International Journal of Drug Policy 26 (2015) 1014–1019

Contents lists available at ScienceDirect

International Journal of Drug Policy

journal homepage: www.elsevier.com/locate/drugpo

Research paper

Successful treatment of chronic hepatitis C with triple therapy in an opioid agonist treatment program

Alain H. Litwin [a,b,*], Irene J. Soloway [b], Lauren Cockerham-Colas [b], Sheila Reynoso [b], Moonseong Heo [c], Christopher Tenore [d], Robert J. Roose [b,e]

[a] Division of General Internal Medicine, Department of Medicine, Albert Einstein College of Medicine, Montefiore Medical Center, Bronx, NY, USA
[b] Division of Substance Abuse, Department of Psychiatry and Behavioral Sciences, Albert Einstein College of Medicine, Bronx, NY, USA
[c] Department of Epidemiology and Population Health, Albert Einstein College of Medicine, Bronx, NY, USA
[d] Albert Einstein College of Medicine, Bronx, NY, USA
[e] Department of Family and Social Medicine, Albert Einstein College of Medicine, Montefiore Medical Center, Bronx, NY, USA

ARTICLE INFO

Article history:
Received 20 February 2015
Received in revised form 13 July 2015
Accepted 10 August 2015

Keywords:
HCV
PWID
PWUD
IDU
Injection drug users
Direct-acting antiviral agents

ABSTRACT

Background: People who inject drugs (PWID) constitute 10 million people globally with hepatitis C virus, including many opioid agonist treatment patients. Little data exist describing clinical outcomes for patients receiving HCV treatment with direct-acting antiviral agents (DAAs) in opioid agonist treatment settings.

Methods: In this retrospective observational study, we describe clinical outcomes for 50 genotype-1 patients receiving HCV treatment with triple therapy: telaprevir ($n = 42$) or boceprevir ($n = 8$) in combination with pegylated interferon and ribavirin on-site in an opioid agonist treatment program.

Results: Overall, 70% achieved an end of treatment response (ETR) and 62% achieved a sustained virological response (SVR). These treatment outcomes are nearly equivalent to previously published HCV outcomes shown in registration trials, despite high percentages of recent drug use prior to treatment (52%), ongoing drug use during treatment (45%) and psychiatric comorbidity (86%). Only 12% ($n = 6$) discontinued antiviral treatment early for non-virological reasons. Four patients received a blood transfusion, and one discontinued telaprevir due to severe rash.

Conclusions: These data demonstrate that on-site HCV treatment with direct-acting antiviral agents is effective in opioid agonist treatment patients including patients who are actively using drugs. Future interferon-free regimens will likely be even more effective. Opioid agonist treatment programs represent an opportunity to safely and effectively treat chronic hepatitis C, and PWID should have unrestricted access to DAAs.

Introduction

Hepatitis C virus (HCV) infection affects over 10 million people worldwide and is a major cause of morbidity, mortality, and healthcare expenditure (Nelson et al., 2011; Wong, McQuillan, McHutchison, Poynard, 2000). Although people who inject drugs (PWID) have high HCV infection rates and are likely to transmit HCV by sharing drug paraphernalia, few active or recent PWID have received treatment for HCV (Alavi et al., 2014; Grebely, Raffa, & Lai, 2009; Iversen et al., 2014). Some of the physician reluctance to treat HCV in PWID can be attributed to concerns about poor treatment adherence associated with ongoing substance abuse or comorbid psychiatric disorders, lack of urgency to address HCV, or pessimism regarding HCV treatment tolerability or effectiveness (Davis & Rodrigue, 2001; Edlin et al., 2001). Despite these concerns, several systematic reviews provide support for using interferon and ribavirin to treat HCV in patients with active substance abuse disorders (Aspinall et al., 2012; Dimova et al., 2013; Hellard, Sacks-Davis, & Gold, 2009). These studies show that PWID respond to HCV treatment as well as non-drug using patients.

All of these studies followed PWID who initiated treatment with pegylated interferon and ribavirin. First-generation direct-acting antiviral agents (telaprevir and boceprevir) when used in combination with pegylated interferon and ribavirin (triple therapy) are associated with significantly increased proportions

* Corresponding author at: Albert Einstein College of Medicine, Montefiore Medical Center, Division of General Internal Medicine, 111 East 210th Street, Bronx, NY 10467, USA. Tel.: +1 718 920 5946; fax: +1 718 561 5165.
E-mail address: alitwin@montefiore.org (A.H. Litwin).

http://dx.doi.org/10.1016/j.drugpo.2015.08.008
0955-3959/

of sustained virological response for both treatment-naive and treatment-experienced patients in large registration trials (Bacon et al., 2011; Jacobson et al., 2011; Poordad et al., 2011; Zeuzem et al., 2011). However, triple HCV regimens are associated with increased dosing frequency (three times daily), pill burden (up to 20 pills daily), co-administration of specific dietary requirements (e.g. 20 g fat with telaprevir), as well as additional significant additive and novel side effects (anemia, nausea, severe rash, anal discomfort, and dysgeusia). Indeed, there have been no published real-world reports of HCV treatment outcomes in people who use drugs or opioid agonist treatment patients treated with direct-acting antiviral agents. We have previously demonstrated high percentages of SVR (40% in genotype 1) in opioid agonist treatment patients initiating treatment with pegylated interferon and ribavirin at a comprehensive on-site opioid agonist treatment program (Litwin et al., 2009). We now describe treatment outcomes of the first fifty patients initiating treatment with triple therapy on-site within the same opioid agonist treatment program.

