

Treatment for Co-occurring Substance Abuse and Hepatitis C

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Chronic infection with the hepatitis C virus (HCV) is frequently complicated by the presence of coexisting substance use disorders (SUDs) and mental illnesses. Patients experience multiple barriers to evaluation and treatment services, and health care providers often experience uncertainty and frustration in trying to provide those services.

Chronic hepatitis C is the leading cause of liver failure and subsequent liver transplantation, a trend that will rapidly rise in the next decade as the largest group of patients with chronic HCV infection develops cirrhosis, hepatocellular carcinoma and liver failure (Alter, 1997). Furthermore, antiviral treatment is now achieving viral elimination in a substantial proportion of patients, and efforts to improve treatment outcomes are continuing (Saracco et al., 2003).

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Alcohol Consumption and HCV

Alcohol consumption is considered a cofactor in the natural history of hepatitis C, although some consider that not enough emphasis has been placed on its importance. Drinking eight to 12 or more drinks per day for many years clearly accelerates the progression of chronic hepatitis C to cirrhosis and to hepatocellular carcinoma (HCC), as well as mortality (Bhattacharya and Shuhart, 2003).

The risk for developing HCC is particularly high for heavy drinkers who are infected with HCV. The evidence regarding less extreme drinking levels is not as clear and is limited by retrospective designs relying on remote recall of drinking over several decades and the use of different measures and cutoff levels for analysis.

However, it has been shown that the relationship between drinking and risk of cirrhosis may be additive at lower levels (<3 drinks/day) and synergistic at higher levels (>8 drinks/day) (Corrao and Arico, 1998). Some studies have reported a relationship between light-to-moderate drinking and development of cirrhosis in the context of HCV, while others have found a relationship only with heavy drinking (Donato et al., 2002). The resolution of this question awaits further research.

The effect of alcohol consumption on response to interferon-based treatments is similarly in question. Several small, mostly retrospective studies found that lifetime alcohol use reduces the response to interferon (Okazaki et al., 1994). In addition to the methodological problems already mentioned, most studies were conducted on Japanese patients treated with interferon monotherapy.

Methods for collecting information about alcohol consumption are poorly described, and many studies lack information about genotype or compliance. More recently, however, a history of problematic alcohol use (and almost certainly some ongoing drinking) was not found to affect outcomes in a small sample of male veterans treated with interferon and ribavirin (Virazole, Rebetol) (Dieperink et al., 2003). At this point, it is not possible to develop firm conclusions about the effect of alcohol use on HCV treatment response.

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Injection Drug Use and HCV

Injection drug use (IDU) is the primary mode of HCV transmission. Among people attending drug treatment programs, HCV seroprevalence ranges from 30% to >90%, with 65% to 85% being common (Diaz et al., 2001). Intranasal and crack cocaine use have also been reported to be risk factors for HCV, but this could be due to unreported IDU by these individuals (Thomas, 2001).

Risk of exposure to HCV is greatest during the first period of drug use and increases to >60% after five years of IDU (Cook et al., 2001). Sharing other types of drug-using equipment such as cookers and cotton may transmit HCV. The transferring of drug from one syringe to another (known as frontloading) is another potential mode of transmission.

Although the incidence of HCV in people who inject drugs has been declining, there is evidence that educational prevention efforts such as those used for HIV are ineffective (Hernandez-Aguado et al., 2001) and that new prevention methods are needed.

There is no evidence that IDU by itself alters the course of HCV infection, but IDU is frequently coupled with heavy drinking of ethanol, which increases the rate of fibrosis. Co-infection with HIV ranges from 5% to >30%, depending on the overall prevalence of HIV in the area, and HIV co-infection appears to increase the rate of fibrosis in HCV (Maier and Wu, 2002). Co-infection with the hepatitis B virus and other hepatitis viruses is common in individuals who inject drugs (Estrada, 2002).

SUD in Hepatitis C Treatment

Screening for SUDs must be routine and thorough, incorporating evidence-based screening methods. Screening for alcoholic beverage drinking should include measures of quantity-frequency, as well as screens for alcohol abuse or dependence.

The Alcohol Use Disorders Identification Test (AUDIT) is a well-validated instrument that screens for both nondependent heavy drinking and for alcohol abuse and dependence (Bohn et al., 1995). It is brief (10 items), self-administered and easy to score. The AUDIT-C, composed of the first three items of the AUDIT, appears to accomplish much the same thing in an even shorter format (Bush et al., 1998).

Most other screening tests (e.g., the CAGE) only identify patients with possible abuse or dependence and will miss nondependent heavy drinking. If such screens are used, questions about quantity and frequency of drinking need to be added.

Screening for other drug use is more effective if questions specifically address each class of drugs. Any drug used more than five times in a lifetime deserve further exploration. Screening should also include urine toxicology screening (with the patient's consent). Clinicians should know which drugs their laboratory will routinely test for and which ones need to be specifically ordered. The synthetic opioids are not routinely assessed in many screening procedures. If a drug screen is positive, but the patient denies drug use, the laboratory should be asked to conduct a confirmatory test using gas chromatography/massspectroscopy.

