SUPPLEMENT ARTICLE

Models of Care for the Management of Hepatitis C Virus Among People Who Inject Drugs: One Size Does Not Fit All

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One of the major obstacles to hepatitis C virus (HCV) care in people who inject drugs (PWID) is the lack of treatment settings that are suitably adapted for the needs of this vulnerable population. Nevertheless, HCV treatment has been delivered successfully to PWID through various multidisciplinary models such as community-based clinics, substance abuse treatment clinics, and specialized hospital-based clinics. Models may be integrated in primary care—all under one roof in either addiction care units or general practitioner–based models—or can occur in secondary or tertiary care settings. Additional innovative models include directly observed therapy and peer-based models. A high level of acceptance of the individual life circumstances of PWID rather than rigid exclusion criteria will determine the level of success of any model of HCV management. The impact of highly potent and well-tolerated interferon-free HCV treatment regimens will remain negligible as long as access to therapy cannot be expanded to the most affected risk groups.

Keywords. hepatitis C; integrated care; management; IDU; people who inject drugs.

In developed countries, the main driving force behind hepatitis C virus (HCV) infections is injection drug use. Worldwide, approximately 10 million injection drug users are HCV antibody positive. The midpoint HCV antibody prevalence in this at-risk group is 67.5% [1]. Treatment uptake rates remain low in the drug-using population in particular [2–6]. This major at-risk group of people who inject drugs (PWID) acts as a virus reservoir. They are not yet reached well enough with HCV care. Because PWID will be responsible for the main burden of HCV-induced disease in the future in developed countries, improved access to care for this population must be a priority in the public health efforts of the next few years. Increasing treatment uptake rates in PWID has the potential to significantly reduce prevalence rates and the burden of HCV-related liver disease [7–9]. The impact of highly potent and well-tolerated interferon-free HCV treatment regimens will remain negligible as long as access to therapy cannot be expanded to the most affected risk groups [10]. Reviewing the literature, we can identify a number of different models of hepatitis C care for PWID, which are presented below.

BARRIERS TO CARE ON THE TREATMENT-SETTING LEVEL

Many barriers to HCV care in PWID have been identified [11–13]. One of the major obstacles is the lack of treatment settings that are suitably adapted for the needs of this vulnerable population [14, 15]. Another hurdle is that, when transferred to secondary or tertiary care units, PWID will often miss appointments and/or risk getting exposed and stigmatized [15–17]). Furthermore, limited infrastructure for HCV therapies and a lack of HCV knowledge in addiction clinics and primary care units prevent these institutions from providing treatment to PWID [18–20].

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MULTIDISCIPLINARY APPROACH

HCV treatment has been delivered successfully to PWID through various clinical models, such as specialized hospital-based clinics, drug detoxification program centers, opioid substitution therapy centers, and community-based clinics. What all these models have in common is their multidisciplinary approach. Multidisciplinary teams generally include clinicians and nursing staff for clinical assessment and monitoring, drug and alcohol support services, psychiatric services, social work, and other social support services (including peer support, if available) [21–26]. In a recently published meta-analysis, the involvement of multidisciplinary teams was positively correlated with sustained virologic response (SVR) rates in a multivariable meta-regression analysis [27].

INTEGRATED CARE: ALL ROADS LEAD TO ROME

Evidence from randomized controlled trials in integrated care settings is available for the integration of substance use and psychiatric treatment into primary medical care [28, 29]. In the past few years, a wide variety of different hepatitis C care models for PWID has been published. Almost every described model integrates specific measures to enhance different aspects of hepatitis C management (eg, assessment, treatment uptake, adherence, SVR) for drug users. In the following section, we provide an overview of different models and measures, according to at which point in the healthcare system they were offered.

INTEGRATED IN PRIMARY CARE: ALL UNDER ONE ROOF

The complex medical needs of PWID can be most effectively addressed by linking medical care with services for treatment of substance abuse [30, 31]. PWID are often not able to adhere to the highly structured secondary or tertiary care settings in which HCV assessment and treatment is usually provided, and HCV clinics are normally not adapted to the special, mainly psychosocial needs of the multimorbid population of PWID [15]. Integrating hepatitis C care into both primary addiction care and into general practices has proved to be effective [23, 26, 32–35].

