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Assessing Candidacy for Acute Hepatitis C Treatment Among Active Young Injection Drug Users: A Case-Series Report

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Abstract

Treatment for acute hepatitis C virus (HCV) infection has significantly better outcomes than treatment for chronic infection. The short window of the acute period poses challenges for young injection drug users (IDU), who are at highest risk of HCV infection, to demonstrate treatment candidacy. We recruited patients with acute HCV from a prospective cohort study to examine clinical and behavioral issues related to treatment candidacy. We report on outcomes and how nursing case management affected candidacy. All 5 acutely-infected participants reported daily drug use at baseline. All established primary care and decreased their drug use. None received treatment for their acute infection; one was treated within 12 months of infection. . Establishing treatment candidacy for young IDU in the acute phase involves various health domains. Acute infection's short period poses many challenges to establishing candidacy, but it is a window of opportunity to engage young IDU in health care.

Keywords

acute hepatitis C infection; hepatitis C virus treatment; injection drug use; youth

Recent research has shown that hepatitis C virus (HCV) infection treated during the acute phase is significantly more effective at achieving a sustained virologic response (SVR) than treatment at later stages of infection (Corey, Mendez-Navarro, Gorospe, Zheng, & Chung, 2010; De Rosa et al., 2007; Jaeckel et al., 2001; Kamal, 2008; Santantonio, Wiegand, & Gerlach, 2008). Treatment of acute HCV is associated not only with higher rates of viral eradication than treatment initiated in the chronic stage of the infection, but the course of treatment is also shorter and better tolerated (Corey et al., 2010; Kamal, 2008). Randomized controlled trials of treatment for acute HCV showed higher rates of SVR when treatment initiation took place 8 weeks after infection (87%) compared to 1 year after infection (53%; Nomura et al., 2004). Reviews of literature pertaining to the treatment of acute HCV have found that SVRs obtained during treatment in the acute phase of infection ranged from 75–100%, compared to SVRs ranging from 50–80% in treatment for chronic HCV infection

(Corey et al., 2010; Kamal, 2008; Santantonio et al., 2008). However, these trials were conducted in highly select groups, drawing mostly from needle stick injuries and few injection drug users (IDUs). IDUs, however, are the population at highest risk for contracting HCV (Centers for Disease Control and Prevention, 2010). Transmission rates are high in the early years of injecting (Hagan et al., 2006), potentially a result of poorer injection practices and less access to prevention programs; for instance, syringe exchange may be less likely to be used.

Although recommendations from the National Institutes of Health (2002) and other updated practice guidelines (Ghany, Strader, Thomas, & Seeff, 2009; Wilkins, Malcolm, Raina, & Shade, 2010) no longer summarily exclude active IDU from HCV treatment recommendations, few studies have included IDU in their trials (Kamal, 2008). The lack of data on the population most impacted by HCV has compounded the concerns of clinicians already reluctant to treat IDU for HCV infection (Edlin et al., 2005). Preclusive factors include the safety and logistics of medication administration and monitoring, the possibility of reinfection, the risk of interferon exacerbating co-existing mood disorders, and concerns that continued drug and alcohol use will compromise treatment efficacy (Dalgard, 2005; Grebely et al., 2006; Holtzheimer et al., 2010; Santantonio et al., 2008).

Several non-randomized studies of IDU have demonstrated results nearing the efficacy of HCV treatment for non-IDUs, including a 2007 study conducted in Italy of 23 IDUs treated for acute HCV infection (De Rosa et al., 2007). Seventeen of these patients achieved SVR, demonstrating no statistical difference in acute HCV treatment outcomes between IDU and non-IDU. Similar results have been demonstrated treating IDUs for chronic HCV, notably by Sylvestre and colleagues (2004), and Rifai, Moles, Lehman, and Van der Linden (2006). One random controlled trial of acute HCV treatment efficacy among active IDU has been conducted. Although complete results have not yet been published, early results suggest that the researchers did find successful treatment outcomes nearing those of the non-drug-using population (Holtzheimer et al., 2010). None of these studies examined the effect of age on treatment outcomes.

Acute HCV infection in active young IDUs is easily identifiable using dual testing algorithms including anti-HCV and RNA tests (Page-Shafer et al., 2008). Although many barriers currently exist that impede candidacy and interest in HCV treatment among young adult IDU with chronic infection (Hagan et al., 2006), treatment outcomes are improved with younger age (Asselah et al., 2010). Despite this, little information is available regarding candidacy for treatment of acute HCV infection in young persons. We studied newly infected young IDU enrolled in prospective studies of HCV infection and evaluated clinical and behavioral factors potentially affecting treatment candidacy. In this research report, we present a case series describing the first five participants, including descriptions of individual factors affecting treatment candidacy and how a weekly acute HCV education group and individualized nursing case management affected candidacy outcomes.

