Review

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HCV epidemiology in high-risk groups and the risk of reinfection

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Summary

Injecting risk behaviours among people who inject drugs (PWID) and high-risk sexual practices among men who have sex with men (MSM) are important routes of hepatitis C virus (HCV) transmission. Current direct-acting antiviral treatment offers unique opportunities for reductions in HCV-related liver disease burden and epidemic control in high-risk groups, but these prospects could be counteracted by HCV reinfection due to on-going risk behaviours after successful treatment. Based on existing data from small and heterogeneous studies of interferon-based treatment, the incidence of reinfection after sustained virological response range from 2–6/100 person years among PWID to 10–15/100 person years among human immunodeficiency virus-infected MSM. These differences mainly reflect heterogeneity in study populations with regards to risk behaviours, but also reflect variations in study designs and applied virological methods. Increasing levels of reinfection are to be expected as we enter the interferon-free treatment era. Individual- and population-level efforts to address and prevent reinfection should therefore be undertaken when providing HCV care for people with on-going risk behaviour. Constructive strategies include acknowledgement, education and counselling, harm reduction optimization, scaled-up treatment including treatment of injecting networks, post-treatment screening, and rapid retreatment of reinfections.

Keywords: HCV; Reinfection; Epidemiology; PWID; MSM; Injecting drug use; Risk behaviours.

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Abbreviations: PWID, people who inject drugs; MSM, men who have sex with men; HCV, hepatitis C virus; IDU, injecting drug use; DAA, direct-acting antiviral; PY, person-years; NSP, needle/syringe provision; OST, opioid substitution treatment; HIV, human immunodeficiency virus; SVR, sustained virological response; RNA, ribonucleic acid; NGS, next generation sequencing; PCR, polymerase chain reaction.

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Introduction

In high-income countries, injecting risk behaviours among people who inject drugs (PWID) and high-risk sexual practices among men who have sex with men (MSM) are important routes of hepatitis C virus (HCV) transmission [1–3]. The majority of HCV patients in these populations have been chronically infected for many years and no longer take part in risk behaviour. Still, approximately one in four individuals with chronic HCV acquired through injecting drug use (IDU) have recently injected drugs [4] and thereby continue to be at-risk of new HCV exposure.

People with on-going risk behaviour have been successfully treated for HCV infection [5–7]. However, treatment uptake was low during the interferon (IFN) era, particularly among PWID [8,9]. With the current availability of tolerable and highly effective IFN-free direct-acting antiviral (DAA) drugs, increased treatment rates and subsequent rising reinfection rates might be anticipated in high-risk groups.

The potential impact of reinfection is of considerable clinical and public health interest [10–12]. High levels of reinfection could compromise individual treatment benefits but also impede population efforts to limit the HCV epidemic. This review provides updated information on the epidemiology of HCV infection and the risk of reinfection after successful treatment in high-risk groups of PWID and MSM. Particular emphasis is given to the section on reinfection, in which methodological considerations, incidence rates, risk factors, and preventive strategies are discussed.

HCV epidemiology in high-risk groups

HCV epidemiology among PWID

Prevalence of injecting

Globally, there are an estimated 14 million PWID (range 11.2–22.0 million) who are at-risk of HCV

infection as a result of injecting practices that may expose them to contaminated blood [13]. In most developed countries, IDU increased in the 1970s and 1980s and is now the main risk factor for HCV infection in these countries [14–16]. A recent review estimated the total number of current PWID across Europe to be 4.5 million [17].

Prevalence of HCV infection

Anti-HCV prevalence among PWID has been estimated at 67% worldwide, corresponding to 10 million anti-HCV positive PWID (range 6–15.2 million). While the prevalence varies greatly between countries, the majority report prevalence estimates above 60% [1]. This is the case in Europe, where the recorded midpoint prevalence estimates range from 21.1% to 90.5% with approximately half of all countries estimated to have 60% prevalence and above [1]. By region, the largest anti-HCV positive PWID populations are estimated to live in Eastern Europe (2.3 million) and East and South-East Asia (2.6 million); by country, the largest PWID populations are estimated to live in China (1.6 million), Russian Federation (1.3 million), and the USA (1.5 million) [1]. The total number of anti-HCV positive PWID in Europe is estimated to be 2.7 million, with 2.0 million being chronically infected (Fig. 1) [17]. A European systematic review estimates the viremic prevalence in PWID to be between 53% and 97% [18].

