Do some protease inhibitors interact with lithium?

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Lithium has been licensed for the treatment of bipolar depression for several decades. More recently, a preliminary study suggests that lithium treatment may help reverse some HIV-related brain damage that affects memory, clear thinking and concentration—neuro-cognitive problems. However, this was a small and short study and a much larger controlled clinical trial is needed to confirm these results.

One area of concern about the potential for more widespread use of lithium by people with HIV/AIDS (PHAs) is that highly active antiretroviral therapy (HAART) might interact with this drug, causing problems such as decreased effectiveness of HAART or lithium.

Researchers at Luigi Sacco Hospital in Milan, Italy, recently reviewed data on about 1,000 HAART users and found that three were using lithium. Two of these three PHAs were using combinations of atazanavir (Reyataz) and ritonavir (Norvir) and experienced worsening depression. The third PHA was taking a combination of three nucleoside analogues and did not experience any relapse of depression. These findings underscore the need for caution when using lithium and some combinations of protease inhibitors.

Case details—Patient 1
The first PHA was a 46-year-old man whose depression was treated with 450 mg of lithium taken twice daily. His regimen included the following medications:

- lopinavir/ritonavir (Kaletra)
- 3TC + AZT (Combivir)
- tenofovir (Viread)

His depression went into remission and several years later his HIV treatment was switched to the following medicines:

- atazanavir/r
- tenofovir
- 3TC (lamivudine, Epivir)

After using the new regimen for three weeks, he complained of the following symptoms:

- anxiety
- depression

Lab tests revealed that the level of lithium in his blood and urine was well below normal. This suggested that something in his regimen was interacting with the lithium, either impairing its absorption or causing the body to excrete this drug. Doctors did not think that a lack of adherence to lithium therapy played a role in the appearance of his symptoms.

Case details—Patient 2
This PHA had been stable on her previous regimen of the following medications:

- d4T (stavudine, Zerit)
- 3TC
• saquinavir (Invirase) + ritonavir

In addition to these, her dose of lithium, 450 mg twice daily, placed her bipolar depression into remission. Her anti-HIV therapy was later changed to the following combination:

• atazanavir/r
• 3TC + abacavir (Kivexa)

Within two weeks of this switch she reported feelings of instability, including the following:

• compulsions
• panic attacks
• deep depression

Doctors then doubled her dose of lithium in an attempt to provide relief, but this intervention was unable to maintain adequate lithium levels in her blood. To restore her mental stability, doctors felt compelled to prescribe an interruption of HAART. Once she became stable again, another regimen could be chosen. Her physicians noted that in the past this patient has been “highly adherent.”

Although this report is based on just two cases, the Milan doctors urge other physicians to ensure that their patients using boosted protease inhibitors and who also are prescribed lithium have their lithium levels monitored.

Hopefully, researchers will now study interactions between boosted protease inhibitors and lithium.

—Sean R. Hosein

REFERENCE:

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