, Iran. [2]Department of Internal Medicine, Isfahan University of Medical Sciences, Isfahan, Iran.
***Corresponding Author:** Prof. Hamid Nasri; Email: hamidnasri@med.mui.ac.ir

Implication for health policy/practice/research/ medical education

Oxidative stress has been implicated in various pathological systems that are prevalent in CKD. Chronic inflammation is provoked by oxidative stress and chronic degenerative diseases. The inflammatory cells are sources of free radicals in the forms of reactive O2 and nitrogen species, although ROS are considered as the most responsible factor in CKD.

is also the main reason for tissue injury or even cell death which can occur essentially by mechanisms of necrosis, apoptosis and inflammation. It speeds up aging, and attributes to variety of degenerative situation (5). Kidney is an organ which is highly at risk to injury caused by free radicals. Free radicals are concerned with the pathogenic mechanisms of conditions such as tubulointerstitial fibrosis and glomerulosclerosis (6). Oxidative stress, induced by free radicals, plays a very important role in the pathogenesis and progression of renal disease (7,8).

Common and serious problem worldwide is chronic kidney disease (CKD) that adversely affects human health, limits long life and increases expenses to health care systems (9). Oxidative stress is dominant in CKD patients and is considered to be an important pathogenic mechanism. In the kidney disorders, cellular oxidant effect on kidney cells can induce apoptosis and senescence, reduce degenerative capability of cells, and fibrosis (10).

Generally uremia is associated with enhanced oxidative stress in renal patients who under treatment by hemodialysis. It has been found the contribution of oxidative stress and antioxidant concentration reduced in these patients. ROS such as hydrogen peroxide (H_2O_2) or hypochlorous acid (HOCl), and free radicals such as superoxide (O_2^-), hydroxyl radical (OH^-), and nitric oxide ($NO^\bullet$), are continuously formed *in vivo* (11). ROS is produced by a univalent diminution of oxygen (O2). After exposure to provocations, both polymorphonuclear neutrophils and monocyte macrophages are activated and, as a result, raise their O2 use (12). Free radicals produce structural injury to all tissue in the body and attribute to disease generation through activation of gene regulatory proteins. ROS are also considered to play a role in the pathogenesis of ischemia/reperfusion injury. Moreover, according to their effect on cell cycle regulation, O2 radicals may attribute to hypertrophy of tubular cells (13,14). Imbalance between ROS and antioxidants results in destructive effect on mesangial cells by varying lipid metabolism. This result is frequently observed in patients with glomerulonephritis and nephritic syndrome.

Factors correlated with oxidative stress

Creation of O2 and hypoxanthine in the mechanism of reperfusion may damage renal cells by the produced ROS in patients with acute kidney failure. Deactivation of $NO^\cdot$ by superoxide anion radical increases vascular resistance in renal arteries and contributes to the development of hypertensive nephropathy. Oxidative stress and decrease of antioxidant mechanisms are other mechanisms in nephropathy associated with antioxidant/oxidant unbalance (15,16). Pro-inflammatory processes with activation of nonspecific system cells and destruction of kidney structure by free radical processes play important roles in urinary system infections. Inflammation is the main cause for the increased oxidative stress detected in patients with advanced kidney disease. Various investigations have revealed that myeloperoxidase is generated in response to activation of polymorphonuclear neutrophils, and as a result trigger inactivation of nitrogen dioxide (NO) and activation of ROS (17,18). The equilibrium between formation of ROS and antioxidative defense mechanisms depends on the activity of enzymes such as superoxide dismutase, NO synthase, and catalase and also glutathione peroxidase. This equilibrium is relatively fragile, difficult to predict, and strongly dependent on environmental conditions.