When patients have a positive screen for an SUD, further evaluation is required to determine whether substance abuse or dependence is present. This can be done in the hepatitis clinic or through referral to an addiction treatment specialist. Patients who are using heroin or other opioids should be specifically referred for opioid agonist therapy such as methadone (Methadose, Dolophine) or buprenorphine (Buprenex, Subutex) maintenance.

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Opioid agonist therapy is the most effective treatment for opioid dependence; most addicted people relapse even when extended detoxification and enhanced psychosocial services are provided (Sees et al., 2000). The best procedure to follow when a patient with a positive screen refuses such a referral is unclear. Patients may be more open to an assessment if the addiction specialist can see patients in the hepatitis clinic.

If SUD treatment is recommended, then hepatitis and addiction treatment personnel need to work closely together to support completion of both treatments.

Current guidelines call for abstinence from IDU for at least six months prior to initiating interferon-based treatment for HCV, but available evidence suggests that recent or ongoing IDU does not adversely affect outcomes. In a five-year follow-up of 27 Norwegians who were successfully treated for HCV while injecting drugs, only one case of re-infection was found, even though 33% returned to IDU (Dalgard et al., 2002).

Backmund et al. (2001) inducted 50 individuals who were undergoing detoxification for injected drugs into hepatitis C treatment. The patients demonstrated excellent sustained virologic response rates (36%), and 39 patients did not miss one interferon injection, despite an overall relapse to IDU of 80%. One-half of those who returned to injecting heroin demonstrated sustained virologic response.

Former patients who were heroin-addicted who are currently receiving opioid agonist therapy with methadone or buprenorphine should not be excluded from treatment for HCV, and withdrawal from opioid agonist therapy is contraindicated, since relapse to IDU typically follows.

There are no published studies addressing cannabis use in the context of hepatitis C treatment. There is also no evidence that cannabis use interferes with response to hepatitis treatment. Frequent cannabis users or those with symptoms of dependence should be offered referral to an addiction specialist, but if they are otherwise good candidates for hepatitis treatment, there is no reason at this time to deny them that opportunity.

Role of Psychiatrists

Psychiatrists can play an important role in identification, education and referral for chronic HCV infection. Mental disorders, as well as SUDs, place patients at higher risk for contracting HCV infection (Alter et al., 1999; Dieperink et al., 2000), and many HCV infections are not symptomatic.

All patients with mental and addictive disorders need to be screened for their risk of HCV infection, and there should be a low threshold for testing, especially among patients with SUDs. All patients with a history of IDU or significant intranasal drug use should be tested.

Prevention plays an important role for patients with chronic hepatitis C infection. All patients should be educated about decreasing the risk for transmission to others. This includes not sharing razors, using condoms and avoiding sharing drug paraphernalia, including needles, cookers, filters (cotton) and nasal tubes.

Most studies have found a low risk for long-time sexual partners and other household members. Alcohol use should be avoided or at least minimized. Caution must be used in prescribed medications with potential liver toxicity, although there is no evidence at this time that usual doses of medications such as acetaminophen, divalproex (Depakote) or naltrexone (ReVia) are more likely to be harmful in patients with HCV infection who are not in liver failure. More frequent monitoring of serum transaminases is indicated. In patients with HCV infection and those at high

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risk (e.g., IDU, intranasal cocaine use, unsafe sexual practices), consideration should be given to vaccination for hepatitis A and B virus infections if immunity is not present already.

Psychiatrists need to provide consultation, support and treatment for patients undergoing antiviral treatment for HCV infection. Antiviral treatment is associated with a high rate of depression and other neuropsychiatric symptoms, and pre-existing psychiatric symptoms are likely to get worse during antiviral treatment (Dieperink et al., 2003).

Although no controlled trials are available examining efficacy for treating depression related to interferon treatment, case reports and clinical experience suggest that selective serotonin reuptake inhibitors are safe and effective. Citalopram (Celexa) and sertraline (Zoloft) may be the best first-line agents, as they have few drug-drug interactions and tend to be well-tolerated.

Irritability in the absence of a full depressive syndrome may be quite troublesome, and antidepressants may be of significant benefit in this instance as well. One study identified the Beck Depression Inventory (BDI), given at two to four week intervals, as helpful in early identification of depression (Dieperink et al., 2003).

Suicide is an issue as well, especially among patients whose liver disease does not respond to antiviral treatment and who may become hopeless. Suicidal ideation of some kind is endorsed by 20% to 30% of patients during interferon treatment (Dieperink et al., unpublished data), and needs to be further explored so that appropriate treatment can be offered.

A common complaint among gastroenterologists treating HCV infection is that they are unable to receive the support they need from psychiatrists. Psychiatrists can improve access to antiviral therapy for patients by educating ourselves about HCV infection and treatment, and by providing support to patients and to hepatitis providers.

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Source

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