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Paraoxonase enzyme activity and dyslipidemia in chronic kidney disease patients

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Recent studies have focused on decrease activity of paraoxonase (PON) in chronic kidney disease (CKD) patients. Paraoxonase (PON) enzyme is altered in many diseases and is related to lipid abnormalities and antioxidant activities. Patients with CKD often have lipid abnormalities. Lipid abnormalities in CKD patients increase the risk of cardiovascular diseases in CKD patients. In CKD patients, PON activity and its mechanism have developed a new idea for treatment options to reduce the risk of cardiovascular disease. This review article is focused on the role of PON in dyslipidemia in the CKD patients.

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Dyslipidemia is a common abnormality among chronic kidney disease (CKD) patients and is responsible for a large proportion of mortality and morbidity in these patients (1). Paraoxonase (PON) enzyme is altered in many diseases and is related to lipid abnormalities and antioxidant activities. Patients with CKD often have lipid abnormalities. CKD is associated with dysregulation in high density lipoprotein (HDL) and triglyceride metabolism(1,2). Therefore in the plasma of these patients, the level of triglyceride-rich lipoproteins is increased considerably. Moreover, some alterations occurred

in composition of these lipoproteins (1,2). Lipid abnormalities in CKD patients increase the risk of cardiovascular diseases in CKD patients (1,2). In addition to increase the risk of cardiovascular diseases in CKD, dyslipidemia causes the development of renal diseases. Some studies have reported the association of glomerular and tubule-interstitial injuries and dyslipidemia (2). Therefore, the treatment of dyslipidemia in CKD is indicated with lipid lowering drugs such as statins (3). PONs are a group of HDL related enzymes with antioxidative activities. These enzymes are including PON1, PON2, and PON3.

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Among them PON2 and PON3 are expressed primarily in liver and then is secreted into serum. While PON2 is expressed and remain in cells (4). In this regard, PON activity is related to diabetes, thyroid diseases, metabolic syndromes, renal failure and increased age (4 -6).

PON activity decreases in patients with hyperthyroidism, hypothyroidism, and also subclinical forms of thyroid diseases, and it is shown that the treatment of thyroid abnormalities can improve the enzyme activity in these patients (6-9). Also some studies have found an association between some PON gen polymorphisms with metabolic syndrome (10,11). PON activity is altered by lipoproteins and their metabolism, biologic macromolecules, some medications, nutritional factors and life style (9,10). Low HDL levels is one of the characteristics in metabolic syndrome. At least in one part of the antioxidant activity, this enzyme is low in metabolic syndrome. PON activity prevents LDL oxidation, atherosclerosis and cardiovascular diseases(9-11). Recent studies have focused on decreased PON1 activity in CKD which is associated with lower HDL level and higher cardiovascular diseases in these patients. It is logical that maintaining or enhancing PON1 activity in CKD may decrease the rate of cardiovascular events. However, there are limited studies to test this hypothesis and future studies can focus on this issue (8-12). It is well documented that patients with CKD who were under conservative or hemodialysis treatment have reduced level of PON1 activity. This may be responsible for increased risk of cardiovascular events in these patients (10-13). Despite of these findings, various studies have shown that in CKD, lower PON1 activity is not related to the low HDL-c level and increased risk of the cardiovascular diseases morbidity in CKD which is due to low HDL-c may be independent of PON1 activity (12-14). Serum PON activity in CKD is reduced and it is more obvious in patients under

hemodialysis. This reduction is in correlation with oxidative stress markers (13-15). Furthermore, studies in children have reported an increased oxidative stress and decreased antioxidants and serum PON level in CKD (12-16). Serum PON1 level is associated with hyperlipidemia in patients with renal failure but it seems that serum PON level and HDL concentration are not the only determining factors for development of hyperlipidemia (14-17). Hemodialysis can lower the acrolein level which is a very reactive aldehyde. Lowering acrolein level in CKD patients after hemodialysis is in association with increase in PON activity. These findings may explain low PON1 activity in smokers and renal failure individuals (13-18). Also, some studies have suggested that renal transplantation could decrease the risk of premature vascular aging by increase in PON activity and its anti-atherogenic properties (15-19). Treatment of CKD can increase PON activity and lower the risk of cardiovascular diseases in these patients. PON has an important role in dyslipidemia in CKD and is related to the cardiovascular disease and atherosclerosis. New findings in this area are in favor of the decrease in the risk of cardiovascular event by maintaining or enhancing PON activity in CKD patients. However, further studies are needed to reach new treatment options for dyslipidemia in CKD patients.

Authors' contributions

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Conflict of interest

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