



Administration of antioxidants in chronic kidney disease

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Chronic kidney disease has been a health problem in the past, however, today has become a global health threat. The number of chronic renal failure patients is increasing and more than one million people in the end-stage of chronic renal failure are dying annually (1). These patients experience various problems and creating a change in their life is very useful. Fatigue is a common problem in dialysis patients. Fatigue is the most important complication of vitamin C deficiency. Vitamin C is a well-known antioxidant (2).

Hemodialysis process decreased the necessary antioxidants and chronic renal failure associated with stress oxidative (3). Excessive production of free radicals is a state that called stress oxidative which is one of the reasons for vascular lesions (4). Free radicals affect on carbohydrates, protein, fat and DNA (5,6). Free radicals cause lipid peroxidation and degradation of molecules and cellular structures (endothelial cells and red blood cells) (7). Some studies have indicated to the increasing of free radicals caused by dialysis (8-10). Small proteins such as immunoglobulin G and complements attached to the dialyzer membrane and activate granulocytes which resulting in production of free radicals (11,12).

One of the main causes of death in chronic dialysis patients is cardiovascular events. Increasing of peroxidation products and also antioxidant depletion are effective actors of atherosclerosis in patients who undergoing hemodialysis (13).

Chronic kidney disease associated with high incidence

of cardiovascular disease which is common cause of mortality and also imposes high costs (5,6). Chronic renal insufficiency even if you eliminate the initial cause progress to end-stage renal disease, because the initial injury eventually leads to scarring and loss of renal nephrons and resulting in end-stage kidney disease (7-14).

Various investigations mentioned the positive effects of antioxidants in chronic diseases, cardiovascular diseases, hypertension and kidney disease, although some studies have been reported no beneficial effect on reducing mortality and cardiovascular disease (15-21).

Antioxidants are in foods and some studies mentioned to their beneficial role in chronic kidney disease or hypertension (22,23).

This article, reviews some articles regarding the role of antioxidants in hemodialysis patients.

We searched scientific sources and article index databases including PubMed and Scopus by key words including antioxidants, antioxidant therapy in hemodialysis patients, hemodialysis and antioxidants. From the existing articles we reviewed 48 articles.

In study by Santana-Santos *et al.* (24), administration of N-acetylcysteine was effective in reducing of acute kidney injury in patients with kidney disease who underwent CABG surgery and mentioned that prevented from oxidative stress.

However, other study implied that it had not any effect in acute renal injury and chronic kidney disease (25).

Tbahrity *et al.* (26), in their study detected the antioxidant

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enzyme activities change under the influence of renal dysfunction and dialysis.

In another study prescription of an antioxidant, alpha lipoic acid has been useful for diabetic and dialysis patients, while, the most common cause of reaching to the end-stage renal disease in the most communities is diabetes (27).

However, various studies have been reported conflicting results. In a study, antioxidants have been effective in patients with non-dialysis kidney diseases but were not effective in dialysis patients (28-30). Additionally, the impact of anti-oxidants to reduce mortality resulting from cardiovascular diseases has been of much interest (31-33). Some studies reported that cytokines level is higher in hemodialysis patients and have important pathological role in oxidative stress, progression of diabetes complications and increasing the oxidative stress intensity after hemodialysis and emphasized to antioxidants benefits in diabetic and end-stage renal disease patients who are under dialysis (34-36).

It is possible that, reducing the activity of antioxidant enzyme in red blood cells and increasing of lipid peroxidation in hemodialysis patients play a role in progression of cardiovascular disease and antioxidants are effective to reduce cardiovascular events (37-39).

Moreover, some studies point out that the use of dialyzer with antioxidant membrane, taking vitamin D and iron supplements and prescribed antioxidants such as vitamin E and C increase the quality of dialysis and reduce the incidence of oxidative stress and some complications (40-45). Likewise, the effect of low doses of vitamin C on the inflammatory process and reducing of fatigue in hemodialysis patients was emphasized in recent studies (46-48).

According to these findings more studies are necessary to exactly find the effects of antioxidants in hemodialysis patients and reducing complications from dialysis and kidney disease. We recommend to assess their effects and determining a comprehensive therapeutic protocol for antioxidants therapy in hemodialysis patients.

Conclusion

Majority of studies indicated that, antioxidants are helpful in hemodialysis patients, reducing the risk of cardiovascular events and increasing the quality of dialysis.

Authors' contributions

All authors contributed to the manuscript equally.

Conflict of interests

The authors declared no competing interests.

Ethical considerations

Ethical issues (including plagiarism, misconduct, data fabrication, falsification, double publication or submission, redundancy) have been completely observed by the authors.