Methods

Study Population and Eligibility

Subjects were participants in an ongoing study of HCV in young IDU, the `You Find Out' (UFO) Study in San Francisco, that has prospectively followed young (< age 30), active IDU at risk for HCV and with newly acquired HCV, described in detail elsewhere (Page et al., 2009). In brief, using street outreach methods, young active IDU were screened for anti-HCV and HCV RNA; eligible HCV negative participants were invited to enroll in follow-up, which included quarterly testing for HCV infection by anti-HCV (EIA-3, Ortho Clinical Diagnostics, Raritan, NJ) and HCV RNA using qualitative nucleic amplification testing

(NAT; Procleix HIV-1/HCV test, Gen-Probe Inc., San Diego, CA). Participants found to have new HCV infections were offered enrollment into a second study assessing natural history factors associated with spontaneous resolution of acute HCV infection.

Participants eligible for our observational study assessing Acute Treatment Candidacy (ATC; described here) were UFO Study cohort subjects with documented acute HCV infection defined by either: (a) a new anti-HCV positive test result with a negative anti-HCV result in the prior 6 months and alanine aminotransferase (ALT) at least three times the upper limit of normal; or (b) anti-HCV negative and HCV RNA positive test results with a repeatedly positive (confirmatory) HCV RNA testing by either NAT or HCV viral load. Potential participants were excluded if they were unwilling or unable to provide informed consent. Each participating subject was remunerated $20 for each of 12 scheduled study visits over a 6-month period. All subjects gave informed consent to participate in this study and all study procedures were approved by the Institutional Review Board of the University of California, San Francisco.

Procedures

Participants were assessed at baseline, 3, and 6 months. Each assessment period consisted of two study visits 1 week apart and included: (a) interviewer- and self-administered surveys concerning subjects' drug and alcohol use, mental health, and knowledge, attitudes, and beliefs regarding HCV infection and treatment; (b) a brief medical history, symptom review, and physical exam; (c) laboratory testing, including phlebotomy for blood testing and urine specimen collection for toxicology and pregnancy screening; (d) individual consultation with a study clinician; and (e) medical and social service referrals. Surveys, history and physical, and laboratory testing occurred at the initial visit. Results of laboratory tests, individual clinical consultation, and referrals were discussed during the second study visit of each assessment period. The clinician provided the subject with written information about acute HCV, the risks and benefits of early HCV treatment, treatment adherence, and re-infection risk. Individualized nursing assessment and case management offered referrals for primary medical and mental health care, as well as drug and alcohol treatment as indicated. The investigators included a study physician; the study nurse who collected the bulk of the data for the study, with some assistance from counselors; and other nursing staff. Subjects returned for follow-up assessments at 3- and 6-month intervals to undergo similar study activities completed at the initial assessment (above), and for follow-up on the outcome and impact of referrals.

In addition, all participants were invited to participate in an acute HCV education and support group, which met weekly during evenings at the research site. Sessions included HCV prevention education to teach attendees about HCV disease, treatment, and prevention, as well as to provide an opportunity for young IDU to discuss their concerns about HCV. HIV prevention counseling was included in the education sessions. Participants in the ATC study were not required to take part in the support group as a condition of the study, or to receive medical referrals, or nursing case management. Participants referred for HCV treatment were asked to sign a release of medical information so that their clinical eligibility test results could be communicated with the treating provider and so that treatment outcomes could be documented by the study. Provision of HCV treatment was not a study activity, and completing the treatment referral or signing a release of medical information were not requirements for ATC study participation.

Measures

Substance use assessments—Self-reported drug and alcohol use over three time periods (ever, previous 3 months, and previous week) were obtained from surveys

administered as part of the UFO Study. Participants were queried about non-injected and injected use of heroin, methamphetamine, crack, cocaine, prescription opioids, benzodiazepines, and alcohol, as well as drug or alcohol treatment in the week prior to the ATC assessment.

The Alcohol Use Disorders Identification Test (AUDIT) was administered to identify participants at risk for hazardous drinking or active alcohol use disorders, including alcohol abuse or dependence (Bradley et al., 2007; Saunders, Aasland, Babor, De La Fuente, & Grant, 1993)?. The AUDIT, a screening tool developed by the World Health Organization (WHO), is a 10-item tool used to assess problem drinking and alcohol dependence (Saunders et al., 1993). The AUDIT assessment is a preferred tool for persons with HCV and has been validated with youth and with drug users (Cook, Chung, Kelly, & Clark, 2004; Skipsey, Burleson, & Kranzler, 1997; Sylvestre et al., 2004). The AUDIT collects data on the quantity and frequency of consumption, as well as alcohol-related problems that have occurred within the previous year. A score of 8 or more indicates harmful or hazardous drinking; a score of 13 for females or 15 for males indicates alcohol dependence (Saunders et al.. 1993).