Pathway and antioxidant protection of co-enzyme Q10

ROS can be created from vascular and glomerular cells including fibroblasts, leucocytes, and from renal interstitial cells. Another cellular enzymes, including myeloperoxidase, cyclooxygenase, mitochondrial oxidases, xanthine oxidase, lipoxygenase, nicotinamide adenine dinucleotide (NADPH) oxidase, and in the case of L-arginine or tetrahydrobiopterin depletion, NO synthase have been recognized as cellular sources of ROS formation (19). Comparing to other organs, kidney involves the highest endogenous levels of co-enzymes (Co)Q9 and CoQ10. CoQ10 is an essential lipid solvable component of all cell membranes containing those enclosing sub-cellular partitions. The function of CoQ10 within the mitochondria are: 1) transferring electrons from complexes I and II to complex III, 2) generated pro-oxidant $O2^{\bullet-}$ and H2O2, and 3) the antioxidant transitive free radicals. Oxidized form of ubiquinone or CoQ10 is able to accept electrons, first and foremost from nicotinamide adenine dinucleotide (NADH), to become effusive reduced.

The reduced form of CoQ10 is able to give up electrons, as follows scavenging free radicals (20). The arbitrate of ubiquinol and ubiquinone is the univalently reduced ubisemiquinone which acts as a pro-oxidant to form $O2^\bullet$ and, consequently, H2O2. The main antioxidant role of CoQ10 is in inhibiting lipid peroxidation directly, and by interactions with α-tocopherol. Ubiquinol is able to give a hydrogen atom and therefore quenchperoxyl radicals, preventing lipid peroxidation chain reactions. CoQ10, acting as a pro-oxidant in all biological membranes has led to much denigration as regards the demanded antioxidant power of CoQ10 supplementation in humans (21). Nevertheless, lots of studies show antioxidant properties of CoQ10 in single cells, and benefit of CoQ10 supplementation in humans are attributed to its ability to preserve effective mitochondrial energy metabolism and so prevent mitochondrial dysfunction, before act as a direct cellular antioxidant. Indicating Co-enzyme Q10 is diminished $O2^{\bullet-}$ levels in hemi- nephrectomized

rat kidneys on a Co-enzyme Q10 supplemented diet, and increased kidney function compared with rat on a control regime (22-24). In aerobic situation, all biological systems are exposed to oxidative stress. The impressive mainstream of these free radicals are generally O2 radicals and other ROS. Oxidative stress can be pondered an imbalance in the ROS production/degradation ratio. In usual conditions, ROS such as superoxide anions radical, hydroxyl radical, and hydrogen peroxide are produced in cells throughout energy formation in mitochondria by reducing O2 during aerobic respiration. Mitochondria are considered the major source of reactive O2 spices. Molecular O2 is converted to the ROS, $O2^{\bullet-}$, and H2O2. Even if cellular H2O2 is stable in this type, it has the potential to interrelate with a variety of substrates to cause destruction, especially in the attendance of the ferrous iron, which causes to cleavage and formation of the most reactive and damaging of the ROS and the $OH^{\bullet}$ (34). In healthy metabolic cells, harmful production of H2O2 is countered by the catalyzing actions of mitochondrial or cystolic catalase or thiol peroxidases into water and O2. The electron transport chain consists of five multi enzyme complexes responsible for maintaining the mitochondrial membrane potential and adenosine triphosphate generation. Each of these complexes presents a site of ROS generation, though complexes I and III have been identified as the first sites of $O2^{\bullet-}$ generation. A certain correlation was found between serum uric acid and serum creatinine with impaired kidney function. While serum uric acid levels increasing can arise from purine metabolism, aging and decreased renal excretion, and have impairing systemic effects. Hyperuricemia is associate with an increased risk for development and progression of CKD. Preservation of uremic toxins promotes inflammation and oxidative stress, throughout priming the severe inflammatory polymorphonuclear and lymphocytes and also activating interleukin 1β and interleukin 8. Furthermore, uric acid synthesis can defend oxidative stress directly by the activity of xanthine oxidoreductase. This enzyme is synthesized as xanthine dehydrogenase, which can be converted to xanthine oxidase by calcium dependent proteolysis or alteration of cysteine residues. In doing so, the enzyme loses its ability to combine NADH by alteration in its catalytic site and, as a substitute for, transfers electrons from O2, thus generating O2– (25-27). The production of ROS is generally in balance with the accessibility and cellular localization of antioxidant enzymes such as superoxide dismutase, catalase and glutathione peroxidase. Mitochondria have their own lake of antioxidants to resist their generation of ROS. The role of oxidative stress in upstream transcriptional gene regulation is increasingly identified. Not only does this provide insight into the physiological role of oxidative stress, but existing regulatory systems that are possibly tending to dysregulation (28). Free radicals are chemical species which are highly reactive and when, they formed, they can react with another molecules to construct other free radicals or non-radical molecules. Therefore, a chain reaction of free radicals take place, leading to damaging biological systems and tissues (29).