HEPATITIS C CARE IN PRIMARY ADDICTION CARE UNITS

Several reports on the successful integration of hepatitis C treatment into opioid substitution clinics have been published. In a community-based opioid substitution treatment clinic in New York, a team consisting of an internal medicine specialist, a psychiatrist, nurses, and substance abuse counseling staff successfully administered hepatitis C treatment to PWID [23]. Patient groups commonly excluded from treatment in tertiary care units, such as patients with ongoing alcohol and drug use and psychiatric comorbidities, were successfully reached for HCV assessment and therapy in this model of integrated community-based care.

In a similar model in Vancouver, Canada, a team of physicians, specially trained nurses, addiction counselors, and on-site infectious diseases specialists provided hepatitis C treatment for PWID [21]. In addition, this multidisciplinary, community-based health clinic offered primary care and addiction services including methadone maintenance therapy (MMT), as well as needle exchange and counseling services. Treatment response and adherence rates achieved were comparable to those in non–drug users, despite ongoing drug use during treatment.

In London, United Kingdom, a consultant hepatologist and a nurse monthly reviewed patients of an addiction unit that the homeless attended to exchange needles and/or access healthcare services and opiate replacement treatment programs [36]. A team consisting of a specialized nurse and a psychiatrist treated PWID within this community-based setting. Neither intravenous drug use nor alcohol consumption affected the treatment outcome or the adherence rate of patients treated.

Moussalli et al report on their model implementing a multidisciplinary on-site HCV team into an addiction unit [37] and therefore providing efficient HCV assessment and treatment. The team consisted of general practitioners (GPs), a hepatologist on loan from a hospital, psychiatrists, nurses, and health counselors. The GPs' task was to treat the addiction and hepatitis C simultaneously, as instructed by the hepatologist.

Brunner et al demonstrated the feasibility of achieving favorable SVR rates in a collective of patients with mostly active ongoing drug use. They provided HCV and human immunodeficiency virus (HIV) assessment and therapy in a setting of opioid substitution treatment with integrated primary care–based multidisciplinary health services, all under one roof [38]. A part of participants were receiving prescription heroin therapy, and SVRs were also very favorable in this group.

In contrast, a Canadian study indicates the feasibility of integrated HCV care outside the context of addiction treatment programs, focussing mainly on substance users in whom opioid substitution is not indicated [34]. SVR rates (70% overall, n = 24) comparable to those of large randomized controlled trials were demonstrated for a collective of crack cocaine users with high rates of mental health comorbidities, participating in psychoeducational support groups and integrated, multidisciplinary, community-based health services.

GENERAL PRACTITIONER–BASED MODELS

In their analysis, Seidenberg et al proved the feasibility of providing hepatitis C treatment in the setting of a single-handed general practice offering opioid substitution treatment. A GP with additional training in both hepatitis C care and addiction medicine can set up a most efficient "all under one roof" model [32]. Merging different disciplines into one general practice forms the simplest model of them all. But offering everything under one roof requires a highly committed GP who is prepared to undergo training in addiction and HCV medicine.

Another primary care–based model in the United Kingdom involved a clinical nurse specialist in hepatitis working under the supervision of a consultant in infectious diseases [25]. They formed a partnership with the drug workers and GPs. Clients were referred to the clinical nurse specialist before or after their appointment with their GP or drug worker. The clinical nurse specialist assessed risk factors and carried out a pretest assessment. Treatment indication was then made by the whole team. Studies have shown that HCV treatment provided in this specialized multidisciplinary unit within a primary care setting proved to be as effective (SVR, 61%, n = 21) as HCV treatment provided in secondary care.

An innovative setting of GP-based integrated hepatitis C care provides the Extension for Community Healthcare Outcomes model [39]. In a prospective cohort study, HCV treatment provided at a tertiary care center was compared with HCV treatment provided by GPs supported and trained via telehealth technology. Similar rates of treatment success were achieved in both groups. Several factors were identified by the authors as potentially contributing to the success of the telehealth model: GPs have a more patient-centered approach, which improves the doctor–patient relationship as well as patient education; furthermore, they are able to offer more personal contact with the patient, hence enhancing adherence and side-effect management.

