Coffee consumption and reduced self-reported side effects in HIV-HCV co-infected patients during PEG-IFN and ribavirin treatment: Results from ANRS CO13 HEPAVIH

To the Editor:

Constentin and colleagues [1] reported key results about the protective effect of elevated coffee consumption (three or more cups/day) on histological activity in patients with chronic hepatitis C. These findings bring additional evidence to the potential hepatoprotective properties of coffee in chronic liver diseases, as already suggested in studies showing its beneficial effects on liver cancer [2].

More recently, Freedman and colleagues [3] showed associations between elevated coffee consumption (three or more cups/day) and early, week-20 and sustained virological response (SVR) during re-treatment with peginterferon alfa-2a (180 μg/wk) and ribavirin (1000–1200 mg/day) in the HALT trial. The study also highlighted that the proportion of individuals tolerating the full dose of treatment was significantly higher in those patients drinking more than three cups of coffee/day. In addition, during treatment, coffee drinkers were significantly less likely to have a dose reduction due to either low neutrophils or platelets.

These results provide important insights into the double role that coffee consumption may play in slowing HCV progression, reducing medical side effects and improving response to HCV treatment. However, whether and to what extent elevated coffee consumption may also reduce the burden of patients’ “personal experience” with HCV disease and/or HCV treatment, as expressed by self-reported symptoms/side effects, has not yet been documented.

Individuals receiving HCV treatment experience a considerable range of symptoms/side effects [4], in particular fatigue, neurocognitive symptoms, depression, and problems of anger control which can seriously compromise their quality of life [5] and undermine adherence and continuity of treatment [6]. On the other hand, several performance benefits are attributed to coffee consumption including physical endurance, fatigue reduction, and improvements in mental concentration and alertness [7].

Medically reported side effects document major toxicity events during HCV treatment, whereas self-reported discomforting symptoms are known to express perceived toxicity and disease burden on patients’ daily life more accurately.

To test whether elevated coffee consumption can indeed relieve the discomfort caused by side effects, we used data from the HEPAVIH ANRS CO13 cohort of HIV-HCV-infected patients [8]. Selection criteria for this analysis targeted patients receiving antiretroviral therapy (ART) who started peginterferon alfa-2a and ribavirin during follow-up and who had both complete data about coffee consumption before starting treatment and self-reported discomforting side effects during treatment at 3 months and before the end of treatment, collected through self-administered questionnaire (N = 106, 138 visits). A five-category variable measured coffee consumption on a five-point scale: “no consumption”, “occasional consumption”, “one cup per day”, “two cups per day”, “three or more cups of coffee per day”.

Self-reported symptoms [9] detailed 30 treatment-related symptoms (defined here as “self-reported side effects”) over the previous 4 weeks and the discomfort they caused. This scale has already been shown to capture HCV-treatment toxicity in HIV-HCV infected patients [4].

Among the 106 selected patients, median [IQR] age was 44 [41–46] years, men accounted for 71% and most of the participants (80%) were HIV-infected through injecting drug use (IDU). At enrollment, 86% of the patients had undetectable plasma HIV RNA, 52% presented with severe fibrosis (F3–4) and 13% had a CD4 count <200/mm3. The median [IQR] number of self-reported side effects causing discomfort was 3 [0–8] and 31% did not report any discomforting side effects. A mixed model confirmed that individuals drinking more than three cups a day did not significantly change their consumption over time. A logistic regression model based on Generalized Estimating Equations was used to study the relationship between coffee consumption before
starting treatment and the presence of discomforting side effects at 3 months and before the end of treatment.

Patients drinking >3 cups of coffee per day were less likely to report discomforting side effects than non-drinkers of coffee (OR [95% CI] = 0.19 [0.05–0.78], p = 0.02). The association between drinking three or more cups and self-reported side effects remained significant (AOR [95% CI]: 0.17 [0.03–0.96], p = 0.04) even after multiple adjustments for gender, age, history of opioid use, and liver fibrosis (F3–F4 vs. F0–F1–F2) which are known correlates of reporting a higher number of discomforting side effects [10]. In addition, the likelihood of reporting discomforting side effects during HCV treatment linearly decreased across the five categories of coffee consumption (OR [95% CI] = 0.67 [0.49–0.90], p = 0.008) and remained significant after multiple adjustment for age, gender, liver fibrosis, and history of opioid use (AOR [95% CI] = 0.62 [0.43–0.90], p = 0.01).

These results outline an association between elevated coffee consumption and reduced perceived toxicity during HCV treatment, which needs confirmation in future studies.

Although the study population may be particularly vulnerable to treatment toxicity and more prone to reporting discomforting side effects because of their double viral infection, our findings suggest the additional potential benefits of coffee consumption in patients receiving peg-IFN + ribavirin therapy. While newer treatment options will soon become available, this combination will remain the only one available in resource-limited settings where treatment success is still greatly subordinate to patient readiness to start, strict adherence, and receipt of adequate side effects management and counseling. In the meantime, Costentin’s and Freedman’s results, together with our own, may provide an inexpensive and simple suggestion to lower necroinflammatory injury and potentially reduce the progression of liver fibrosis, improve response to HCV treatment as well as alleviating treatment-related toxicity once patients engage in HCV treatment.

Conflict of interest

The authors declared that they do not have anything to disclose regarding funding of conflict of interest with respect to this manuscript.

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References

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