Indicators of oxidative stress in chronic kidney disease

CKD, consisted of inflammation and fibrosis. Chronic inflammation is induced by infections, autoimmune disease, chemical drugs, and oxidative stress (30). Inflammation is imperative reason for the increased oxidative stress observed in patients with proceed renal disease, with factors such as, malnourishment, autonomic dysfunction, chronic volume excess being amid some factors concerned in the increased inflammatory state seen in renal injury. Activation of polymorphonuclear neutrophils is a well-recognized feature in CKD patients, with documented association between renal dysfunction and the different mediators and markers of inflammation for example C-reactive protein, interleukin-6, and tumor necrosis factor-α and fibrinogen, suggesting that CKD is a low-grade inflammatory process by itself (31). The inflammatory cells are cause of free radicals in the forms of reactive O2 and nitrogen species, while ROS are considered the most general. The main reactive O2 spices are hydroxyl radical, superoxide and hydrogen peroxide that able to destruct various structures and functional pathways in cells. In consequence, the occurrence of inflammatory cells is stimulated by cell injury caused by ROS producing a cycle of chronic injury that is complicated to break. Oxidative stress rises from alterations in the oxidation-decline balance of cells. Generally, ROS are countered by endogenous natural defenses known as antioxidants, and it is the lack of equilibrium between ROS and antioxidants which favors greater relative levels of ROS, hence giving rise to a state of oxidative stress (32-35). Interstitial fibrosis is the common feature of most diseases progressing to chronic kidney failure. Kidney fibrosis in aging, ischemia/reperfusion injury, and diabetes has been linked to excessive produce yielded of ROS, which is considered the major pathogenic pathway in these disorders. The ROS excess is associated to alterations in mitochondrial metabolism leading to cell damage fibrosis. Aging increased proportion of mutations in nuclear and mitochondrial DNA, advanced glycation end products (AGEs), and lipofuscin increased oxidative stress and consequent increased apoptosis. Ischemia/reperfusion injury in the kidney produces excess of ROS beyond this organ's scavenging capacity, causing cell damage, surplus of ROS has been associated with chronic allograft nephropathy after kidney transplantation (36). An ordinary feature of all these situations is the ROS overproduction, which principal to renal fibrosis and progressive chronic disease. Inflammation and oxidative stress go hand-in-hand in many tissues. Oxidative stress produces the production of inflammatory cytokines that will generate free radical production. One specific aldehyde is 4-hydroxynonenal, which is increasingly recognized as a mediator and marker of cellular dysfunction. Also renal fibrosis is the major determinant of CKD progression and typically results from chronic inflammation. Most

chronic fibrotic disorders have in common a persistent production of fibrogenic cytokines, growth factors, proteolytic, angiogenesis factors enzymes, and ROS. These conditions stimulate deposition of extracellular matrix that progressively destroys the organ's structural design and as a result its function. Recently, ROS have been related with kidney fibrosis in different diseases such as chronic allograft nephropathy following transplantation, and diabetic kidney disease. In addition, ROS have been shown to be an important mediator of the harmful effects of the rennin angiotensin aldosterone system in renal and vascular tissues (37,38). Previous studies have shown an important imbalance in pro-oxidant and antioxidant activities in patients with renal dysfunction. Oxidative stress has been found even in the first stages of CKD, as revealed through plasma 8-isoprostane levels. Moreover, oxidative stress increases the intensity of CKD proceed the level of glomerular filtration rate diminishes (39,40). Additionally, other markers of oxidative stress are malondialdehyde which oxidized serum albumin, and glutathione peroxidase.