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References

- Hamer RA, El Nahas AM. The burden of chronic kidney disease. *BMJ* 2006; 323: 563-4.
- Singer R, Rhodes H, Chin G, Kulkarni H, Ferrari P. Highprevalence of ascorbate deficiency in an Australianperitoneal dialysis population. *Nephrology* 2008; 13: 17-22.
- Kohen R, Chevion S, Scharzt R, Berry EM. Evaluation of the total low molecular weight antioxidant activity of plasma in health and diseases: a new approach. *Cell Pharmacol* 1996; 3: 355-9.
- Loughrey CM, Young IS, Lightbody JH, McNamee PT, McNamee PT, Trimble ER. Oxidative stress in haemodialysis. *QJM* 1994; 87(11): 679-83.
- Bast A, Haenen RM, Cees JA. Oxidants and antioxidants: state of the art. *Am J Med* 1991; 91(3c): 25-13s.
- Stocks J, Kemp M, Dormandy TL. Increased susceptibility of red blood cell lipids to autoxidation in haemolytic states. *Lancet* 1971; 6(7693): 266 -70.
- Bery EM, Kohen R. Is the biological antioxidant system integrated and regulated? *Med Hypotheses* 1995; 53: 397-401.
- Hussain SA, Hassan MQ, Zeki MA. Antioxidant profile human erythrocytes after kidney transplantation. *Clin Biochem* 1995; 28(16): 607-10.
- Dasgupta A, Hussain S, Ahmad S. Increased lipid peroxidation in patients on maintenance hemodialysis. *Nephron* 1992; 60(1): 56-9.
- Sanaka T, Higuchi C, Shinobe T, Nishimura H, Omata M, Nihei H, et al. Lipid peroxidation as an indicator of biocompatibility in haemodialysis. *Nephrol Dial Transplant* 1995; 10(3): 34-8.
- Luciak M, Trznadel K. Freeoxygen species metabolism during hemodialysis in the different membranes. *Nephrol Dial Transplant* 1991; 6(3): 66-70.
- 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* 1991; 16(3): 339-46.
- 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(8 Pt 1): 1135-8.
- Dincer Y, Sekercioglu N, Pekpak M, Gunes KN, Akcay T. Assessment of DNA oxidation and antioxidant activity in hypertensive patients with chronic kidney disease. *Ren Fail* 2008; 30(10): 1006-11.
- Atamer A, Kocyigit Y, Ecder SA, Selekt S, Ilhan N, Ecder T, et al. Effect of oxidative stress on antioxidant enzyme activities, homocysteine and lipoproteins in chronic kidney disease. *J Nephrol* 2008; 21(6): 924-30.
- Konta T. Renal disease-related clinical examination in a cohort study. *Rinsho Byori* 2014; 62(2): 190-6.
- Himmelfarb J, Ikizler TA, Ellis C, Wu P, Shintani A, Dalal S, et al. Provision of antioxidant therapy in hemodialysis (PATH): a randomized clinical trial. *J Am Soc Nephrol* 2014; 25(3): 623-33.
- Gómez-Guzmán M, Jiménez R, Romero M, Sánchez M, Zarzuelo MJ, Gómez-Morales M, et al. Chronic hydroxychloroquine improves endothelial dysfunction and protects kidney in a mouse model of systemic lupus erythematosus. *Hypertension* 2014; 64(2): 330-7.