Methods

Treatment setting

The Division of Substance Abuse of the Department of Psychiatry and Behavioral Sciences at Albert Einstein College of Medicine operates three large methadone maintenance treatment clinics in three Bronx communities, serving approximately 3200 adults with opioid dependence. In addition to comprehensive substance abuse treatment, clinics offer medical and psychiatric care to Medicaid-insured patients choosing on-site care. Approximately 65% of all patients are HCV-antibody positive, and 50% have chronic hepatitis C.

In October 1, 2010, New York State Department of Health funded Albert Einstein College of Medicine to continue to provide on-site hepatitis C medical, care coordination, treatment and supportive services for hepatitis C mono-infected persons at two of our Einstein clinics (n = 2000). HCV evaluation and treatment were provided by internists and physician assistants with expertise in both HCV and addiction medicine, using a standardized protocol. Patient with chronic hepatitis C were referred by medical and non-medical providers, HCV program staff (coordinator or health educator), and self-referred. HCV medical care was supervised by an experienced HCV provider (AL). Of the 2000 patients, 850 patients were eligible to receive medical care on-site due to having appropriate Medicaid managed care insurance coverage, and approximately 425 patients had chronic hepatitis C. Most patients with current psychiatric comorbidities were eligible for HCV treatment. Formal psychiatric criteria were used to determine treatment ineligibility (e.g. active suicidal ideation, any psychiatric condition significantly disrupting activities of daily living, and nonadherence to psychotropic medications). HIV/HCV coinfected patients also received on-site HIV-related primary care, including highly active antiretroviral treatment when appropriate.

Staging was performed either by Fibrosure or liver biopsy. The treatment program is explained in detail in an earlier publication (Litwin, Soloway, & Gourevitch, 2005).

All patients were treated on-site at the opioid agonist treatment program and received weekly directly administered pegylated interferon injections. Many patients were treated within a group model of treatment (Stein et al., 2012), and some were treated with modified directly observed treatment (oral medications taken at the methadone window). All patients initiating treatment with telaprevir-based regimens were provided with monthly food bags containing fatty snacks (20 g of fat).

HCV treatment eligibility criteria

Patients with active drug or alcohol use, HIV/HCV coinfection, current psychiatric illness, and compensated cirrhosis were all eligible for HCV treatment.

Treatment

Our standardized protocol for genotype-1 infected patients called for treatment with either telaprevir or boceprevir plus once-weekly pegylated interferon in combination with twice-daily ribavirin for either 24 or 48 weeks (Ghany, Nelson, Strader, Thomas, & Seeff, 2011). Genotype-1 infected patients received treatment with these regimens because it was endorsed by AASLD/IDSA, was the standard of HCV care in the United States, and covered by Medicaid. Pegylated interferon alfa-2a was dosed subcutaneously at 180 ucg weekly. The dose of ribavirin was weight-based and taken with food: 1000 mg if $\leq$75 kg or 1200 mg if $>$75 kg. Patients received telaprevir for 12 weeks – 750 mg three times daily with high-fat food (20 g of fat). After results of the Optimize trial were available, patients received telaprevir at a dose of 1125 mg twice daily (Buti et al., 2014). Patients starting boceprevir-based treatment received 800 mg three times daily taken with food after a four week lead-in period of pegylated interferon alfa-2a in combination with ribavirin. Standard futility rules were applied, and patients without cirrhosis were eligible for response guided treatment if they achieved an extended rapid virological response (Ghany et al., 2011).

Key definitions

Rapid virological response (RVR) is an undetectable viral load at week 4 after initiating either telaprevir or boceprevir.

Extended rapid virological response (eRVR) is an undetectable viral load at weeks 4 and 12 after initiating either telaprevir or boceprevir.

End of treatment response (ETR) is an undetectable viral load at the end of treatment.

Sustained virological response (SVR) is an undetectable viral load 24 weeks after completion of treatment.

Psychiatric diagnoses (depression, anxiety, psychosis, bipolar disorder, and post traumatic stress disorder) were determined by either psychiatrists or internists. Internists determined psychiatric diagnoses by structured interviews, screening tools (e.g. PHQ-9), and patient self-report. Psychiatrists determined psychiatric diagnoses by structured interviews.

Medical comorbidities included diabetes mellitus, hypertension, asthma, chronic obstructive pulmonary disease, renal disease, seizure disorder, thyroid disease, congestive heart failure, coronary artery disease, or HIV.

Recent drug use was defined as at least one positive monthly urine toxicologies (either opioids, cocaine, or benzodiazepines) in the 6 months preceding HCV treatment initiation. Patients with prescriptions in the chart for either opioids or benzodiazepines were not considered to be using drugs if toxicologies were positive for opioids and benzodiazepines, respectively.

Active drug use was defined as any positive urine toxicology within 1 month of HCV treatment initiation.

Drug use during treatment was defined as any positive urine toxicology during the period of HCV treatment.

Alcohol abuse or dependence was determined through review of most recent Addiction Severity Index-lite (administered by substance abuse counselor on intake and annually), problem list and most recent annual physical exam.

Tobacco use was determined through review of most recent annual physical exam.