Study participants also completed the Stages of Change Readiness and Treatment Eagerness Scale (SOCRATES 8D), an instrument designed to assess readiness for change in substance users that has been validated as an effective screening tool in the primary care setting (Maisto et al., 1999). The instrument yields three scale scores in the areas of recognition, ambivalence, and taking steps, related to drug or alcohol use behaviors and readiness to change. Raw scores for each category in the 70th decile or greater are considered “high.” Scores in the 30th decile or below are considered “low.” Those with high recognition scores acknowledge that they have problems related to their use, tending to express a desire for change and a perception that harm will occur if they do not change. Those with low recognition scores (< 30) deny that their use causes problems and do not express a desire to change (Miller & Tonigan, 1996). High ambivalence scores reflect uncertainty of the individual's belief in his or her ability to control the use or the impact use has on her- or him-self or others. High scores reflect contemplation, a stage of change. Low ambivalence scores can suggest that the individuals “know” they are drug dependent and have a problem, or that they “know” they are not drug dependent and do not have a problem with drug use. Ambivalence scores are evaluated in conjunction with recognition scores (Miller & Tonigan, 1996).

High scores in the taking steps category suggest that the individual is already doing positive things to make behavior changes. A high score in this category has been found to be predictive of successful change (Miller & Tonigan, 1996). Low scorers report not taking action to change current drug use habits.

Mental health and social support assessment—Characteristics, attitudes, and symptoms of depression were measured using the Beck Depression Inventory (BDI), a 21-item self-administered inventory that has shown good reliability and consistency among young people and substance users (Seignourel, Green, & Schmitz, 2008; Osman, Barrios, Gutierrez, Williams, & Bailey, 2008). Scores of 10 to 18 indicate mild to moderate depression; scores of 18 to 29 indicate moderate to severe depression; scores above 29 indicate severe depression.

The Primary Care Post-Traumatic Stress Disorder (PTSD) Screen is a 4-item screen designed for use in primary care and other medical settings to screen for PTSD (Kimerling, Trafton, & Nguyen, 2006). Questions focus on potential responses to traumatic events, such as sleeplessness or nightmares due to an event, but not on specific traumatic events that may

have occurred. The results of the PTSD screen are considered positive if the respondent answers “yes” to any 3 items.

The presence of emotional and tangible support (through the provision of finances, food, or shelter) was determined by a series of seven self-administered questions adapted from the Norbeck Social Support Questionnaire (Gigliotti, 2006). The standard Norbeck Social Support Questionnaire was adapted for this study. Participants were asked to consider if anyone in their lives provided a particular aspect of social support rather than considering individuals in their personal networks. Subjects identified as having emotional and tangible support answered “yes” to at least five questions; persons who did not have such support had fewer than five “yes” answers (Gigliotti, 2006).

Laboratory tests—We conducted testing for HCV using anti-HCV (EIA-3 -Ortho Clinical Diagnostics, Raritan, NJ), HCV RNA quantitative viral load (Roche Amplicor Monitor HCV 2.0, Roche Molecular Systems, USA), qualitative HCV RNA using NAT testing (Procleix HIV-1/HCV test, Gen-Probe Inc., San Diego, CA), and HCV genotype (LiPA Line Probe Assay; Bayer Diagnostics, Tarrytown, NY). Additional blood tests included serological testing for HIV-1, HBsAg, anti-HBc, anti-HBs, anti-HAV (total); biochemical markers of liver injury and assessment of hepatic function including alanine aminotransferase (ALT), albumin, bilirubin, and prothrombin time; white blood cell counts with differential, hemoglobin, hematocrit, and platelets; thyroid function tests; and serum creatinine, ferritin, antinuclear antibody, alpha-fetoprotein, and ceruloplasmin. Urine toxicology screening tests were used to detect metabolites indicative of recent use of marijuana, methamphetamine, opiates, cocaine, and benzodiazepines; urine pregnancy testing was conducted among all females. HIV counseling and testing was done on a quarterly basis.

Acute HCV infection was defined as either: (a) a new anti-HCV positive test result following a negative anti-HCV result in the previous 3 months and ALT at least three times the upper limit of normal, or (b) anti-HCV negative and HCV RNA positive test results with a repeatedly positive (confirmatory) HCV RNA test by either NAT or quantitative HCV viral load. The date of HCV infection was estimated as the midpoint between last negative HCV RNA test and the first positive HCV RNA test or anti-HCV test (whichever was first). Spontaneous clearance of HCV infection was defined as two sequential negative qualitative HCV RNA tests 1 month apart following a confirmed new infection.

Treatment candidacy—We determined clinical eligibility for HCV treatment based on the subject's most recent laboratory, psychiatric, and behavioral data. Criteria were adapted from chronic HCV treatment guidelines developed by the Veteran's Administration (Yee, 2006). Laboratory criteria included: persistent HCV RNA; absolute neutrophil count (ANC) > 1.5 k/mm^3, platelet count > 70 k/mm^3 and no evidence of uncompensated liver disease, uncontrolled diabetes, or autoimmune disease. Eligible females required a negative urine pregnancy test and testament to a reliable contraceptive method. Psychiatric criteria consisted of: BDI score < 10, negative PTSD screen, and no current serious suicidal ideation or suicide plan. A participant with a BDI score between 10–18 was considered clinically eligible if s/he had completed a mental health referral and had been evaluated for a major depressive disorder. A participant with a BDI score between 18–29, a diagnosis of a major depressive disorder, or a positive screen for PTSD was considered clinically eligible, if s/he was actively engaged in mental health services, including antidepressant medication, education, cognitive behavioral therapy, and/or other social supports. Substance use criteria required an AUDIT-C score less than 8. Participants with scores of at least 8 could be considered eligible for acute HCV treatment if they were actively engaged in alcohol use treatment or participating in counseling and education to learn about the risks of alcohol use

related to HCV treatment and to reduce current alcohol use. Current injectors were clinically eligible if they were actively engaged in substance use treatment or participating in counseling and education to learn about the risks of continued use related to HCV treatment and how to reduce further HCV transmission and re-infection. Other criteria considered in determining eligibility included housing status and ability to attend scheduled appointments.

