New Guidelines: Anti-Seizure Drug Selection for People Living With HIV

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New guidelines from the American Academy of Neurology (AAN) and the International League Against Epilepsy (ILAE) have been published online ahead of print by the journal Neurology to help people living with HIV and their care providers choose seizure drugs that do not interact negatively with antiretrovirals (ARVs).

“Drug interactions between AEDs [antiepileptic drugs] and ARVs could result in progression to AIDS and/or reduced seizure control,” said Gretchen Birbeck, MD, MPH, of Michigan State University and a lead author of the recommendations in an accompanying announcement. “Providing guidelines that help physicians select appropriate therapies for their patients with epilepsy and HIV/AIDS will ultimately improve patient outcomes and possibly decrease the public health threat of the development of drug-resistant HIV.”

Seizure disorders, such as epilepsy, are common among people living with HIV, Birbeck and her colleagues note. Up to 55 percent of the 33 million people living with HIV worldwide require treatment with AEDs—used to manage epilepsy, a variety of mood disorders and other neurological complications including peripheral neuropathy—at some point in their lives.

Numerous AEDs are available to these neurological problems, and many can be combined, safely, with ARVs. However, some AEDs are associated with potentially dangerous interactions with available HIV medications.

Because of the way certain AEDs and ARVs are broken down (metabolized) in the body, some seizure medications can significantly increase or decrease blood levels of some HIV drugs, potentially increasing the risk of side effects or HIV drug resistance. Similarly, some ARVs can increase or decrease blood levels of some AEDs, which can also increase the risk of side effects or reduce the effectiveness of anti-seizure therapies.

Unfortunately, the guidelines note, evidence from studies looking at specific drug-drug interactions is weak and, as a result, firm AED selection and dosing recommendations are limited. However, a number of interactions are known and should be considered. Some of the key recommendations in the published guidelines include:

AEDs and Protease Inhibitors

Dylantin (phenytoin) and Kaletra (lopinavir/ritonavir)
People living with HIV receiving phenytoin may require a Kaletra dosage increase of about 50

percent to maintain adequate blood levels of lopinavir, the active protease inhibitor in Kaletra.

Lamactil (lamotrigine) and Norvir (ritonavir)–boosted Reyataz (atazanavir)
People living with HIV receiving Norvir-boosted Reyataz may require a lamotrigine dosage increase of about 50 percent to maintain adequate blood levels of atazanavir.

AEDs and Integrase Inhibitors

Lamactil (lamotrigine) or Versed (midazolam) and Isentress (raltegravir)
Isentress may not require doses of either lamotrigine or midazolam to be adjusted.

AEDs and Nucleoside/Non-Nucleoside Reverse Transcriptase Inhibitors

Depakote (valproic acid) and efavirenz (found in Sustiva and Atripla)
People living with HIV receiving Sustiva or Atripla may not require the dose of valproic acid to be adjusted.

Depakote and zidovudine (found in Retrovir, Combivir and Trizivir)
People living with HIV receiving valproic acid may require a zidovudine dose reduction to maintain normal blood levels of zidovudine.

“Future research should target epilepsy and HIV/AIDS drug combinations where choices are limited, such as in developing countries”—where both AED and ARV drug choices are limited—“to better understand the risks,” Birbeck said. “It also is important that patients know exactly which drugs they are taking and provide that information to all prescribing health care providers caring for them.”

To establish the guidelines, Birbeck and her colleagues systematically reviewed studies published in the medical literature between 1950 and 2010 to determine the prevalence of co-usage of anti-epileptic drugs and antiretrovirals and drug interactions. Nearly 4,500 articles were identified, 68 full studies were reviewed and data from 42 articles were used in the analysis.

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