

Methadone Usage Associated with Lower Rate of Chronic Hepatitis C

Those with HCV antibodies who were taking methadone were significantly less likely to have detectable HCV RNA even without differences in liver biopsy

Approximately 80-85% of persons with past HCV (* hepatitis C virus) infection have chronic hepatitis C, as determined by the presence of HCV RNA. Specific factors that determine which persons will have chronic infection currently are under investigation. Some of those factors might include lacking symptoms of acute hepatitis C and lacking a breadth of immune responses to HCV antigens. Now, researchers from the University of Missouri have determined that methadone users with antibodies to HCV are significantly less likely to have chronic hepatitis C than non-methadone users.

The results do not necessarily mean that methadone causes clearance of HCV RNA or resolution of infection, and there are a few potential confounding factors that might explain the findings. Injection drug use is a major risk factor for HCV infection, while methadone is a long-acting opiate drug that helps heroin users abstain from illicit narcotic injection.

Dr. Wendell K. Clarkston and colleagues performed a retrospective chart review of 285 consecutive HCV antibody positive patients referred for evaluation to the Hepatology (liver) clinic at the School of Medicine there. None had treatment for HCV infection. Their hypothesis was to determine whether injection drug use or methadone use effected the outcome of HCV infection.

The results showed that 52 patients (18%) were taking a mean methadone dose of 63 mg daily. Methadone users were slightly more likely to be men (54%) than non-methadone users (48%). Also, methadone users were slightly younger (mean age 47 years) than non-methadone users (mean age 49 years).

Interestingly, methadone users were significantly more likely to have a negative test for HCV RNA (21%) than non-methadone users (9%). The type of test was PCR (polymerase chain reaction), although the lower limit of detection was not stated. Stated in the opposite way, methadone users were significantly less likely to have chronic hepatitis C (79%) than non-methadone users (91%). Also, the researchers reported that methadone users with detectable HCV RNA were significantly more likely to have a normal ALT (alanine aminotransferase, liver enzyme, 63%) than non-methadone users with a detectable HCV RNA (31%).

The researchers said that there were no significant differences between the two groups in terms of HCV genotypes. However, the specific genotypes were not listed for each group. The mean viral load was identical for methadone users and non-users, 3.1 million (6.5 log) copies per milliliter. Also, there were no significant differences on liver biopsies when comparing the two groups. The mean liver inflammation score was 2.2 in methadone users and 2.1 in non-users. Similarly, the mean liver fibrosis scores were quite similar in the two groups: 1.5 in users and 1.9 in non-users.

When the researchers determined from chart records whether there was a history of injection drug use (IDU), there were insignificantly more patients with an IDU history with undetectable HCV RNA (23 of 184, 13%) than those without such a history (8 of 101, 8%). Stated in the opposite way, those with an IDU history were insignificantly less likely (87%) to have chronic hepatitis C than those without such a history (92%).

The authors concluded, "Methadone treatment for narcotics dependency is associated with a reduced risk of chronic HCV infection (defined by the presence of detectable HCV RNA) in patients who are positive for HCV antibody." Also, "Methadone therapy is associated with an increased incidence of normal ALT in chronically infected patients." In addition, "A history of previous IVDA [intravenous drug abuse] is not associated with a significant reduction in the incidence of chronic HCV infection." Lastly, "Further studies to determine the reasons for the reduced risk of chronic infection (e.g., immunologic modulation or enhanced spontaneous viral clearance), the increased incidence of normal ALT [among those with chronic infection], and the response rate to available antiviral therapy in methadone patients are warranted."

While the authors give two factors that might explain their findings ("immunologic modulation or enhanced

spontaneous viral clearance"), they certainly have no evidence that either was a reason. There are several potential confounding factors that account for some the differences. First, the absence of an IDU history in those 101 patients does not mean that such a history did not exist. Patients often are reluctant to admit such behavior. Second, there was no breakdown of race-ethnicity in either group. Past studies have shown that African-Americans have a higher rate of chronic hepatitis C than other race-ethnicities. Perhaps the non-methadone users were more likely to be African-American. This is possible, since the rate of chronic infection in the methadone users was similar to other studies, while the rate in non-users was more similar to what has been reported for African-Americans. Third, the authors did not indicate whether any of those who were not taking methadone at that time had taken it in the past. It is possible that some in the non-user group had taken methadone in the past and if those had been included in the methadone user arm, there might not have been a significant difference in the percentage with detectable HCV RNA. Fourth, there was no mention of co-infection with other viruses, including hepatitis B, D or HIV. Past studies have shown that those with HIV/HCV co-infection have different mean levels of HCV RNA than HCV-mono-infected patients. (Although that would not necessarily account for the difference in detectable versus non-detectable HCV RNA.)

Other information was omitted that has not been associated with a differential in HCV viral loads in past studies, but might still represent potential confounding factors. First, ongoing IDU behavior in the non-methadone users might be much more frequent than among the methadone users.

Second, (also related to potential ongoing IDU behavior) methadone users might have a better nutritional status, since they almost by definition are no longer injecting at least heroin or other opiates. The factors of ongoing IDU or alcohol use might be ruled out if spot urine/blood tests for illicit drugs (including alcohol) were performed. Specifically, it might be that ongoing illicit drug usage in the non-methadone users that could be contributing to an increase in the rate of detecting HCV RNA.

Third, it would have been helpful if the authors had made an estimate of the duration of HCV infection in both groups. Even though the liver biopsy results were nearly equivalent in the two groups, a longer (or shorter) estimated duration of infection might represent a possible co-factor to explain the findings. Fourth, the authors did not specifically indicate what percentage of those with an IDU history were taking methadone. The number of methadone users was 52 (18%), while the number with an IDU history was 184 (65%). Twenty-three of 184 (13%) with an IDU history were HCV RNA negative. Were all of those 23 patients taking methadone or not? Lastly, were there HCV RNA viral load levels in the methadone patients prior to their starting the drug? That last bit of information might be important to consider.

Addressing these potential confounding factors would be helpful in determining whether the association between methadone and a lower rate of chronic hepatitis C might be causative. That also would be better answered by a prospective study.

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Reference:

Clarkston WK and others. Methadone therapy is associated with a reduced risk of chronic hepatitis C virus infection in patients who are positive for HCV antibody. Abstract and poster presentation 241 at *Digestive Disease Week 2000*; May 21-24, 2000; San Diego, California.