Norvir and Viral Hepatitis Increase HIV Drug levels, Risk of Side Effects

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The ability of Norvir (ritonavir) to boost the blood levels of other antiretroviral (ARV) drugs is amplified in HIV-positive people who are also infected with either hepatitis B virus (HBV) or hepatitis C virus (HCV), according to a study published online in the Journal of Acquired Immune Deficiency Syndromes. As a result, researchers warn, people coinfected with HIV and hepatitis may be at an increased risk for ARV side effects.

Liver damage, including fibrosis and cirrhosis, progresses faster in people infected with both HIV and hepatitis, compared with people infected only with HBV or HCV. Additionally, coinfected people are at an increased risk of liver side effects caused by ARV medications, compared with those only infected with HIV. However, the reason for this is not clear.

One suggestion is that coinfection alters the liver's ability to break down (metabolize) medications in the body, causing increased drug levels and, consequently, a higher risk of drug-induced liver damage. If this theory is correct, using Norvir to boost drug levels in coinfected people may further increase the possibility of drug-related side effects, including damage to the liver.

To explore this possibility, Tamsin Knox, MD, MPH, from Tufts University School of Medicine in Boston and her colleagues conducted a study involving 30 HIV-positive individuals, 17 of whom also had chronic viral hepatitis and 13 of whom did not. In both groups, roughly half were on an ARV regimen containing at least 100 mg of Norvir. Dr. Knox and her team looked specifically at Norvir's ability to inhibit production of a liver enzyme known as CYP3A4. With less of the enzyme present to metabolize other drugs, the blood levels of those drugs can end up many times higher than normal.

Knox's team found that, as expected, the patients taking Norvir had CYP3A4 levels that were reduced by more than 90 percent. In people taking Norvir who were also coinfected with hepatitis, however, CYP3A4 levels were reduced by an additional 70 percent. This was the case even in people with evidence of very little liver damage from their hepatitis infection. This change is large enough, Knox's team writes, that it could easily result in greater drug toxicity, including an increased risk of liver damage. They recommend further studies on drug blood levels in people coinfected with both HIV and HBV or HCV in an effort to decrease the chance of serious side effects.

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