

## **Acute hepatitis C virus infection in HIV+ MSM: Should we change our screening practice?**

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**Dear Editor:**

Current guidelines recommend anti-HCV antibody testing in patients presenting with HIV infection, and HCV-RNA testing should be performed in those with a positive antibody response.<sup>1</sup> However, direct testing for HCV-RNA is recommended in patients with previous intravenous drug abuse (IVDA) and in HIV+ persons with unexplained transaminase elevations<sup>1</sup>, since occult HCV infection can be found in some of these patients.<sup>2</sup> Noteworthy, this would not include HCV-RNA screening of HIV-infected men who have sex with men (MSM), an important risk group according to numerous reports on the rising number of acute hepatitis C virus infections (AHCs) in MSM in the last decade<sup>3-6</sup>

However, there is often a gap between the recommendations by guidelines and the actual clinical practice. This is clearly demonstrated by the study of Dr. Freiman et al.<sup>7</sup> published in this issue of CID. While the majority of patients (85%) were screened by anti-HCV antibody testing within 3 months after first presentation at HIV primary care clinics, the follow-up HCV screening modalities did not follow the guidelines in a substantial proportion of patients, with only 55.6% receiving additional HCV tests after initial screening.<sup>7</sup> Most interestingly, even patients with elevated transaminases (ALT>100IU/L) did not receive additional HCV screening tests in the majority of cases (only 26.7% of those patients were tested for HCV infection).<sup>7</sup> As that the study population was enrolled between 2000 and 2011, it has to be emphasized, that in the first years of the study period the guidelines on when, how, and which HIV+ persons should be tested for HCV had not been as clear as today. Over the last decade the important clinical impact of HCV co-infections in HIV+ individuals attracted more attention among clinicians, and especially now – when novel directly acting antiviral agents (DAAs) can achieve impressive cure rates<sup>8-10</sup> - HCV screening represents an even more critical issue.

However, there is still need for improvement<sup>11</sup> of HCV screening - especially in the setting of AHC, as anti-HCV testing is recommended as the primary screening test for AHC in HIV+ MSM. In this issue, Vanhommerig et al.<sup>12</sup> provide important data on the dynamics of anti-HCV development (HCV seroconversion) and loss of anti-HCV (sero-reversion) following AHC in the “at-risk” population of HIV-infected MSM. In brief, the main finding was an average duration of 2.5 months (74 days) for seroconversion and a rate of up to 51% of sero-reversion following spontaneous clearance or successful HCV-treatment.

It seems that anti-HCV testing is a reliable screening tool for diagnosis of AHC in MSM, since – at least in this cohort of HIV+ MSM – there was not a single case of “occult” AHC infection. However, since the average time to HCV seroconversion was 74 days (around 11 weeks) - which implies that “early” diagnosis of AHC is often missed when only anti-HCV testing is performed HIV+ MSM.

Why is “early” diagnosis of AHC relevant? First of all there is still discussion if early liver fibrosis progression is particularly pronounced in HIV+ MSM after acute HCV as compared to other patients with AHC infection.<sup>13</sup> Second, early diagnosis might also allow prevention of transmission of HCV by the HIV+MSM patients unaware of their HCV infection. Third, the response to antiviral therapy – at least to pegylated interferon alpha (PEGIFN)-based regimens – seems better when treatment is initiated early.<sup>14</sup> Current EACS guidelines<sup>15</sup> even recommend initiation of treatment with pegylated interferon alpha and ribavirin in absence of a significant decline in viral load within 4 weeks of diagnosis of AHC in HIV+ patients.

Another important finding of this study was the high rate of sero-reversion which was observed in almost one third of the patients (8/31 subjects) and the fact that AHC re-infections were diagnosed in absence of significant transaminase elevations. Thus, anti-HCV testing might be of diagnostic value even after

resolution of AHC with sero-reversion in HIV+ MSM and should not only triggered by elevated levels of transaminases.

These novel data on anti-HCV dynamics in HIV+ MSM are highly relevant, since they support a broader use of a sensitive quantitative PCR-based HCV-RNA testing in this high-risk population to prevent potential transmission during the early phase of AHC (as the patient is otherwise unaware of the HCV co-infection) and to allow early administration of antiviral therapy (that is likely associated with improved response rates). Indeed, the authors conclude that screening for AHC is ideally performed using HCV-RNA testing.

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