Lipids and Renal Disease

Anita Shah, M.D.[a]; *Juan Jose Olivero,* M.D.[b]

[a]BAYLOR COLLEGE OF MEDICINE, HOUSTON, TEXAS; [b]HOUSTON METHODIST HOSPITAL, HOUSTON, TEXAS

The column in this issue is supplied by Anita Shah, M.D., and Juan Jose Olivero, M.D. Dr. Shah is a first-year nephrology fellow at Baylor College of Medicine in Houston, Texas. She earned her medical degree from The University of Texas Medical Branch at Galveston and completed an internal medicine residency at Houston Methodist Hospital. Dr. Olivero is a nephrologist at Houston Methodist Hospital and a member of the hospital's Nephrology Training Program. He obtained his medical degree from the University of San Carlos School of Medicine in Guatemala, Central America, and completed his residency and nephrology fellowship at Baylor College of Medicine in Houston, Texas.

The management of hyperlipidemia in those without renal dysfunction is based on multiple factors, including age, low-density lipoprotein (LDL) cholesterol levels, the presence of diabetes mellitus, a history of cardiovascular disease (CVD), and the 10-year risk of atherosclerotic cardiovascular disease (ASCVD).[1] However, primary and secondary prevention of CVD in patients with chronic kidney disease (CKD) and end-stage renal disease (ESRD) differs from that of the general population. Multiple trials and meta-analyses have been done to determine how aggressively hyperlipidemia should be treated to reduce morbidity and mortality in this unique population. The following are points to remember when treating hyperlipidemia in patients with CKD and ESRD.

- Hypertriglyceridemia is the most common dyslipidemia in patients with CKD who require hemodialysis, whereas high LDL cholesterol is more commonly seen in those requiring peritoneal dialysis or who have nephrotic syndrome.[2]
- Hypertriglyceridemia in CKD is likely due to decreased lipoprotein lipase (LPL) activity, leading to less catabolism of chylomicrons and very low-density lipoproteins (VLDL). Secondary hyperparathyroidism also contributes to lowered LPL synthesis.[3,4]
- In nephrotic syndrome, hypoalbuminemia results in hepatic overproduction of lipoproteins containing apolipoprotein B and their impaired catabolism, which leads to hyperlipidemia.[3,5]
- According to the 2011 Study of Heart and Renal Protection (SHARP) trial, recommendations vary regarding statin initiation for primary prevention in patients with CKD who do not require dialysis and have no CVD risk factors. Some clinicians prescribe statins for all patients with an eGFR < 60 mL/min/1.73 m^2 while others will initiate only if the patient's 10-year ASCVD risk score is > 7.5%.[6]
- The SHARP study illustrated a lower composite outcome of coronary death, myocardial infarction, stroke, and revascularization procedures at 5 years in patients with CKD who underwent dialysis and received simvastatin and ezetimibe versus placebo. However, there was no difference in all-cause mortality between the groups.[6]
- Based on a meta-analysis of more than 50,000 patients, it is recommended that a statin be initiated for secondary prevention in those with CKD who do not require dialysis but have cardiovascular risk factors such as diabetes mellitus, coronary artery disease (CAD), history of ischemic stroke, transient ischemic attack (TIA), or peripheral arterial disease.[7]
- In contrast, the Die Deutsche Diabetes Dialyse (4-D) trial showed no significant effect of atorvastatin on the primary composite outcome of cardiovascular death, nonfatal myocardial infarction, and stroke in patients on hemodialysis with type II diabetes mellitus and elevated LDL cholesterol at 4 years.[8] However, there was a significant reduction in cardiac events in the statin group.[8] The AURORA (A Study to Evaluate the Use of Rosuvastatin in Subjects on Regular Hemodialysis: An Assessment of Survival and Cardiovascular Events) trial showed similar findings.[9]
- For hyperlipidemia and hypertriglyceridemia in nephrotic syndrome, treatment of the underlying disease is the main form of management. Adjunctive treatments include diet modification, statins, bile acid sequestrants, and fibrates.[5]
- Fenofibrates are commonly avoided in patients with CKD but may be indicated in uncontrolled hypertriglyceridemia. Of note, fenofibrates can cause a reversible increase in serum creatinine and decrease in estimated glomerular filtration rate that resolves upon medication discontinuation. The etiology of this occurrence is not currently known.[10,11]
- Based on these studies, the Kidney Disease Improving Global Outcomes (KDIGO) organization published lipid management guidelines in 2013 recommending statins for all patients with CKD who do not require dialysis and are at least 50 years of age. For adults 18 to 49 years of age who have CKD and do not require dialysis or kidney transplantation, statins are recommended if there is a history of coronary artery disease, diabetes mellitus, stroke, or an ASCVD risk > 10%. Statin

initiation is not recommended for patients starting dialysis who are not currently on a statin; however, KDIGO supports continuing a statin if the patient is already taking one prior to starting dialysis.[10]

REFERENCES

1. Stone NJ, Robinson JG, Lichtenstein AH, et al; American College of Cardiology/American Heart Association Task Force on Practice Guidelines. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. Circulation. 2014 Jun 24;129(25 Suppl 2):S1-35.

2. Massy ZA, de Zeeuw D. LDL cholesterol in CKD–to treat or not to treat? Kidney Int. 2013 Sep;84(3):451-6.

3. Trevisan R, Dodesini AR, Lepore G. Lipids and renal disease. J Am Soc Nephrol. 2006 Apr; 17(4 Suppl 2):S145-7.

4. Appel G. Lipid abnormalities in renal disease. Kidney Int. 1991 Jan;39(1): 169-83.

5. Grundy S. Management of hyperlipidemia in kidney disease; Kidney Int. 1990;37:847-53.

6. Baigent C, Landray MJ, Reith C, et al.; SHARP Investigators. The effects of lowering LDL cholesterol with simvastatin plus ezetimibe in patients with chronic kidney disease (Study of Heart and Renal Protection): a randomised placebo-controlled trial. Lancet. 2011 Jun 25;377(9784): 2181-92.

7. Palmer SC, Craig JC, Navaneethan SD, Tonelli M, Pellegrini F, Strippoli GF. Benefits and harms of statin therapy for persons with chronic kidney disease: A systematic review and meta-analysis. Ann Intern Med. 2012 Aug 21;157(4):263-75.

8. Wanner C, Krane V, Marz W, et al.; German Diabetes and Dialysis Study Investigators. Atorvastatin in patients with type 2 diabetes mellitus undergoing hemodialysis. N Engl J Med. 2005 Jul 21;353(3):238-48.

9. Fellstrom BC, Jardine AG, Schmieder RE, et al.; AURORA Study Group. Rosuvastatin and cardiovascular events in patients undergoing hemodialysis. N Engl J Med. 2009 Apr 2;360(14):1395-407.

10. KDIGO clinical practice guideline for lipid management in chronic kidney disease. Kidney Int, Suppl. 2013 Nov;3:259-305.

11. Lipscombe J, Lewis GF, Cattran D, Bargman JM. Deterioration in renal function associated with fibrate therapy. Clin Nephrol. 2001 Jan;55(1):39-44.