

A Call to Action for the Prevention of Hepatitis C Infection Among Intravenous Drug Users in Turkey

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Hepatitis C Epidemiology in Population and Intravenous Drug Users

With an estimated global prevalence of 2.8%, hepatitis C virus (HCV) causes chronic infection which may result in potentially lethal chronic liver diseases such as cirrhosis and hepatocellular carcinoma (1). Epidemiological studies revealed that the number of anti-HCV positive people has increased from 122 million to 185 million between 1990 and 2005 and this indicated that this virus is a global public health threat (1). Although the transmission of HCV infection may occur due to blood transfusion, unsafe therapeutic injections, and other health-care related procedures; the majority of HCV infections are transmitted via illicit drug injections, especially in the developed countries (2,3).

In spite of the efforts to prevent it, drug use

continues to be an important health problem in both developed and developing countries (4). Recent reports suggest that approximately 10.0 million people who inject drugs (PWID) worldwide may be exposed to the HCV (5). These data reveal that with an prevalence up to 80%, HCV infection is more common than HIV infection among PWID and its prevention must be the major concern for the health policy makers (5).

Interestingly, the characteristics of HCV infection among PWID are different than those in the general population (6). In addition to the social factors and psychiatric comorbidities which are affecting the treatment access of PWID, the genotypes of the HCV may be different in this population (7,8). Six major genotypes of HCV have been defined so far and genotypes 1a and 3 have a significantly greater prevalence among the PWID population compared with the general population (8). Moreover, PWID have

relatively high rates of reinfection with hepatitis C following successful cure, similar to HIV-infected men who have sex with men (MSM) (9). All these psychosocial and biological factors necessitate adopting different strategies and individualizing HCV treatment interventions for the PWID population.

Targets of World Health Organisation and Turkish Ministry of Health to HCV elimination

Considering the fact that viral hepatitis was a leading cause of death in 2013 (1.46 million deaths worldwide), World Health Organization (WHO) decided to initiate a combat against hepatitis B (HBV) and HCV to eliminate them by the year 2030 (10,11). WHO officials underlined the importance of combining prevention methods and recently developed treatment alternatives, which makes elimination of these two infections feasible. This new generation of highly effective medications has the potential of suppressing HBV replication and may cure chronic HCV infection (11).

Considering the limited efficacy of the traditional primary prevention methods (e.g. opiate substitution treatment and needle and syringe programs) in reducing the HCV transmission among PWID in the recent years, there is an increased interest in the role of HCV treatment as prevention to improve the efficacy of those primary interventions and decrease the HCV related morbidity and mortality in this population (12,13). In addition to the individual benefits of HCV cure (e.g. prevention of cirrhosis and hepatocellular carcinoma, reduction in complications and disease related mortality, and improvement in the quality of life), curing the HCV infection has the potential to improve public health by preventing onwards transmission and reducing health service costs (14-17). Considering the results of mathematical models that demonstrated how treatment of HCV infection among PWID reduces both the prevalence and economic burden of this chronic disease, recent guidelines underline the importance of the "treatment for prevention" concept and recommend providing treatment for people at high risk of

transmission (e.g. PWID and MSM) irrespective of fibrosis stage (14,18,19). Combining primary prevention methods with effective treatment strategies are the key factors for eliminating HBV and HCV by 2030 and averting 7.1 million deaths (20).

The prevalence of HCV is around 0.5-0.9% in Turkey whereas it is much more common among PWID. Recent data suggested that anti-HCV positivity has gradually increased up to 50.1% in 2012 among PWID who have been treated in inpatient addiction centers (21,22). There is a slight decrease to 45.7% in 2013, probably due to the use of primary prevention methods in these centers effectively. Similar to the other countries, genotype 3 is more common than genotype 1 in the Turkish PWID population (58.6% vs 11.5%), although genotype 1 prevalence is around 90% in the non-PWID population (23). Furthermore, studies revealed that anti-HCV positivity increases with increasing age and there is a positive correlation between the age of the first injection and the probability of anti-HCV positivity (22,24).

Why is Routine Screening Essential?

Reports suggesting that about half of HCV-infected people are unaware of their condition, suggests how important screening for this chronic infection (25).

HCV screening and treatment may be challenging for PWID due to patient, health care staff and health system related factors. For these reasons, HBV, HCV and HIV must be routinely screened for inpatient PWID in order not to miss this opportunity of their diagnosis (26). American Association for the Study of Liver Diseases (AASLD) and Infectious Diseases Society of America (IDSA) guidelines recommend annual HCV testing for PWID whereas the European Association for the Study of the Liver (EASL) underlines that screening strategies for HCV infection should be defined according to the local epidemiology and demographic characteristics of HCV, prior exposures, high-risk behaviours, and medical conditions. Based on the conditions in Turkey once or twice a year HCV screening can be

Table 1: Interpretation of the HCV status of the patients according to the HCV testing results

Anti HCV	HCV RNA	Interpretation
Positive	Positive	Acute or chronic HCV infection depending on the clinical context
Positive	Negative	Resolution of HCV; Acute HCV infection during period of low-level viremia
Negative	Positive	Early acute HCV infection; Chronic HCV infection in setting of immunosuppressed state; False positive HCV RNA test
Negative	Negative	Absence of HCV infection

suggested (14,19). Other guidelines specifically emphasize the need for annual HCV testing for PWID and HIV-infected MSM because of the high incidence of HCV infection (27).

