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EDITORIAL COMMENTARY

Is Moderate Alcohol Consumption Safe for Human Immunodeficiency Virus/Hepatitis C Virus–Coinfected Women?

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(See the Major Article by Kelly et al on pages 2050–6.)

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Alcohol consumption is common among chronic hepatitis C virus (HCV)–infected patients [1]. Unhealthy alcohol use can accelerate HCV-related liver fibrosis and increase the risk of cirrhosis, hepatocellular carcinoma, and death [2]. Excessive alcohol consumption may also prevent providers from prescribing HCV treatment [3].

Chronic HCV patients with human immunodeficiency virus (HIV) coinfection may be particularly susceptible to harm from alcohol use. HIV-infected patients experience physiologic injury and increased mortality at lower levels of alcohol use than uninfected persons [4]. Moreover, unhealthy alcohol use in HIV has been associated with liver disease [5], decreased adherence to antiretroviral therapy [6], and immune dysfunction [7], and these factors increase the risk of HCV-related liver complications in HIV [8].

Despite alcohol's role as an important co-factor in liver disease, few studies have evaluated the effects of different levels of alcohol consumption on liver outcomes, especially among HIV/HCV-coinfected patients. A key question often posed to providers by patients with HIV/HCV coinfection is whether light or moderate alcohol use will accelerate their hepatic fibrosis progression. One study among HIV/HCV-coinfected US Veterans demonstrated a stepwise increased prevalence of advanced hepatic fibrosis with greater severity of alcohol use, but this analysis excluded individuals who were abstinent from alcohol so could not determine associations between light or moderate levels of alcohol consumption and advanced fibrosis [9]. Other studies of coinfected patients have focused primarily on hepatic outcomes of heavy alcohol use or abuse/dependence among samples comprised of mostly men. However, sex differences exist in the effect of alcohol on liver fibrosis [2]. Women may be more sensitive to the adverse effects of alcohol and experience ill effects at a lower level of intake. Thus, studies that specifically evaluate the impact of different quantities of alcohol, particularly light or moderate use, on liver disease among HIV/HCV-coinfected women have been sorely needed.

Investigators from the Women's Interagency HIV Study (WIHS), an ongoing, National Institutes of Health–funded, multicenter study of adult women with HIV or at high risk of acquiring HIV, examined rates of liver fibrosis progression associated with different alcohol use categories among HIV/HCV-coinfected women; their findings are reported in this issue of *Clinical Infectious Diseases* [10]. Established in 1994, the WIHS collects demographic, behavioral, and medical information on participants every 6 months from structured interviews, physical examinations, and biological specimens. In this study, data were obtained prospectively over a median follow-up of 10 years, allowing determination of the long-term consequences of different levels of alcohol use on liver fibrosis progression.

Alcohol consumption was ascertained semiannually based on self-reported average number of drinks per week during the preceding 6 months. Alcohol use was categorized as light (1–3 drinks per week), moderate (4–7 drinks per week), heavy (8–14 drinks per week), or very heavy (>14 drinks per week). Participants were considered abstinent if they reported no alcohol consumption at WIHS enrollment or during follow-up.

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Importantly, cumulative exposure to each alcohol use category was determined over each patient's observation period.

The main outcome was the rate of liver fibrosis progression, defined as a change in the Fibrosis-4 Index for Liver Fibrosis (FIB-4) per year. FIB-4 is a noninvasive measure of hepatic fibrosis that is calculated using alanine aminotransferase, aspartate aminotransferase, platelet count, and age and has been shown to identify advanced hepatic fibrosis/cirrhosis with a high degree of accuracy in HIV/HCV-coinfected patients [11]. In this study, FIB-4 was calculated annually among patients in the cohort, and the mean change in FIB-4 per year was determined for each alcohol use category compared to periods with no consumption. Although biopsy has been the gold standard for staging liver disease, it is not feasible to perform liver biopsies in large cohort studies because of the costs and risks to patients. Noninvasive markers of hepatic fibrosis, such as FIB-4, have therefore been valuable for evaluating liver fibrosis in population-based studies. The WIHS previously showed that FIB-4 was independently associated with mortality among HCV/HIV-coinfected women [12].

The study provides important observations on the drinking patterns of coinfected women. Those with higher categories of alcohol use at study entry were more likely to smoke tobacco and use injection/noninjection drugs and were less likely to be on antiretroviral therapy. Alcohol consumption varied during follow-up, with 30.5% increasing their alcohol consumption over time, 14.5% decreasing consumption over time, and 55.0% having the same level of alcohol use at entry and during follow-up. This variation in alcohol use provides strong support for the evaluation of alcohol consumption as time-varying.

Importantly, after controlling for age, race/ethnicity, and HIV RNA load, women with light or moderate alcohol use (≤7 drinks per week) had a similar rate of liver fibrosis progression as those who were abstinent from alcohol throughout their follow-up. As expected, the heaviest level of alcohol use (>14 drinks per week) was associated with the highest rate of hepatic fibrosis progression. Fibrosis progression rates for each alcohol use category were not reported according to baseline stage of hepatic fibrosis, likely because such stratification would have led to very small subgroup sizes that would have yielded imprecise results. However, it will be important to know if liver fibrosis progression rates associated with levels of alcohol use vary by baseline FIB-4 category (eg, <1.45 [no/minimal hepatic fibrosis]; 1.45–3.25 [moderate liver fibrosis]; >3.25 [advanced hepatic fibrosis/cirrhosis] [11]). The analysis by Kelly and colleagues [10] provides new insights on the impact of small quantities of alcohol on liver fibrosis progression among HIV/HCV-coinfected women. This study also demonstrates the value of large observational HIV cohort studies for understanding important associations in the setting of HCV coinfection.

This study highlights the importance of assessing alcohol consumption during routine practice (eg, with the Alcohol Use Disorders Identification Test) to classify patients' level of use. HIV/HCV-coinfected women should be counseled to minimize alcohol consumption, and any patient with evidence of advanced hepatic fibrosis/cirrhosis should avoid alcohol use given that the risk of liver complications, such as decompensated cirrhosis and hepatocellular carcinoma, associated with light or moderate use remains unknown in this group. However, some may be unable or unwilling to completely abstain from alcohol because of mental health or substance use disorders. This study suggests that light or moderate alcohol use by coinfected women is not associated with accelerated liver fibrosis progression as measured by changes in FIB-4.

The work by Kelly and colleagues [10] provides important information on the impact of alcohol on liver fibrosis progression among women with HIV/HCV coinfection, but many critical questions remain regarding the interactions between alcohol, chronic HCV, and HIV [2]. Future studies should determine the effects of light and moderate alcohol consumption on changes in other noninvasive measures of liver fibrosis (eg, transient elastography) and on rates of liver complications, such as hepatic decompensation and hepatocellular carcinoma, in HIV/HCV-coinfected men and women to confirm this study's findings. Additional research is also needed to evaluate the effects of alcohol use categories on adherence to direct-acting antiviral therapy and HCV treatment response and examine whether these outcomes differ by HIV status and sex. These data will further help inform whether there is a "safe" level of alcohol intake in patients coinfected with HIV and HCV.

Notes

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