Why oxidative stress increased in CKD?

Different mechanisms are explained its basic characteristics of renal patients such as diabetes, elderly and renal hypertension would influence them to rising levels of oxidative stress compared with the normal population. Kidney disease patients at end stage, with their nutritional limitation of fresh vegetables and fruits because of avoid hyperkaliemia, would a have lesser levels of vitamin C. Each hemodialysis session induces oxidative stress, with ROS being produced by dialysis membranes through the activation of polymorphonuclear neutrophils by cause of bio-incompatibility, and also relative loss of antioxidant vitamins during the dialysis itself (41,42). Renal dysfunction is often related with oxidative stress, as levels of different markers comprising plasma F_2-isoprostanes, malondialdehyde and advanced oxidation protein products are increased in patients with varying degrees of renal dysfunction, including patients with end-stage renal failure too (43). An antioxidant defense mechanisms such as manganese superoxide dismutase and copper zinc superoxide dismutase have also been shown to be down regulated in patients with kidney dysfunction (44). Myeloperoxidase is generated in retort to activation of polymorphonuclear neutrophils, and this must trigger ROS activation and inactivation of nitrogen oxide. Serum myeloperoxidase was found to be correlated with markers of both inflammation and mortality in hemodialysis patients (45).

Conclusion

Oxidative stress has been implicated in various pathological systems that are prevalent in CKD. Chronic inflammation is provoked by oxidative stress and chronic degenerative diseases. The inflammatory cells are a source of free radicals in the forms of reactive O2 and nitrogen species, although ROS are considered as the most responsible factor in CKD.

Authors' contribution

HN and SBR wrote the paper equally.

Conflicts of interest

The authors declared no competing interests.

Ethical considerations

The authors of this manuscript declare that they all have followed the ethical requirements for this communication. Also, Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors.

Funding/Support

None.

