ARV Liver Toxicity in HIV/Hep C Coinfected Patients on the Decline

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For people living with HIV, coinfection with HCV is known to increase the risk for, and rate of, liver toxicity from ARV therapy. Hepatotoxicity was a particular concern with commonly prescribed ARVs during the early years of combination HIV treatment, notably the late 1990s and early 2000s. In more recently years, the approval of newer agents has permitted health care providers to prescribe HIV combinations heralded as being safer than their predecessors, yet it hasn't been clear whether evolved regimens have reduced the incidence of liver toxicity among people with HIV/HCV coinfection.

To explore this question, Mark Hull, MD, from Canada's BC Centre for Excellence in HIV/AIDS in Vancouver and his colleagues followed 748 people living with HIV—196 (26 percent) of whom were coinfected with HCV—over a span of 12 years. The study subjects were divided into three groups: those observed between January 1, 1997, until December 31, 1999 (period one); those observed between January 1, 2000, and December 31, 2003 (period two); and those observed between January 1, 2004, and December 31, 2009 (period three).

In this mostly male group averaging 42 years old, HIV treatment uptake increased over the years. During period one, 107 people (14 percent) started ARV treatment for HIV. In period two, 208 (28 percent) started ARV therapy. In period three, 433 (58 percent) began ARV treatment.

Liver toxicity was defined as an increase in alanine aminotransferase (ALT)—a liver enzyme that signals liver inflammation—using any of three criteria: Five times higher than pre-treatment levels, five times higher than the upper limit of normal or 3.5 to 5 times higher than pre-ARV therapy levels when pretreatment ALT was abnormally high. Liver enzyme levels were checked at 1,3, 6, 9 and 12 months after starting HIV treatment.

No matter which criteria were used to assess liver toxicity, it was much more likely among people living with HIV and HCV compared with those living with HIV alone. According to the researchers' report, the average time to liver toxicity after starting ARV therapy was 10 months, when ALT levels increased from a pretreatment average of between 33 to 35 international units per liter (IU/L) to an on-treatment average of 508 to 515 IU/L.

During each time point, however, the estimated incidence rate of liver toxicity dropped.

During period one, the overall incidence of liver toxicity—among all people living with HIV on ARV therapy, irrespective of their HCV coinfection status—was roughly 17 per 100 person-years (PY). In other words, roughly 17 (17 percent) of 100 people included in the analysis who started HIV

treatment between January 1997 and December 1999 and remained on ARV therapy for one year (or 34 percent of 50 people who started and remained on treatment for a two-year period) were estimated to have experienced liver toxicity.

Looking specifically at those with HIV/HCV coinfection starting ARV treatment during period one, the estimated incidence of liver toxicity was 37 per 100 PY. As for those with HIV but not HCV infection, the estimated incidence was roughly four per 100 PY.

During period two, the overall incidence of liver toxicity decreased to approximately 10 per 100 PY. Among people coinfected with HIV and HCV, the estimated incidence of liver toxicity dropped to 30 per 100 PY, versus roughly one per 100 PY among those living with HIV alone.

During period three, the overall estimated incidence of liver toxicity dropped further, to nearly seven per 100 PY. Among people coinfected with HIV and HCV, the estimated incidence decreased to roughly 24 per 100 PY, compared with approximately two per 100 PY among those infected only with HIV.

“The overall incidence rate of hepatotoxicity after [ARV therapy] initiation has diminished in the modern era, but remains significantly higher in those with underlying HCV infection,” Hull and his colleagues remarked. “Coinfected patients should be assessed for consideration of HCV therapy prior to [ARV therapy] as a means of decreasing subsequent [ARV] -related hepatotoxicity,” they added, alluding to data from other studies showing that HCV treatment, when successful, lowers the risk for and rate of liver toxicity from HIV treatment.