Barriers to HCV screening of PWID may vary from one country to another, therefore, there is an urgent need for expanding the access to addiction centers in order to address the unmet need for PWID who are at a high risk for HCV (28). Unfortunately, only limited numbers of inpatient addiction centers are routinely screening PWID for HBV, HCV and HIV in Turkey whereas outpatients PWID are not routinely screened. Therefore, routine inpatient and outpatient screening programs should be established in all AMATEMs (Research, Treatment and Training Center for Alcohol and Substance Dependence) in Turkey immediately.

How can Serologic Test Results be Interpreted?

People, who recommended HCV screening, should be tested for HCV antibody (anti-HCV) first (29,30). Anti-HCV test positivity does not always represent an active HCV infection. Anti-HCV positivity means, the patient is currently active HCV infection (acute or chronic) or has had HCV infection in the past and it has been decreased, or a false-positive test result (31). In order to Active HCV diagnosis, to initiate HCV treatment HCV-RNA nucleic acid test (NAT) is necessary to confirm the HCV viremia (14). If the patient is immunocompromised or may have been exposed to HCV within the last six months, an HCV-RNA test is also necessary because these people may be anti-HCV negative (14). An HCV-RNA test is also essential to detect reinfection in anti-HCV-positive

people after previous spontaneous or treatment-related viral clearance (14). Table 1 summarizes the interpretation of the HCV status of the patients according to the HCV testing results.

What to do in The Presence of Infection?

Considering the beneficial effects of HCV treatment for both the patient and public health, all HCV infected PWID should access to a proper health service and must be treated with highly effective new generation antiviral treatments. Before the initiation of HCV therapy, quantitative HCV-RNA testing may be used to determine the baseline level of viremia (i.e. viral load) in order to determine the duration of treatment regimens. Testing for HCV genotype helps to guide the selection of the most appropriate treatment regimen. Moreover, preventive measures such as alcohol consumption reduction must be taken among HCV-infected PWID, in order to prevent further damage of alcohol to the liver (32). Many studies have found a strong association between excessive alcohol use and development (or progression) of liver fibrosis and hepatocellular carcinoma development (33-35).

In addition to organizing HCV screening programs, healthcare providers in the addiction centers must adopt an effective referral system as HCV infection management requires adequate expertise in the liver diseases and antiviral treatments. Recent studies revealed that only around 15% of HCV-infected people could receive treatment in the USA due to lack of appropriate screening and problems in the consultation systems (25,36). Lack of an easy access to the treatment, lack of expertise in HCV treatment and

lack of specialty for consultation systems are the major barriers to initiation of the effective HCV therapy, and healthcare providers in the addiction centres must adopt proper strategies for addressing these barriers. Health care personal in AMATEMs should be trained to overcome these shortcomings (37-40).

Integrated HCV screening, evaluation, consultation and treatment services may increase the number of HCV infected PWID who access to appropriate treatment and improve their health conditions (41-43). Such integration requires close collaboration between addiction center physicians and subspecialists who are experienced in viral hepatitis (44).

Treatment Options

Direct-acting antiviral (DAA) agents revolutionized the management of this chronic infection and significantly improved the health-related outcomes of HCV infected individuals. Due to concerns about poor treatment adherence and reinfection risk, HCV infected PWID used to be considered as a “difficult to treat” population. However, recent analyses demonstrated that treatment adherence and sustained virologic response (SVR) rates among PWID are comparable to those among people who do not inject drugs (45-47). In light of the these studies, AASLD and EASL guidelines recommend that HCV therapy must be considered PWID who are actively using illicit drugs or on opioid substitution therapy, if they wish to receive treatment and are willing to maintain regular appointments (19).

How does a Referral Cascade Organize?

There are no infectious diseases and/or gastroenterologists in AMATEMs. Therefore, patients with HCV infection are referred to the department of

infectious diseases and/or gastroenterology in the hospital to which the AMATEM affiliated. Patients assessed in these departments may need to be referred to other centers to begin their treatment because of the reimbursement conditions for antiviral treatments used in the treatment of HCV.

In the current referral cascade; most patients do not admit to the clinics which are specialized on HCV infection management due to the complexity of procedures, underestimating the severity of the disease and inexperience of the addiction center in terms of HCV infection management.

It is highly recommended to AMATEMs, evaluating their current referral cascade for HCV infected patients, updating it or developing a new one that defines the responsibility of each healthcare staff (physicians, nurses, administrative personnel). The new cascade must explain a route how patients reach a center that specialized in HCV infected patient management.

CONCLUSION

Reducing HCV prevalence by declining the re-infection risk is the most important step towards HCV elimination thus “treatment as prevention” paradigm must be strictly adopted by the public health authorities who aim to reduce the burden of HCV (48). The reservoir for re-infection in PWID cannot be reduced unless strategies for engagement and retention of PWID in treatment and follow-up are developed. Moreover, targeting PWID for treatment is proven to be a cost-effective approach for reducing long-term health costs (49). Therefore, there is an urgent need for developing routine HCV screening in outpatient and inpatient settings of AMATEMs for all PWID and breaking down the barriers against prioritization of HCV treatment among the PWID in the DAA for reaching the HCV elimination target (48).

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