References

1. Dounousi E, Papavasiliou E, Makedou A, Ioannou K, Katopodis KP, Tselepis A, et al. Oxidative stress is progressively enhanced with advancing stages of CKD. Am J Kidney Dis. 2006;48:752-60.
2. Small DM, Coombes JS, Bennett N, Johnson DW, Gobe GC. Oxidative stress, anti-oxidant therapies and chronic kidney disease. Nephrology. 2012;17:311-21
3. Block G, Dietrich M, Norkus EP, Morrow JD, Hudes M, Caan B, et al. Factors associated with oxidative stress in human populations. Am J Epidemiol. 2002;156:274-85
4. Boaz M, Smetana S, Weinstein T, Matas Z, Gafter U, Iaina A, et al. Secondary prevention with antioxidants of cardiovascular disease in endstage renal disease (SPACE): randomised placebo-controlled trial. Lancet. 2000;356:1213-8
5. Erdoğan C, Unlüçerçi Y, Türkmen A, Kuru A, Cetin O, Bekpinar S. The evaluation of oxidative stress in patients with chronic renal failure. Clinica Chimica Acta. 2002;322:157-61.
6. Rodrigo R, Rivera G. Renal damage mediated by oxidative stress: a hypothesis of protective effects of red wine. Free Radical Bio Med. 2002;33:409-22.
7. Ward RA, Ouseph R, McLeish KR. Effects of high-flux hemodialysis on oxidant stress. Kidney Int. 2003;63(1):353-9.
8. Dahwa R, Fassett RG, Wang Z, Briskey D, Mallard AR, Coombes JS. Variability of oxidative stress biomarkers in hemodialysis patients. Biomarkers 2014;19;154-8.
9. Tucker PS, Dalbo VJ, Han T, Kingsley MI. Clinical and research markers of oxidative stress in chronic kidney disease. Biomarkers. 2013;18:103-15.
10. Ichikawa I, Kiyama S, Yoshioka T. Renal antioxidant enzymes: their regulation and function. Kidney Int. 1994;45:1-9.
11. Galle J. Oxidative stress in chronic renal failure. Nephrol Dial Transplant. 2001;16:2135-7.
12. Kao MP, Ang DS, Pall A, Struthers AD. Oxidative stress in renal dysfunction: mechanisms, clinical sequelae and therapeutic options. J Hum Hypertens. 2010;24:1-8.
13. Choksi KB, Nuss JE, Boylston WH, Rabek JP, Papaconstantinou J. Age-related increases in oxidatively damaged proteins of mouse kidney mitochondrial electron transport chain complexes. Free Radic Biol Med. 2007;43:1423–38.
14. Shackelford RE, Kaufmann WK, Paules RS. Oxidative stress and cell cycle checkpoint function. Free Radic Biol Med. 2000;28:1387-404.
15. Pedzik A, Paradowski M. Oxidative stress in nephrology. Pol Merkur Lekarski. 2010;28:56-60.
16. Lizarraga KJ, Nayer A. Dengue-associated kidney disease.J Nephropathol. 2014;3:57-62.
17. Gagnon AL, Desai T. Dermatological diseases in patients with chronic kidney disease. J Nephropathol. 2013;2:104-9.
18. Gupta K, SahniN. Dietary antioxidents and oxidative stress in predialysis chronic kidney disease patients. J Nephropathol. 2012;1:134-42.

