Hepatitis C in injection drug users: It is time to treat

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Abstract

Injection drug users (IDUs) are at risk of hepatitis C virus (HCV) infection, due to needle and syringe sharing. Chronic HCV infection is a major cause of liver-related morbidity and mortality but can be cured with antiviral treatment leading to sustained viral response (SVR). It is well demonstrated that, when close cooperation between specialists in drug addiction and psychiatrists is assured, patients on maintenance treatment with methadone/buprenorphine can be treated for HCV with response rate, tolerability and side effects similar to those reported in non-IDUs. Current guidelines recommend that active injection drug use should not exclude patients from HCV treatment, but many services remain reluctant to treat IDUs. No significant pharmacodynamic interactions were reported between approved direct anti-viral agents (DAAs) and buprenorphine or methadone. Dose adjustments are not recommended; therefore DAAs appear to be the “perfect” therapy for patients taking opiate substitutive therapy. These suggestions have been recently recognized by the European Association for the Study of the Liver (EASL) and included in EASL Recommendations on Treatment of Hepatitis C 2016. Guidelines confirm that HCV treatment for IDUs should be considered on an individualized basis and delivered within a multidisciplinary team setting; a history of intravenous drug use and recent drug use at treatment initiation are not associated with reduced SVR and decisions to treat must be made on a case-by-case basis.

Key words: Hepatitis C; Drug users; Peg-interferon; Direct antiviral agents; Hepatitis C virus treatment

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Core tip: It is well demonstrated that injection drug users (IDUs) on maintenance treatment with methadone/buprenorphine can be treated for hepatitis C virus (HCV) with response rate, tolerability and side effects similar to those reported in non-IDUs. European Association for the Study of the Liver Recommendations on Treatment of Hepatitis C 2016 confirm that HCV treatment for IDUs should be considered on an individualized basis and delivered within a multidisciplinary team setting; a history of intravenous drug use and recent drug use at treatment initiation are not associated with reduced sustained
viral response and decisions to treat must be made on a case-by-case basis.

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INTRODUCTION

It is well established that injection drug users (IDUs) are at risk of hepatitis C virus (HCV) infection, due to needle and syringe sharing. Chronic HCV infection is a major cause of liver-related morbidity and mortality but can be cured with antiviral treatment leading to sustained viral response (SVR).

Treatment with pegylated interferon (PEG-IFN) and ribavirin (RBV) leads to SVR in 46%-52% of patients with genotype 1 (GT1) infection, and 76%-80% of those with genotype 2 or 3 (GT2/GT3) infection. It should be noted that these outcomes have been reported in large clinical trials that excluded patients with a recent history of drug addiction[1,2].

It is well demonstrated that, when close cooperation between specialists in drug addiction and psychiatrists is assured, patients on maintenance treatment with methadone/buprenorphine can be treated for HCV with response rate, tolerability and side effects similar to those reported in non-IDUs[3]. On the contrary, IDUs are still often considered to be poor candidates for HCV treatment due to concerns about psychiatric and other medical disorders as well as ongoing drug use, eventually leading to inadequate adherence to treatment and risk for reinfection. Similar concerns were previously raised with the advent of highly active antiretroviral therapy for HIV, but clinical studies suggested that DUs with HIV could achieve similar adherence to non users[4]. Current guidelines recommend that active injection drug use should not exclude patients from HCV treatment, but many services remain reluctant to treat IDUs.

In a meta-analysis, Aspinall et al[5] demonstrated that acceptable treatment outcomes can be achieved in patients with active drug injection who are eligible and committed to starting HCV treatment. Nevertheless, a considerable uncertainty remains around the risk of HCV reinfection following treatment. To assess reinfection risk, cases of HCV reinfection should be clearly distinguished from cases of HCV relapse. All studies in this review excluded individuals with a positive HCV test within 6 mo from end of treatment date, but, despite this, some of these individuals might have experienced early reinfection with HCV, rather than early relapse.

Further crucial points are the low prevalence of DUs referring to specialty clinics for evaluation of HCV related disease and the low percentage (20%) of DUs who have considered to start antiviral therapy[6].

DUs often cite discomfort encountered in conventional medical venues as a primary obstacle limiting pursuit of an HCV evaluation; consequently, HCV therapeutic effectiveness in DUs is an issue of treatment access, acceptance and adherence rather than drug efficacy[7].

