CKD in HIV-Infected Patients: From the New Plague to Chronic Care Management

ARTICLE *in* AMERICAN JOURNAL OF KIDNEY DISEASES · FEBRUARY 2015

Impact Factor: 5.76 · DOI: 10.1053/j.ajkd.2015.01.007 · Source: PubMed

2 AUTHORS, INCLUDING:

Joseph A Vassalotti
Icahn School of Medicine at Mount Sinai
74 PUBLICATIONS **1,327** CITATIONS

SEE PROFILE

AJKD

In the Literature

CKD in HIV-Infected Patients: From the New Plague to Chronic Care Management

Commentary on Lucas GM, Ross MJ, Stock PJ, et al. Clinical practice guideline for the management of chronic kidney disease in patients infected with HIV: 2014 update by the HIV Medicine Association of the Infectious Diseases Society of America. Clin Infect Dis. 2014;59(9):e96-e138.

In just 2 decades, antiretroviral therapy (ART) has transformed HIV (human immunodeficiency virus) infection from an almost universally fatal disease to a condition in which people can live long productive lives with chronic care management. Similarly, HIV-associated nephropathy (HIVAN), originally described in 1984[1,2] and once identified as a common cause of end-stage renal disease in young African American men, may be vanishing with ART. HIV infection in people with end-stage renal disease once was considered a potential indication for palliative-focused care; now the full spectrum of kidney replacement therapies are offered, including kidney transplantation in selected cases.[3] Current therapeutic challenges are posed by ART nephrotoxic effects, drug interactions, and the interplay of HIV infection with other chronic diseases characteristic of a sedentary lifestyle, unhealthy diets, and aging.[3]

WHAT DOES THIS IMPORTANT GUIDELINE SHOW?

The 2014 update of the Infectious Diseases Society of America (IDSA) clinical practice guideline for the management of chronic kidney disease (CKD)[3] in patients infected with HIV is a comprehensive and authoritative review of what is currently known about kidney disease and how clinicians managing HIV infection should apply that information in practice. Monitoring kidney function, using creatinine-based glomerular filtration rate (GFR) estimating equations, and assessing kidney damage using urinalysis or a quantitative measure of albuminuria/proteinuria is emphasized at ART initiation and should be repeated semiannually and annually, respectively, thereafter.[3] Nephrology consultations are recommended for severe CKD (estimated GFR [eGFR] < 30 mL/min/1.73 m^2 or urinary albumin-creatinine ratio > 300 mg/g) and for acute kidney injury (AKI) or CKD progression (eGFR decline $> 25\%$ from baseline and to a level < 60 mL/min/1.73 m^2) that does not resolve after withdrawal of potentially nephrotoxic agents.[3]

The guideline includes an important review of potential adverse kidney effects of ART useful for the nephrology consultant. Tenofovir receives the most attention, addressed in 3 of 24 guideline statements: avoid initiation of tenofovir therapy at eGFR < 60 mL/min/1.73 m^2, substitute alternative ART when eGFR decreases by $>25\%$ and <60 mL/min/1.73 m^2 in a treated patient, and avoid tenofovir use in prepubertal children.[3] Tenofovir effects can include AKI, CKD, proximal tubular dysfunction, nephrogenic diabetes insipidus, and combinations of these patterns. Methods for proximal tubular toxicity monitoring are outlined (Table 5 in the guideline), although their use is not specifically recommended.[3] Kidney safety signals also are described for the protease inhibitors: atazanavir, lopinavir, and indinavir. Indinavir is rarely used in the United States because of drug-containing radiolucent nephrolithiasis and intratubular drug-crystalline formation. Atazanavir and lopinavir are associated with decreases in eGFR in large cohort studies, but the interpretation is complicated in part by inclusion of concomitant ritonavir that inhibits tubular creatinine secretion (discussed next). Two useful and extensive guideline tables (6 and 7) provide guidance for ART and antimicrobial dosing, respectively, for both kidney failure treated by dialysis and earlier stages of CKD.[3]

Also highlighted is the fact that many ART combinations contain a pharmacoenhancer, an agent that impairs hepatic cytochrome P450 3A metabolism of an active antiretroviral to enhance blood levels and reduce dosing requirements.[3] Cobcistat is the newest of these agents, currently coformulated with tenofovir, elvitegravir, and emtricitabine, but coformulations with protease inhibitors and formulation as a monodrug are anticipated. Ritonavir is a protease inhibitor that often is formulated as a pharmacoenhancer to boost activity of another protease inhibitor. Both pharmacoenhancers block tubular secretion of creatinine, thereby increasing serum creatinine level without reducing the true GFR. Two drugs that do not act as boosters, dolutegravir, a new integrase inhibitor, and rilpivirine, a nucleoside reverse-transcriptase inhibitor, also inhibit tubular creatinine secretion. The prescriber and consultant must be aware of these features in order to distinguish predictable declines in eGFR from declines in GFR. Last, the guidelines recommend avoidance of central venous catheters for hemodialysis by considering peritoneal dialysis and

Address correspondence to Joseph A. Vassalotti, MD, Icahn School of Medicine at Mount Sinai, One Gustave L. Levy Pl, Nephrology, Box 1243, New York, NY 10029-6574. E-mail: joseph.vassalotti@mssm.edu

0272-6386
http://dx.doi.org/10.1053/j.ajkd.2015.01.007