19. Carr AC, McCall MR, Frei B. Oxidation of LDL by myeloperoxidase and reactive nitrogen species—reaction pathways and antioxidant protection. Arterioscler Thromb Vasc Biol. 2000;20:1716-23.
20. Frei B, Kim MC, Ames BN. Ubiquinol-10 is an effective lipid-soluble antioxidant at physiological concentrations. Proc Natl AcadSci U S A. 1990;87:4879-83.
21. Stoyanovsky DA, Osipov AN, Quinn PJ, Kagan VE. Ubiquinone-dependent recycling of vitamin E radicals by superoxide. Arch Biochem Biophys. 1995;323:343-51.
22. Jun M, Venkataraman V, Razavian M, Cooper B, Zoungas S, Ninomiya T, et al. Antioxidants for chronic kidney disease. Cochrane Database Syst Rev. 2012;10:CD008176.
23. James AM, Smith RA, Murphy MP. Antioxidant and prooxidant properties of mitochondrial Coenzyme Q. Arch Biochem Biophys. 2004;423:47-56.
24. Linnane AW, Kios M, Vitetta L. Coenzyme Q(10) - its role as a prooxidant in the formation of superoxide anion/hydrogen peroxide and the regulation of the metabolome. Mitochondrion. 2007;7:51-61.
25. Nishino T, Okamoto K, Kawaguchi Y, Hori H, Matsumura T, Eger BT, et al. Mechanism of the conversion of xanthine dehydrogenase to xanthine oxidase: identification of the two cysteine disulfide bonds and crystal structure of a non-convertible rat liver xanthine dehydrogenase mutant. J Biol Chem. 2005;280:24888-94.
26. Martinon F, Petrilli V, Mayor A, Tardivel A, Tschopp J. Gout-associated uric acid crystals activate the NALP3 inflammasome. Nature. 2006;440:237-41.
27. Chen YC, Su CT, Wang ST, Lee HD, Lin SY. A preliminary investigation of the asso- ciation between serum uric acid and impaired renal function. Chang Gung Med J. 2009;32:66-71.
28. Pieczenik SR, Neustadt J. Mitochondrial dysfunction and molecular pathways of disease. Exp Mol Pathol. 2007;83:84-92.
29. Ozbek E. Induction of Oxidative Stress in Kidney. Int J Nephrol. 2012;2012:465897.
30. Whaley-Connell A, Pavey BS, Chaudhary K, Saab G, Sowers JR. Renin-angiotensinaldosterone system intervention in the cardiometabolic syndrome and cardio-renal protection. Ther Adv Cardiovasc Dis. 2007;1:27-35.
31. Zhuang S, Yan Y, Daubert RA, Han J, Schnellmann RG. ERK promotes hydrogen per- oxide-induced apoptosis through caspase-3 activation and inhibition of Akt in renal epithelial cells. Am J Physiol Renal Physiol. 2007;292:440-7.
32. Pias EK, Aw TY. Apoptosis in mitotic competent undifferentiated cells is induced by cellular redox imbalance independent of reactive oxygen species production. FASEB J. 2002;16:781-90.
33. Maia L, Duarte RO, Ponces-Freire A, Moura JJ, Mira L. NADH oxidase activity of rat and human liver xanthine oxidoreductase:potential role in superoxide production. J Biol Inorg Chem. 2007;12:777-87.
34. Miller NJ, RiceEvans CA. Spectrophotometric determination of antioxidant activity. Redox Report. 1996;2:161-71.
35. Small D, Gobe G. Oxidative stress and antioxidant therapy in chronic kidney and cardiovascular disease. Agric Biol Sci. 2013.
36. Souza G, Karina N. Superoxide overproduction and kidney fibrosis: a new animal model**.** Einstein (São Paulo). 2015;13:79-88.
37. Djamali A, Reese S, Yracheta J, Oberley T, Hullett D, Becker B. Epithelial-to-mesenchymal transition and oxidative stress in chronic allograft nephropathy. Am J Transplant. 2005;5:500-9.
38. Fujita H, Fujishima H, Chida S, Takahashi K, Qi Z, Kanetsuna Y, et al. Reduction of renal superoxide dismutase in progressive diabetic nephropathy. J Am Soc Nephrol. 2009;20:1303-13.
39. Tepel M, Echelmeyer M, Orie NN, Zidek W. Increased intracellular reactive oxygen species in patients with end-stage renal failure:effect of hemodialysis. Kidney Int. 2000;58:867–872.
40. Dounousi E, Papavasiliou E, Makedou A, Ioannou K, Katopodis KP, Tselepis A, et al. Oxidative stress is progressively enhanced with advancing stages of CKD. Am J Kidney Dis. 2006;48:752–760.
41. Peuchant E, Carbonneau MA, Dubourg L, Thomas MJ, Perromat A, Vallot C, et al. Lipoperoxidation in plasma and red blood cells of patients undergoing haemodialysis: vitamins A, E, and iron status. Free Radic Biol Med. 1994;16:339-46.
42. Jackson P, Loughrey CM, Lightbody JH, McNamee PT, Young IS. Effect of hemodialysis on total antioxidant capacity and serum antioxidants in patients with chronic renal failure. Clin Chem. 1995;41:1135-8.
43. Lahera V, Goicoechea M, de Vinuesa SG, Oubiña P, Cachofeiro V, Gómez-Campderá F, et al. Oxidative stress in uremia:the role of anemia correction. J Am Soc Nephrol. 2006;17:S174-7.
44. Cachofeiro V, Goicochea M, de Vinuesa SG, Oubina P, Lahera V, Luno J. Oxidative stress and inflammation, a link between chronic kidney disease and cardiovascular disease. Kidney Int Suppl. 2008;(111):S4-9.
45. Kalantar-Zadeh K, Brennan ML, Hazen SL. Serum myeloperoxidase and mortality in maintenance hemodialysis patients. Am J Kidney Dis. 2006;48:59-68.