Key point

Combined harm reduction interventions (needle/syringe provision and opioid substitution treatment) could reduce HCV transmission among PWID, but effective interventions to prevent HCV transmission among MSM have not been developed.

Incidence of HCV infection

In contrast to prevalence, no pooled global estimate of incidence among non-incarcerated PWID has been reported; however, a number of studies have reported incidence rates among selected local PWID populations. A systematic review (comprising data from nine European countries) identified 11 studies that reported a median incidence of 26/100 person-years (PY) among current PWID in the community [18]. A review and meta-analysis of HCV in prisons found a summary incidence rate of 16.4/100 PY among prisoners with a history of injecting [19].

Risk factors for HCV acquisition

Sharing needle/syringes is acknowledged to be the main route of HCV acquisition among PWID since direct percutaneous exposure to contaminated blood from a needle/syringe has been demonstrated to transmit HCV [20–22]. The risk of transmission associated with a given sharing event would, however, depend on a number of factors, such as the quantity of blood inoculated and the viral load. Ancillary injecting equipment (spoons/cookers, filters, and water) may also become contaminated with HCV during the process of preparing and injecting drugs. Sharing cookers and filters has been associated with an increased risk of HCV in epidemiological studies: while the probability of HCV transmission associated with the latter is likely less than that for sharing needles/syringes, the generally higher prevalence of sharing cookers/filters may increase their contribution to the proportion of new HCV infections [23–25]. While there is evidence of a decline in the rates of needle/syringe sharing in some countries, this risk behaviour nevertheless persists among PWID [26–28]. A similar decline has been seen in Western European countries [29–32]; however, the prevalence of sharing needles/syringes may remain high in Eastern Europe [33]. Furthermore, the sharing of ancillary injecting equipment appears to remain more prevalent than needle/syringe sharing [29,34].

Key point

Sharing needle/syringes and contaminated ancillary injecting equipment (spoons/cookers, filters, and water) are the main risk factors for HCV acquisition among PWID.

Harm reduction

Harm reduction is defined as the policies, programmes, and practices that aim to reduce the harms associated with the use of psychoactive drugs among people who are unable or unwilling to stop [35]. The main harm reduction interventions are generally considered to be sterile needle/syringe provision (NSP) and opioid substitution treatment (OST). There is evidence to support the effectiveness of NSP and OST in reducing injecting risk behaviour, and some evidence to support their effectiveness in preventing blood-borne virus transmission among PWID [36,37].

More recently, studies have demonstrated that the combined impact of NSP and OST can produce a greater reduction in HCV transmission than either intervention alone [32,38–40]. These interventions have been endorsed by national, regional, and international authorities for the prevention of HCV [41–44]. However, despite the availability of, and evidence for, effective harm reduction, most countries have not achieved a level of intervention coverage that would likely be required to curb new HCV infections: on a global level, there is generally poor coverage of interventions, with NSP coverage estimated at 22 sterile needles/syringes per PWID per year and OST coverage estimated at 8 OST recipients per 100 PWID. The highest NSP coverage is in Australia & New Zealand (202 needles/syringes per PWID per year) and the highest OST coverage is in Western Europe (61 OST recipients per 100 PWID) [45].

The experience of some countries that have achieved high levels of harm reduction intervention coverage is, however, that they can reduce, but not fully control, HCV transmission among PWID [32,46]. This may be because high coverage needs to be sustained for decades in order to have an impact. For example, model projections have shown that, in a scenario of 40% viremic prevalence, reducing HCV prevalence by a third would require more than 60% coverage of both OST and high coverage NSP for 15 years [47]. More impact could probably be achieved through a treatment-as-prevention strategy: modelling studies have suggested that scaling up HCV therapy among active PWID (in addition to the existing harm reduction interventions) is necessary if substantial reductions in HCV

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