Role of High-density Lipoprotein Cholesterol in Renovascular Disease Treatment

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Ischemic renal or renovascular disease is a reduction in glomerular filtration rate (GFR) and loss of renal parenchyma, caused by renal artery stenosis. Ischemic renal disease presents itself in the setting of extrarenal arteriosclerotic vascular disease, endothelial dysfunction, and also azotemia in older patients. Atherosclerotic renal artery disease is common in individuals with coronary artery disease and aortic and peripheral vascular disease.[1] Risk factors for ischemic nephropathy are the same as those for coronary artery disease, so it seems that patients with renovascular disease die because of cardiovascular complications more than the progress to end-stage renal disease.[2]

In patients with atherosclerosis, the initiator of endothelial injury is not clear but hypertension, dyslipidemia, diabetes mellitus, cigarette smoking, viral infection, immune injury, and increased homocysteine levels may contribute to endothelial injury. Endothelial dysfunction is implicated in lesion creation by the support of both the early and late mechanisms of atherosclerosis including up-regulation of adhesion molecules, increasing chemokine secretion, leukocyte adherence and cell permeability, enhanced low-density lipoprotein cholesterol oxidation, platelet activation, and vascular smooth muscle cell proliferation and migration. Nitric oxide production is diminished, and an imbalance in the role of endothelium-derived relaxing factor and contracting factor would appear, corresponding to the endothelium actions moved toward reduced vasodilation, a proinflammatory state with prothrombic properties.[3-5]

Reactive oxygen species (ROS) are produced at inflammation and injury sites. When ROS concentration growth interacts with nitric oxide (NO), it decreases its bioavailability and results in formation of the pro-oxidant peroxynitrite. Lessening of NO activity dominates vasopressors activity and leads to vasoconstriction and GFR decrease.[2,3] On the other hand, cholesterol levels even in the normal range, may be linked inversely to endothelium-dependent vasodilation and lowering its levels may progress the production and release of endothelium-dependent NO and endothelial function.[3,6] Different studies show that in addition to the cholesterol-lowering effect, statins can also stimulate endothelial NO synthase activity and changing the balance toward vasodilation.[7-10] Also some findings suggest that abnormal high-density lipoprotein cholesterol (HDLC) function and capacity can increase risk of cardiovascular disease in patients with end-stage renal disease and patients on chronic hemodialysis.[11]

High-density lipoprotein cholesterol has an anti-atherosclerotic and atheroprotective property which acts by reverse cholesterol transport and its anti-inflammatory and antioxidant effects.[12-14] Therefore, in the artery wall, the critical step to leukocyte infiltration and ROS production will be inhibited. High-density lipoprotein cholesterol stops production of monocyte chemo-attractant protein-1 and inhibits the expression of endothelial adhesion molecules such as vascular cell adhesion molecule-1 and intercellular adhesion molecule-1. It is linked with some anti-oxidant enzymes, such as paraoxonase, glutathione peroxidase, lecithin cholesterol acyltransferase, and platelet-activating factor acetylhydrolase, and transfers oxidized lipids for clearing by the liver.[12] A recent study

has been shown that each 1 mg/dL increase in HDLC results in 2% to 3% decrease in coronary artery disease incidence.[15] Thus, because HDLC plays a very important role in the prevention of atherosclerosis progression and abnormal capacity of HDLC mediates cholesterol efflux, we can explain the restricted effect of statins alone in reducing atherosclerosis events and as mentioned in the article by Yasmeen and colleagues published in this issue of the *Iranian Journal of Kidney Diseases*.[16-18] The decrease in total cholesterol or increase in HDLC level with some available medications, such as niacin, when combined with statins, could provide better results and improves endothelial function in renovascular disease.

CONFLICT OF INTEREST

None declared.

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