INTEGRATED HEPATITIS C MANAGEMENT IN SECONDARY/TERTIARY CARE SETTING

In a randomized controlled trial, the integration of psychologist-led interventions into a hepatology unit increased HCV treatment eligibility in an underserved population with mental health and substance abuse comorbidities [40]. The monthly interventions were individually tailored and based on motivation-enhancing techniques.

The effect of systematic consultations after each medical visit from a nurse vs standard clinical follow-up was evaluated in another randomized controlled trial conducted in a hepatology unit [41]. Patients in the intervention group were seen initially monthly, then every 12 weeks, by a nurse to evaluate the patient's understanding of the disease and side effects of treatment and to improve adherence to treatment. Adherence and SVR rates of patients with standardized nurse-led education sessions were significantly higher than in the group with standard clinical follow-up.

The involvement of a clinical specialist psychiatric nurse in a hepatitis C clinic can raise the rate of HCV assessment and treatment uptake [42]. The duty of the specialist nurse in the setting as described by Knott et al [42] was to administer specific psychotherapies including cognitive-behavioral and motivational therapies as well as prescribing psychopharmacological medication in collaboration with a psychiatrist.

An integrated, colocalized care model in which an internist addiction medicine specialist from an opioid substitution program was used in a hepatitis clinic proved to be an effective and efficient way to deliver HCV evaluation and treatment to patients in opioid substitution therapy [43]. Patients in MMT programs were referred to and assessed by the internist, under supervision of a hepatologist, and provided with HCV treatment in the hepatitis clinic. The involvement of both sites proved successful.

DIRECTLY OBSERVED THERAPY

Prior research has shown that treatment adherence and outcomes for other infectious diseases, such as tuberculosis and HIV, is improved among drug users when directly observed therapy (DOT) is administered at MMT programs [44, 45]. Several reports that have integrated DOT into opioid substitution clinics have been published. Most of these studies involved close collaboration between the secondary or tertiary setting that provided the HCV care and the opioid substitution clinic, which provided substance abuse treatment and directly observed dosing of pegylated interferon (peg-IFN) and/or ribavirin (RBV).

A randomized, multicenter trial of HCV treatment in methadone-maintained patients focused on directly observed peg-IFN, and compared weekly provider-administered (DOT) peg-IFN alfa-2a in combination with self-administered RBV to self-administered peg-IFN alfa-2a in combination with self-administered RBV. Although subjects in both study arms took RBV on their own, more subjects in the DOT peg-IFN group were >97% adherent with planned cumulative doses of both peg-IFN alfa-2a and RBV as well as the prescribed duration of treatment [46]. A small prospective study of 11 HIV/HCV-coinfected methadone-maintained patients receiving directly administered peg-IFN demonstrated an SVR rate of 18%. In a small prospective study of 17 HCV genotype 3–infected Norwegian methadone-maintained patients treated with peg-IFN alfa-2a plus RBV with observation of weekly peg-IFN dosing, an adherence rate of 100% and SVR rate of 94% were achieved [47]. A retrospective study evaluated the efficacy and tolerability of DOT with both peg-IFN alfa-2a and once-daily RBV in 49

injection drug users maintained on opiate agonist treatment (either methadone or buprenorphine) participating in a drug treatment program. SVR was achieved by 48 of 49 patients (98%) overall, including 20 of 21 (95%) genotype 1/4-infected patients. When receiving DOT, patients had daily access to and support from specialist physicians, nurses, and counseling services at the center. In addition, a 24-hour helpline was available to all patients for advice and support [48].

All of these studies involved close collaboration between the secondary or tertiary settings that provided the HCV treatment and opiate agonist treatment program, which provided substance abuse treatment and directly observed dosing of peg-IFN and/or RBV. Another randomized controlled trial in which both HCV and addiction treatment were delivered within the MMT program was designed to determine whether enhanced DOT with both peg-IFN alfa-2a plus RBV (only morning dose was observed) was more efficacious for increasing adherence and improving HCV treatment outcomes compared to standard DOT—weekly provider-administered peg-IFN alfa-2a plus self-administered RBV. Preliminary data (n = 40) observed a significant difference in adherence to RBV between the treatment arms (88% in enhanced DOT arm vs 77% in the standard DOT arm; $P = .02$) [23].