Results

Between January 2007 and September 2008, we identified and enrolled six UFO Study participants with acute HCV infection. Two participants were female; four were male. Their ages ranged from 20–31 years, five were Caucasian, one African American. Two of the participants were sex and injecting partners. All participants reported daily injection of opiates or stimulants at baseline. Methamphetamine, heroin, and crack cocaine were the most frequently used drugs. One participant did not return after study enrollment and was lost to follow-up. None of the subjects in this study were infected with HIV and prevention counseling was included in all study activities. The clinical course and characteristics of the five remaining participants are reported in detail below. Demographic and baseline characteristics are summarized in Table 1, and clinical and behavioral characteristics of subjects during acute HCV infection are shown in Table 2.

Patient 1

Patient 1 reported regular (weekly) injection and non-injection methamphetamine use and daily marijuana use at baseline. This patient reported sharing equipment with injectors of known and unknown HCV status. She had a prior history of heroin, cocaine, and crack use. She had received methadone treatment in the past and reported no heroin, crack, or alcohol use in the previous 3 months. She presented with new anti-HCV test results and ALT elevation of 360 IU/L. She was asymptomatic. Her last negative anti-HCV negative test had been 98 days prior to the positive antibody test, resulting in an estimated 49 days to seroconversion. Quantitative HCV RNA was 38.7 million IU/mL and ALT peaked at 785 IU/ml 16 weeks after her estimated initial infection. Her genotype was 1a.

Patient 1 had no significant medical history, including decompensated liver disease or autoimmune disorders. She lived in a family shelter with her young daughter. Baseline screening for depression and PTSD were negative. Emotional and tangible support was perceived as high by the patient. Urine toxicology confirmed methamphetamine and cannabis use, and a urine pregnancy test was negative. Her ANC was greater than 1.5 k/mm^3, platelet count was greater than 70 k/mm^3, and she had no clinical or laboratory evidence of uncompensated liver disease, uncontrolled diabetes, or autoimmune disease. She did not demonstrate serologic immunity against HAV and HBV despite completing the vaccine series several years prior to this study. Booster vaccinations were given. No referrals were accepted at baseline as this patient stated that she had medical care and did not desire substance use or mental health treatment. Given clinical findings at baseline, this patient could be considered a treatment candidate. She expressed interest in receiving treatment for her acute HCV.

At 3-month follow-up, Patient 1 reported continued injection drug use in the 3-month interval, but none in the week prior to the study visit. Urine screening was negative for methamphetamines. Alcohol, depression, and PTSD screens remained negative, while emotional and tangible support remained high. Her SOCRATES 8D score showed very low scores for recognition, ambivalence, and taking steps, suggesting that she was not prepared to undergo drug treatment. Qualitative and quantitative HCV RNA testing were both negative. She was referred to a case manager specializing in homeless families for housing access at this visit. At 6-month follow-up, she reported no injection drug use in the previous

3 months, but tested positive for methamphetamines on urine toxicology. Her SOCRATES scores continued to demonstrate very low recognition, ambivalence, and taking steps to address her drug use. She continued to attend the HCV support group on a regular basis and secured permanent housing through the homeless families' case management referral. HCV RNA tests were again negative at month 6.

Patient 2

Patient 2 reported daily methamphetamine injection and daily cannabis use at baseline. He reported sharing equipment with injectors of known and unknown HCV status and having unprotected sex with a female IDU who was also acutely infected with HCV. Acute HCV infection was determined after he presented with repeatedly positive HCV RNA testing by NAT without antibody seroconversion. At that time, quantitative HCV RNA was 1.1 million IU/mL. He was asymptomatic and his ALT level peaked at 944 IU/ml 3 weeks after his first positive NAT test. Anti-HCV seroconversion was detected an estimated 21 days after infection. His genotype was 1a.

Patient 2 had a history of heroin and cocaine use, but at study enrollment only reported methamphetamine and cannabis use. He had never received drug or alcohol treatment. Urine toxicology was positive for methamphetamines. Baseline AUDIT, BDI, and PTSD scores were 0, 3, and 1, respectively; and emotional and tangible support were high. He had received psychological counseling in his life, but had not received counseling or mental health support in more than 4 years. He demonstrated serologic immunity against HAV and HBV. His ANC was 1.3 k/mm^3 (low) and his platelet count was greater than 70 k/mm^3; he had no clinical or laboratory evidence of uncompensated liver disease, uncontrolled diabetes, or autoimmune disease. Drug treatment, primary care, and mental health referrals were offered at baseline. While Patient 2 expressed interest in receiving treatment for his acute HCV, he did not accept any referrals at that time. Clinically, he was determined to be a candidate for treatment of acute hepatitis C.