19. Prats M, Font R, García C, Muñoz-Cortés M, Cabré C, Jarrod M, et al. Oxidative stress markers in predicting response to treatment with ferric carboxymaltose in nondialysis chronic kidney disease patients. *Clin Nephrol* 2014; 81(6): 419-26.
20. Saddadi F, Alatab S, Pasha F, Ganji MR, Soleimani T. The effect of treatment with N-acetylcysteine on the serum levels of C-reactive protein and interleukin-6 in patients on hemodialysis. *Saudi J Kidney Dis Transpl* 2014; 25(1): 66-72.
21. Che R, Yuan Y, Huang S, Zhang A. Mitochondrial dysfunction in the pathophysiology of renal diseases. *Am J Physiol Renal Physiol* 2014; 306(4): F367-78.
22. Baradaran A, Nasri H, Rafieian-Kopaei M. Oxidative stress and hypertension: Possibility of hypertension therapy with antioxidants. *J Res Med Sci* 2014; 19(4): 358-67.
23. Sahni N, Gupta KL, Rana SV, Prasad R, Bhalla AK. Intake of antioxidants and their status in chronic kidney disease patients. *J Ren Nutr* 2012; 22(4): 389-99.
24. Andreucci M, Faga T, Pisani A, Sabbatini M, Russo D, Michael A. Prevention of Contrast-Induced Nephropathy through a Knowledge of Its Pathogenesis and Risk Factors. *Scientific World Journal* 2014; 2014: 823169.
25. Grebe SO, Langenbeck M, Schaper A, Berndt S, Aresmouk D, Herget-Rosenthal S. Antioxidant treatment and outcome of cortinariorellanus poisoning: a case series. *Ren Fail* 2013; 35(10): 1436-9.
26. Tbahriti HF, Kaddous A, Bouchenak M, Mekki K. Effect of different stages of chronic kidney disease and renal replacement therapies on oxidant-antioxidant balance in uremic patients. *Biochem Res Int* 2013; 2013: 358985.
27. Safa J, Ardalan MR, Rezazadehsaatlou M, Mesgari M, Mahdavi R, Jadid MP. Effects of alpha lipoic acid supplementation on serum levels of IL-8 and TNF- α in patient with ESRD undergoing hemodialysis. *Int Urol Nephrol* 2014; 46(8): 1633-8.
28. Shah SV, Baliga R, Rajapurkar M, Fonseca VA. Oxidants in chronic kidney disease. *J Am Soc Nephrol* 2007; 18(1): 16-28.
29. Wilcox CS, Mendonca M, Kong Y, Brown M, Land Luo Z. Novel catalytic antioxidant for CKD and hypertension. *J Nephrol Therapeutic* 2013; 3: 5.
30. Banach M. Lipid and Blood Pressure Meta-Analysis Collaboration Group. Statins in patients with chronic kidney disease - an attempt at recommendations. *Curr Med Res Opin* 2013; 29(11): 1419-22.
31. 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.
32. Kennedy DJ, Tang WH, Fan Y, Wu Y, Mann S, Pepoy M, et al. Diminished antioxidant activity of high-density lipoprotein-associated proteins in chronic kidney disease. *J Am Heart Assoc* 2013; 2(2): e000104.
33. Luciak M. Antioxidants in the treatment of patients with renal failure. *Rocz Akad Med Bialymst* 2004; 49: 157-61.
34. Lee HB, Seo JY, Yu MR, Uh ST, Ha H. Radical approach to diabetic nephropathy. *Kidney Int Suppl* 2007; 106: S67-70.
35. Ghobrial EE, Mahfouz NN, Fathy GA, Elwakkad AA, Sebaii HM. Oxidative stress in Egyptian hemodialysis children. *Iran J Kidney Dis* 2013; 7(6): 485-91.
36. Hemmati M, Kadkhodae M, Zahmatkesh M, Mahdavi-Mazde M, Ghaznavi R, Mirershadi F. Blood antioxidant levels and alterations of serum calcium and pH in hemodialysis patients. *Tehran Univ Med J* 2008; 66(1): 12-7.
37. Marjani AJ, Mojerloo M, Mansourian AR, Rabiei MR. Effect of hemodialysis on plasma Lipid peroxidation and erythrocyte antioxidant enzyme in Gorgan. *J Gorgan Uni Med Sci* 2004; 6(1): 83-9.
38. Sarnak MJ, Levey AS, Schoolwerth AC, Coresh J, Cullerton B, Hamm LL, et al. Kidney Disease as a Risk Factor for Development of Cardiovascular Disease, A Statement From the American Heart Association Councils on Kidney in Cardiovascular Disease, High Blood Pressure Research, Clinical Cardiology, and Epidemiology and Prevention. *Circulation* 2003; 108(17): 2154-69.
39. Solati M, Etemadi A, Pezeshk P, Rahbar K, Azizi F. Lipids, apolipoproteins, lipid oxidation and paraoxonase enzyme activity in diabetic and non-diabetic end stage renal disease patients. *Iranian Journal of Endocrinology and Metabolism* 2003; 5(1): 27-32.
40. Chen HC, Lin HC, Chen HH, Mai FD, Liu YC, Lin CM, et al. Innovative strategy with potential to increase hemodialysis efficiency and safety. *Sci Rep* 2014; 4: 4425.
41. Kuo KL, Tarng DC. Oxidative Stress in Chronic Kidney Disease. *Adaptive Medicine* 2010; 2(2): 87-94.
42. Rojas-Rivera J, Ortiz A, Egido J. Antioxidants in Kidney Diseases: The Impact of Bardoxolone Methyl. *Int J Nephrol* 2012; 2012: 321714.
43. Santana-Santos E, Gowdak LH, Gaiotto FA, Puig LB, Hajjar LA, Zeferino SP, et al. High dose of N-acetylcystein prevents acute kidney injury in chronic kidney disease patients undergoing myocardial revascularization. *Ann Thorac Surg* 2014; 97(5): 1617-23.
44. Webster AC. Antioxidants for chronic kidney disease. *Nephrology* 2013; 18: 576-8.
45. Dincer Y, Sekercioglu N, Pekpak M, Gunes KN, Akcay T. Assessment of DNA oxidation and antioxidant activity in hypertensive patients with chronic kidney disease. *Ren Fail* 2008; 30(10): 1006-11.
46. Farmahini B, Sajadi A, Esmailpoor S, Dormanesh B, Zare M. The Effect of Oral Vitamin C on Fatigue in Hemodialysis Patients in Selected Hospitals of the Army University of Medical Sciences in 2009. *Ann Mil Health Sci Res* 2009; 7(3): 163-8.
47. Zhang K, Li Y, Cheng X, Liu L, Bai W, Guo W, et al. Cross-over study of influence of oral vitamin C supplementation on inflammatory status in maintenance hemodialysis patients. *BMC Nephrol* 2013; 14: 252.
48. Tamadon MR, Baradaran A, Rafieian-Kopaei M. Antioxidant and kidney protection; differential impacts of single and whole natural antioxidants. *J Renal Inj Prev* 2013; 3(2): 41-2.

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