In the era of potent IFN treatments with potentially simplified dosing (eg, once-daily medications), DOT may be even more effective in improving both rates of adherence and SVR. In addition, a variety of clinical settings (eg, tuberculosis clinics, correctional settings, residential settings, homeless shelters, and substance abuse treatment clinics) may be suited to deliver DOT.

PEER-BASED MODELS OF TREATMENT

Group treatment of HCV and addiction are natural allies, as both peer- and provider-led groups are familiar, well received, and efficient in the substance abuse treatment setting. Like the self-help system, the peer group offers support and influences members to adopt healthy behaviors. The Organization to Achieve Solutions In Substance-Abuse peer-based HCV group began by organizing a small group of patients who had successfully completed HCV treatment and invited other interested patients as they were diagnosed or referred to care. Experienced peers co-led the group with a medical provider, and participants requesting a medical visit were called from the group and offered services including treatment [49]. A key predictor of treatment success was successful pretreatment engagement. This peer-based model led to successful treatment outcomes in many drug users. The peer-based model has been modified in various other settings including Vancouver, Canada, and the Bronx, New York [21, 23].

Group medical visits have been used since the 1990s as a tool in the management of chronic illnesses. Group medical visits combine provider-led group education and peer interaction with elements of individual patient visits. In a model of concurrent group treatment of HCV infection, patients initiated and continued treatment for the entire treatment course, experiencing the same milestones together (eg, 4-week viral load). This pilot program of concurrent group treatment delivered on-site within an MMT program was associated with high rates of SVR for genotype 1–infected patients treated with peg-IFN and RBV and promising early outcomes for patients treated with direct-acting antiviral agents [50]. This model was informed by existing peer-based programs [21, 23, 49] and an innovative model of group HCV treatment funded by the Meyers Primary Care Institute and delivered within a primary care center in Worcester, Massachusetts, where groups of patients (including drug users) were treated using peg-IFN in combination with RBV (T. J. McQuaid, personal communication, 13 November 2012).

DISCUSSION

Various models and settings for successful HCV care for PWID have been described and evaluated. Almost every model constitutes of different measures and disciplines. Therefore, the effects can only partially be compared. In addition, most evidence about these different management types are from observational studies with low numbers of patients. Only a few randomized controlled trials exist. Different models have not been directly compared to each other so far, only to the standard of care for the non–drug using HCV population. From the existing literature, it is not possible to identify how large the impact of the individual factors is on assessment, treatment uptake, adherence, and treatment outcome. A very recent meta-analysis of studies examining treatment outcome of at least 10 patients with injection drug use identified "treatment of addiction during HCV therapy" as a parameter leading to higher treatment completion [27]. This study did not further differentiate between different models of care.

Not all of the above described models are feasible for any healthcare system. Not every studied measure can be implemented into existing clinical settings. None of those models meets all the needs of the heterogeneous patient population of PWID. Therefore, it is important to have a variety of different models and approaches available. HCV treatment settings for PWID should contain a combined appropriate variety of political and financial measures that are practical in order to meet the specific needs of this vulnerable population.

CONCLUSIONS

A multidisciplinary approach is the foundation of each of the above-described settings. According to the current knowledge,

offering a range of different settings per region/city would be the best way to reach a maximum of those in need.

Close collaboration of all involved health professionals is crucial for every model to be successful. This collaboration must exceed the mere exchange of medical information and should involve joint training sessions. To adopt a nonjudgmental attitude toward PWID is essential for all parties involved. A high level of acceptance of the individual life circumstances of PWID rather than rigid exclusion criteria will determine the level of success of any model of hepatitis C management. In regions where need-adapted treatment settings are established, people who use drugs should always be referred to these institutions first.

Further research on the effects of the different models and measures is needed to provide further recommendations on the most efficient and cost-effective ways to provide HCV care to PWID.

Notes

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