At 3-month follow-up, Patient 2 was still HCV RNA reactive with a viral load of 4.2 million IU/mL. He reported a decrease from daily methamphetamine injection to weekly use. His SOCRATES scores were “very low” in all three categories – recognition, ambivalence, and taking steps. Based on his continued viremia, his interest in receiving treatment, his efforts to change his drug use, his attendance at the weekly HCV education group, and laboratory values, he was still considered a candidate for acute HCV treatment. He was referred to a community health clinic for primary medical care, mental health evaluation, and to prepare for treatment. He had difficulty attending appointments and had other problems with the mental health provider at the clinic, including presenting for an evaluation high on cannabis and not communicating with the provider when he did attend scheduled appointments. At 6-month follow-up, qualitative HCV RNA testing remained reactive and HCV viral load was 11.8 million IU/mL. He reported methamphetamine injection in the previous 3 months, but no injecting drug use in the previous week; urine toxicology was positive for methamphetamine. His SOCRATES scores continued to demonstrate “very low” recognition, ambivalence, and taking steps. AUDIT and BDI scores again were normal. However, he screened positive for PTSD and was offered, but declined, a new referral to mental health care. He was seen sporadically by his primary care physician and obtained stable, permanent housing. Appointments to evaluate and treat his chronic HCV infection were coordinated by the study nurse case manager, his primary care provider, and a consulting hepatologist, but he missed three consecutive appointments and did not receive treatment. He continued to attend the weekly support group.

Patient 3

Patient 3 reported daily injection and non-injection crack use, marijuana use, and prescription benzodiazepine abuse. Urine toxicology screens corroborated her self-report. She presented to the ATC study with evidence of acute viremic seronegative HCV infection, complaining of new onset fatigue and right upper quadrant pain with moderate hepatomegaly. She reported sharing injection equipment with her HCV-infected sex partner. Urine toxicology and pregnancy tests were negative. Her baseline AUDIT score was negative for alcohol dependence or abuse. Her BDI score was positive for moderate-severe depression and her PTSD score was positive. She was engaged in primary health care, therapy, and psychiatric treatment at enrollment. This participant reported multiple diagnoses of PTSD, general anxiety disorder, dissociative disorder, and clinical depression. She was being treated with antidepressants and weekly psychotherapy. She had no other significant health history. Baseline quantitative HCV RNA was 12,400 IU/mL; HCV genotype was 3a. She seroconverted to anti-HCV positive approximately 1.5 months after the estimated data of HCV infection. Peak ALT was 195 IU/mL 2 months after estimated infection date. At baseline, this participant was living in a single-room occupancy hotel (SRO) and on methadone maintenance (120 mg. every day). Hepatitis serology indicated prior immunization for HAV and HBV. Her SOCRATES scores for recognition and taking steps were “very low”; her ambivalence was “low,” suggesting that she did perceive some need to change her current habits.

At 3-month follow-up, she had lost her SRO housing and she was living in a shelter. At that time, she denied any crack or heroin use in the previous week or 3 months, but continued abuse of benzodiazepines. SOCRATES recognition continued to be “very low” and ambivalence was unchanged from baseline; however, she did demonstrate some progress in taking steps. The 3-month qualitative HCV RNA test was non-reactive and quantitative testing similarly showed RNA as undetectable (<5 0 IU/mL). Her BDI score improved, showing mild-moderate depression; she remained positive for PTSD. Her score for emotional and tangible support drastically dropped, possibly in association with her loss of housing. She reported ongoing contact with her primary care physician, psychiatrist, and therapist.

At 6-month follow-up her housing had been re-established. She continued to abstain from crack, but her benzodiazepine abuse continued. Her SOCRATES score continued to show that she was taking steps to change her drug-use habits; however, her recognition continued to be “very low” and her ambivalence scores were in the “very low” range. Her BDI score increased again, suggesting ongoing high symptoms of depression, although still on medication and working with her health care team. Her social support score increased. Her AUDIT score was again negative. HCV RNA measures remained negative, indicative of HCV resolution.

Patient 4

Patient 4 presented to the ATC study approximately 18 days after his estimated date of infection with acute HCV viremia; he was seronegative and asymptomatic. He reported sharing injection equipment with an HCV-infected injection partner. Upon enrollment he reported daily polysubstance abuse, including injection and non-injection use of heroin, methamphetamines, and marijuana; he reported weekly crack, alcohol, and prescription opiate use. He had negative screens on the BDI, AUDIT, and PTSD screening tools. Baseline SOCRATES scores showed recognition and ambivalence in the “very low” range; however, his taking steps score was in the highest decile. He reported a moderate level of social support. His peak ALT was 143 IU/mL;. His baseline quantitative RNA was 490,000 IU/mL. He was genotype 1a. He had no significant prior health history. His baseline ANC

and platelets were within normal range. The patient was not immune to HBV and was started on a vaccination series. At baseline, this patient indicated that he was extremely interested in HCV treatment; he also reported that his father had died from liver disease caused by HCV infection.

