Strategies to Reduce Hepatitis C Virus Reinfection in People Who Inject Drugs

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KEYWORDS

• Hepatitis C • Direct-acting antiviral • DAA • Injecting drug use • HIV • Reinfection

KEY POINTS

- Reinfection will occur after direct-acting antiviral therapy in people with ongoing risk behaviors for acquisition.
- The possibility of hepatitis C virus reinfection should be discussed before, during, and after direct-acting antiviral treatment.
- After achieving sustained virologic response, individuals reporting ongoing risk behaviors for transmission/reinfection should be followed at least annually, with liver function tests and hepatitis C virus RNA.
- Education should include discussions of hepatitis C virus transmission, reinfection risk, and harm reduction strategies.
- Retreatment for reinfection should be offered, without stigma or discrimination.

INTRODUCTION

Globally, 71 million people are estimated to be living with chronic hepatitis C virus (HCV) infection, with approximately 2 million new infections annually.[1,2] The majority of new and existing HCV infections in high-income countries occur among people who inject drugs (PWID) with HCV antibody prevalence estimated at 52% (42%–62%).[3]

One of the goals of the United Nations 2030 Agenda for Sustainable Development and the World Health Organization Viral Hepatitis Strategy is the elimination

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of viral hepatitis as a public health threat.[4,5] To realize this goal, strategies to enhance HCV diagnosis, treatment uptake, and prevention are required. Modeling supports HCV treatment scale-up among populations at greatest risk of transmission to reduce incidence and prevalence, including among recent PWID.[6–8] Interferon-based HCV treatment uptake among PWID was low with multiple barriers to care at the patient, provider, system, and societal levels.[9] Concerns regarding adherence, social instability, treatment-related adverse effects, psychiatric comorbidity, and the potential for reinfection have limited interferon-based treatment initiation among PWID.[9,10]

The development and availability of highly effective, well tolerated interferon-free direct-acting antiviral (DAA) therapy has revolutionized HCV therapeutics and provides the therapeutic tools required to strive for elimination.[11,12] One challenge to achieving HCV elimination through therapeutic intervention is reinfection. There is concern that HCV reinfection may compromise HCV treatment outcomes in populations with ongoing risk behaviors, with the risk of reinfection cited as a reason for not offering treatment to PWID.[13,14]

This review summarizes the literature regarding reinfection after successful HCV treatment among PWID, discusses strategies to reduce HCV infection and reinfection, and highlights the potential individual- and population-level impact of DAA treatment-scale up on HCV elimination.

Paul, a 54-year-old man, presents for review with his methadone prescriber and asks to discuss the "new treatments" for chronic HCV infection.

Paul was diagnosed with chronic genotype 1a HCV infection in 1992. He is treatment naive. There is no evidence of significant fibrosis, with recent liver stiffness measurement 5.5 kPa. Quantitative HCV RNA is 6,798,242 IU/mL with and alanine aminotransferase level of 54 U/L.

He reports first injecting heroin in 1979; currently, he injects once per week. He is on methadone 65 mg/d.

After discussion, he is commenced on sofosbuvir/ledipasvir for 12 weeks.

EFFICACY OF DIRECT-ACTING ANTIVIRAL THERAPY FOR CHRONIC HEPATITIS C VIRUS INFECTION AMONG PEOPLE WHO INJECT DRUGS

DAA therapy is safe and effective among PWID and people receiving opioid substitution therapy (OST; **Tables 1** and **2**).[15] However, the majority of phase II and III clinical trials examining DAA efficacy have excluded people with recent drug use.

A small number of clinical trials have been conducted among people who report recent drug use[16–19] (see **Table 1**). In the C-EDGE CO-STAR trial (A Phase III Randomized Clinical Trial to Study the Efficacy and Safety of the Combination Regimen of MK-5172/MK-8742 in Treatment-Naïve Subjects With Chronic HCV GT1, GT4, and GT6 Infection Who Are on Opiate Substitution Therapy), the efficacy and safety of grazoprevir/elbasvir for 12 weeks in chronic HCV genotypes 1, 4, and 6 was assessed among people receiving OST (n = 301), the majority of whom reported drug use during treatment and follow-up.[16] Most (58%) had a positive urine drug screen at treatment initiation with stable patterns of drug use noted throughout treatment. At treatment initiation (immediate treatment arm), recent use of benzodiazepines, opiates, cocaine, or amphetamines/methamphetamines was seen in 25%, 22%, 10%, and 5%, respectively. SVR at 12 weeks (SVR12) was 92%,