Dimova et al[8] conducted a meta-analysis of studies on DUs treated with PEG-IFN/RBV to understand the role of different support services in assisting DUs to complete HCV therapy and improve treatment outcome. They observed that addiction-treated DUs have higher PEG-IFN/RBV completion rates than non-addiction-treated DUs and that the availability of support services during HCV treatment significantly increased the treatment completion rates. They reported a SVR rate of 55.5% among all PEG-IFN/RBV-treated DUs and of 53% for those treated for addiction during HCV treatment; these are comparable to those obtained in PEG-IFN/RBV registration trials[1,2]. Finally, they observed that involvement of multidisciplinary team led to higher SVR rates among DUs.

In accordance with these findings, we designed a collaborative programme between our hospital’s Hepatology Outpatient clinic and SERT (Drug Addiction Local Outpatient Service) to manage DUs with chronic hepatitis C together. This plan involves scheduled interdivisional meetings (including hepatologists, psychiatrists and SERT physicians) to evaluate IDUs with chronic hepatitis C and selecting the most suitable candidate to receive antiviral therapy. This plan provided IDUs with weekly direct/reserved access to SERT and the Hepatology Outpatient clinic to examine these IDUs’ hepatitis C status and to prescribe antiviral therapy. Ultimately, we treated 23 DUs for HCV related liver disease with PEG-IFN/ RBV with a 61% (14 patients) SVR rate (data not published).

Despite the possibility of reinfection, antiviral treatment to IDUs represents the most cost-effective policy option, at least in scenarios with prevalence of chronic disease less than 60%[9]. Unfortunately, despite attaining the optimal treatment outcome, it has been demonstrated that an increasing significant minority of IDUs continue to inject post-SVR at an intensity which leads to either hospitalisation or death and increased risk of reinfection[10].

This current scenario is mainly referred to “old” PEG-IFN based therapy, used in the last twenty years; however, it will be substantially modified by the arrival of interferon-free, new direct anti viral agents (DAAs). DAAs are expected to eliminate HCV in most persons who receive treatment, without significant side effects, even in advanced disease[11].

No significant pharmacodynamic interactions were
reported between approved DAAAs and buprenorphine or methadone. Dose adjustments are not recommended; therefore DAAAs appear to be the "perfect" therapy in patients taking opiate substitution therapy.[12]

These patients often suffer from psychiatric comorbidities and thus have contraindications to interferon-based antiviral treatment. They frequently have a borderline compliance to PEG-IFN while their compliance is excellent with respect to their daily visits at the low-threshold facility or pharmacy for ingestion of their opioid substitution therapy.

Recently, Schitz et al.[13] used DAAAs to treat fifteen consecutive IDUs with chronic hepatitis C (5 cirrhotics, 4 with METAVIR fibrosis score F3) and borderline compliance, together with opioid substitution therapy under direct observation of a physician or nurse at the "Ambulatorium Suchthilfe Wien" - a low-threshold drug treatment facility in Vienna, Austria. The results were excellent: all patients completed treatment, with 100% of SVR at 12 wk post the end of therapy. In our experience, in the last two years, we treated nine IDUs with advanced HCV related disease (89% cirrhotic; 3 GT1, 6 GT3) with DAA ± RBV obtaining an 89% SVR rate (data not published).

It should be stressed that successful treatment of these patients is beneficial not only for themselves but also for the general population because transmission of the virus is prevented.

These suggestions have been recently recognized by the European Association for the Study of the Liver (EASL) and are included in EASL Recommendations on Treatment of Hepatitis C 2016. Guidelines confirm that HCV treatment for IDUs should be considered on an individualized basis and delivered within a multidisciplinary team setting; a history of intravenous drug use and recent drug use at treatment initiation are not associated with reduced SVR and decisions to treat must be made on a case-by-case basis. The anti-HCV regimens that can be used in IDUs are the same as in non-IDUs; they do not require specific methadone and buprenorphine dose adjustment[14].

In conclusion, considering efficacy, tolerability and the indirect beneficial effect due to prevention of HCV transmission in the general population, at present, treatment of HCV related infection in IDUs appears mandatory: it is time to treat!

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