At 3-month follow-up, the participant had started on methadone maintenance at 80 mg per day, and was working with a caseworker to establish housing. He self-reported continued use, albeit decreased, of heroin, methamphetamines, marijuana, and benzodiazepienes on a weekly basis. Recognition of and ambivalence about his drug use remained very low. Despite self-reported decreases in injecting frequency, his taking steps score dropped, placing him in the “medium” range. His AUDIT score decreased slightly. The participant's BDI score increased, demonstrating mild-moderate depression. He accepted referrals for primary care and mental health care. HCV RNA tests were non-reactive 2 months after enrollment. Difficulties with phlebotomy resulted in no further testing until 5 months after enrollment. At month 5, the participant was found to be HCV RNA reactive (using qualitative testing), and at month 6, HCV viremia was quantified at 1,820 IU/mL. While this was potentially a case of re-infection after spontaneous clearance of acute infection, it did not meet our definition of clearance. We proceeded as if this were the same infection identified at enrollment. His BDI score indicated no presence of depressive disorder. His PTSD and AUDIT scores were negative. Social support had not significantly changed from baseline. Housing had been established in an SRO with a guarantee from his caseworker that the housing would be stable until treatment was completed. He was then referred to hepatology for evaluation of treatment readiness. The participant was still injecting on a weekly basis at that point, again self-reporting a significant decrease from his practices at baseline. His 6-month SOCRATES scores placed him in the same categories for recognition, ambivalence, and taking steps as he had demonstrated at 3-month follow up.

At this point he was approximately 7 months after his estimated date of infection. The consulting hepatologist felt that the participant was not yet ready for treatment. He continued to attend weekly support groups and indicated great desire for treatment. After demonstrating a strong ability to follow through with appointments and reporting a complete cessation of injection use, he was cleared for treatment by the hepatologist and his primary care physician. Although no longer in the window for acute infection by this time, the participant began treatment with PEG-IFN and ribavirin combination therapy in March 2008. Initially, he demonstrated good tolerability to the treatment regimen, showing an early virologic response at 4 weeks. Fatigue, depression, and irritability began to bother him around that time, and an anti-depressant was added to his medication regimen. The participant received 11 weeks of combination therapy when he began to suffer from debilitating depression. A second antidepressant was added to his regimen. The patient, however, chose to stop taking the first anti-depressant at this point. He elected not to receive his PEG-IFN injection in the 12^{th} week of treatment and stopped taking ribavirin that same week. After discussions involving the participant, the treating physician, and the study nurse, treatment was stopped.

Patient 5

This patient presented to ATC as a seroconverter. He reported a single event sharing injection equipment with an HCV-infected partner and denied other risk activities. At baseline, he was homeless, reported daily injection and non-injection crack use, weekly heroin use, abuse of prescription opioids, and alcohol abuse. Baseline SOCRATES scores placed him in the very low range for recognition and ambivalence and showed a low level of taking steps. He had no primary care provider. His initial BDI score indicated moderate-severe depression. He had a positive AUDIT score for alcohol abuse or dependence; his PTSD was negative. This participant reported no evidence of symptomatic disease at

baseline. He reported a history of renal calculi and a recent related hospitalization. The participant had no immunity to HAV or HBV and was started on an immunization series. His baseline HCV viral load was 1,850,000 IU/mL. His peak ALT was 482 IU/mL, about 2 months after initial infection. He was genotype 1a. A referral was offered to primary care for the participant to meet with a therapist. At the initial study visit, this referral was declined. This participant reported no interest in treatment of his acute HCV infection.

At 3-month follow-up, the participant went to a detoxification center for his alcohol and crack use. He was released after 7 days and began using crack and opioids (injecting heroin and pills) again, but he reported a significant decrease in his alcohol use. SOCRATES scoring placed him in the “very low” range for recognition, ambivalence, and taking steps. At that time he accepted referrals for primary care. His 3-month BDI indicated mild-moderate depression; his PTSD score was negative. Qualitative HCV RNA testing was reactive; viral load was 163,000 IU/mL. He continued to come to paid study visits but still reported no desire for treatment.

At 6-month follow-up, the participant reported heroin use in the previous 3 months and no crack use. AUDIT score indicated no change in alcohol use in the previous 3 months. He demonstrated “medium” recognition, low ambivalence, and placed in the “very high” range for taking steps in relation to his drug use. His PTSD score was still negative, but he was found to have severe depression per his BDI score. The participant was given a mental health referral but did not follow through. HCV RNA qualitative tests remained reactive and his viral load at 6 months was 1,130,000 IU/mL. He continued attending the HCV education and support group sporadically despite completing the study enrollment period.

