Drug Interactions Might Provoke Tenofovir-Associated Renal Failure

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A review of 27 cases suggests that ritonavir, ddI, and atazanavir might raise the risk for tenofovir-associated renal failure.

Tenofovir seldom causes patients to complain of side effects, and some studies have suggested that it is free of major toxicity. However, its use has been associated with the development of acute, sometimes irreversible, renal dysfunction, and risks for this complication are not well understood. Researchers reported on 5 new cases of tenofovir-associated renal failure and reviewed 22 cases previously reported in the literature.

All 27 patients were receiving tenofovir in a combination antiretroviral regimen that included ritonavir (21 patients), ddI (9 patients), and atazanavir (5 patients). Duration of tenofovir use ranged from 1 to 29 months (mean, 11 months). CD4-cell counts and viral loads ranged widely. All patients had normal serum creatinine levels at baseline. Renal failure was accompanied by Fanconi syndrome in 16 patients, proteinuria in 6, and urinary sediment characteristic of acute tubular necrosis in 8. Two patients briefly required dialysis. After tenofovir was discontinued, urinary abnormalities resolved in all patients, although five still had some degree of renal dysfunction after a mean follow-up of 7.5 months.

The authors hypothesize that interactions with other antiretrovirals are responsible for sporadic cases of tenofovir-associated renal failure. Ritonavir inhibits secretion of tenofovir into the urine and may raise serum tenofovir levels considerably. ddI may compete with tenofovir for urinary secretion, resulting in elevated serum levels of ddI and ddI-associated renal damage. Atazanavir also reportedly increases serum tenofovir levels. The authors call for close monitoring of renal function and serum electrolyte and cation levels in patients beginning tenofovir with any of these drugs, in the hopes that early diagnosis of altered renal function will prevent permanent damage.

Comment

Renal function in HIV-infected patients is often overlooked until it deteriorates beyond repair (ACC May 11 2005). Certainly, clinicians often forget that a normal creatinine level does not always mean normal renal function, especially in sick patients with reduced muscle mass. Although tenofovir deserves its reputation as an unusually safe and well-tolerated drug, it can cause enduring kidney damage. Clinicians should be vigilant about monitoring renal function and should dose other antiretrovirals carefully in patients taking tenofovir.

Source

- Zimmermann AE et al. Tenofovir-associated acute and chronic kidney disease: A case of multiple drug interactions. *Clin Infect Dis* 2006 Jan 15; 42:283-90.