Discussion

This study described five young active IDU patients identified with acute HCV who were enrolled in HCV education and support, and assessed for HCV treatment candidacy and principal social and clinical outcomes. Of six acutely infected participants enrolled, one was lost to follow-up before any study activities could take place, two (both females) spontaneously cleared the virus, and one declined a referral for treatment. Of the two participants who did want treatment for acute HCV infection, only one actually initiated treatment. These results illustrate the real-world experiences and outcomes of care and follow-up for HCV-infected young IDU.

Both of the women in our patient group spontaneously cleared HCV, which may be interpreted as a higher than expected rate of clearance. Although the etiology of spontaneous clearance is not completely understood, females do clear HCV far more often than do males (Page, Hahn et al. 2009). The overall proportion (40%) of patients with HCV clearance is not interpretable as higher than normal due to the small sample size.

Treatment candidacy for acute HCV infection not only includes physiological factors that can indicate treatment readiness, such as evidence of virus in the blood and no contraindications to IFN therapy, but also a host of psychosocial factors that can impact treatment readiness. These factors include alcohol use, housing status, lack of social support, mental illness, access to health care, and continued drug use.

Even when this population willingly engages in support and education around acute HCV, becoming “good” candidates is an intensive process for both patients and their care providers. Active injectors, who are predominately homeless, lack primary care, and have uncontrolled mental health issues, are asked to change everything in a very short time. This study had the advantage of a very small population, which enabled the study nurse to provide the care, referrals, and advocacy needed to assist subjects in this process. There

were numerous barriers; individual, clinician, social, and psychological, as well as the difficulties presented by continued drug use. While the study aimed to address these barriers through the provision of a weekly support group and individualized nursing case management, the short time frame of the acute period and the multiple co-occurring disorders and social issues presented by each patient posed a significant challenge. It is important to note that, despite the presence of substance use and psychological co-morbidities in Patient 3, her primary care provider stated that he would be willing to treat this participant for her acute hepatitis C if she did not spontaneously clear the virus, given her active engagement with an intricate support system, including her physician, her psychiatrist, her therapist, and the study nurse. Although Patient 4 did not get clearance to begin treatment in the acute period, nor did he complete the duration of treatment, he continued to maintain an SVR more than 6 months after treatment was stopped.

While the acute period of HCV infection lasts only 6 months, enrollment into the ATC study did not always occur immediately after detecting the presence of acute infection; many participants were not able to make it to the group, where study activities took place, until as long as 68 days after the estimated date of infection. The assessments were then carried out over 6 months with an aim to referring to treatment before the 6-month acute window was up. The short time frame from initial infection to chronic infection calls for intense interventions targeted toward IDU in preparation for treatment of acute infection.

None of the participants enrolled in this study were insured, however, through individualized case management and patient advocacy, we enabled these patients to establish primary care while enrolled in the study. All participants demonstrated significant changes in regard to self-care in the context of the HCV education and support supplied by the ATC study. Consistent with other studies of drug users diagnosed with HCV, diagnosis had a significant impact on drug use behaviors and access to health care, regardless of actually getting treatment (Rifai et al., 2006). All five participants who completed the study were assigned primary care providers, engaged with mental health providers when identified as needing support, reported decreases in drug use, and worked to access housing.

The attention given to study participants by the study nurse may have had a significant impact on outcomes and improved the psychosocial candidacy of these patients. While it is important to acknowledge this, it may be that young IDU working to establish treatment candidacy for acute HCV infection need special attention, close monitoring, and support. Future research is needed to establish whether young IDU can establish acute treatment candidacy without the support of a nurse case manager.

We found that while clinical candidacy among this young, relatively healthy cohort was not difficult to establish, psychosocial candidacy posed a much greater barrier to treatment candidacy. Although guidelines on HCV treatment recommend treating active drug users on an individual basis, few primary care providers are comfortable with treating active injectors. More research is needed to understand the barriers to providers initiating treatment for active IDU and ways to improve provider uptake.

Conclusion

Even when systematic screening of at-risk youth for HCV infection provides rapid identification of acute infection, numerous barriers to HCV treatment exist. These include the chaotic lives of young, mostly homeless IDU; other health priorities; lack of access to primary care and mental health support; lack of stable housing; continued drug use; and provider reluctance to initiate treatment. In this young, relatively healthy population, clinical

candidacy is not difficult to establish, while psychosocial candidacy and provider willingness to treat present the most difficult barriers.

Comprehensive, multi-disciplinary programs combining primary care, drug treatment, and mental health as well as HCV treatment education and risk-reduction counseling are essential to establishing candidacy for young people in the acute stages of infection. Individual motivation is key to this process, as are access to supportive services, including community providers willing to treat this special population.

Clinical Considerations

- Frequent screening for HCV infection in young IDU, who are at the highest risk for infection, improves the capacity of providers to identify acute HCV infection.
- Establishing candidacy for treatment of acute HCV infection can be greatly enhanced through the use of educational support groups and nursing case management.
- Acute HCV infection provides a window of opportunity to engage young IDU in their health care needs, regardless of their acceptance of treatment.

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Table 1

Demographics and Baseline Data of Young Injection Drug Users (*N* = 5) With Acute Hepatitis C Infection and Without HIV Infection

Patient	Sex	Estimated Infection Date	First TMA Reactive Date	Days from Last Nonreactive RNA to First Reactive RNA*	Clinical Presentation	ALT Peak Value (IU/L)	Quantitative HCV RNA (viral iu/ml)	First Anti-HCV Positive Date	Days to Anti-HCV Seroconversion	HCV Genotype
1	F	10/10/06	11/28/2006	98	Asymptomatic	785	38,700,000	11/28/2006	49	1a
2	M	10/13/06	11/28/2006	91	Asymptomatic	944	1,110,000	1/30/2007	21	1a
3	F	4/27/07	5/8/2007	21	RUQ pain, nausea	195	13,700,000	6/26/2007	17.5	3a
4	M	4/6/07	4/24/2007	35	Asymptomatic	143	490,000	6/26/2007	17.5	1a
5	M	6/29/07	8/14/2007	91	Asymptomatic	482	1,850,000	8/14/2007	45.5	1a

Note. HCV = hepatitis C virus; TMA = [please provide definition]; RNA = ribonucleic acid; ALT = alanine aminotransferase; HCV = hepatitis C virus; RUQ = right upper quadrant

*Qualitative HCV RNA testing (NAT)

Table 2

Clinical and Behavioral Characteristics of Subjects During Acute Hepatitis C Infection

pt	Self-Reported Drug Use (at 0, 3, & 6 months)	Urine Toxicology Screen (at 0, 3, & 6 mo)*	Alcohol Use: AUDIT (at 0, 3, & 6 months)	BDI (at 0, 3, & 6 months)	PTSD (at 0, 3, & 6 months)	SOCRATES: Recognition	SOCRATES: Ambivalence	SOCRATES: Taking Steps	Referral Outcome	Number of Weekly HCV Education and Support Groups Attended During Study Enrollment*	Meets Treatment Candidacy Criteria? (Y/N)
1	0: Y 3: Y 6: N	0: M 3: M 6: M	0: 0 3: 0 6: 0	0: 1 3: 6 6: 0	0: 0 3: 0 6: 0	0: - 3: 14 6: 7	0: - 3: 8 6: 4	0: - 3: 20 6: 20	family housing obtained; others declined	14	Y
2	0: Y 3: Y 6: Y	0: M 3: M 6: M	0: 0 3: 0 6: 0	0: 3 3: 3 6: 6	0: 1 3: 0 6: 2	0: - 3: 16 6: 12	0: - 3: 10 6: 8	0: - 3: 28 6: 25	family housing obtained; 3 mental health visits; substance use treatment declined	11	N
3	0: Y 3: Y 6: Y	0: CK, C, B 3: B 6: B	0: 0 3: 0 6: 0	0: 29 3: 12 6: 33	0: 4 3: 4 6: 4	0: 26 3: 25 6: 23	0: 15 3: 15 6: 6	0: 26 3: 38 6: 36	Pt had mental health providers (therapists, psychiatrist) at enrollment	14	Y
4	0: Y 3: Y 6: Y	0: P 3: P 6: P	0: 20 3: 11 6: 13	0: 4 3: 12 6: 13	0: 1 3: 1 6: 0	0: 28 3: 26 6: 23	0: 10 3: 6 6: 4	0: 40 3: 37 6: 37	all accepted and followed through	22	Y
5	0: Y 3: Y 6: Y	0: P 3: P 6: P	0: 7 3: 6 6: 4	0: 29 3: 18 6: 12	0: 0 3: 2 6: 4	0: 27 3: 16 6: 34	0: 17 3: 4 6: 11	0: 31 3: 14 6: 39	all referrals accepted; used some detox programs, others not followed through to completion	12	N

Note. Y = yes; N = no; BDI = Beck Depression Inventory; AUDIT = Alcohol Use Disorders Identification Test; PTSD = Post- Traumatic Stress Disorder; M = Methamphetamine; CK = Cocaine; C = Cannabis; B = Benzodiazepine; P = Opiate; SOCRATES = Stages of Change Readiness and Treatment Eagerness Scale

BDI Score interpretive ranges: 0–13 = minimal depression, 14–19 = mild depression, 20–28 = moderate depression, and 29–63 = severe depression; AUDIT Score interpretive ranges: 0–8 = harmful or hazardous drinking, > 13 = alcohol dependence (females), > 15 = alcohol dependence (males); Social Support score interpretive ranges: < 5 yesses = low or no social or tangible support, > 5 yesses = social and/or tangible support presence; PTSD score interpretive ranges: 3 or more yesses = positive PTSD screen; SOCRATES 8D interpretive ranges: Recognition: 7–28 = very low, 29–31 = low, 33 = medium, 34–35 = high, > 35 = very high; Ambivalence: 4–11 = very low, 12–14 = low, 15–16 = medium, 17–18 = high, > 19 = very high; Taking Steps: 8–29 = very low, 30–32 = low, 33–35 = medium, 36–38 = high, > 38 = very high

*Total number of sessions offered: 24

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