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Time for a systematic approach to the treatment of hepatitis C virus infection in injection drug users

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'As IDUs constitute the bulk of the HCV epidemic in developed countries, it is quite clear that any comprehensive approach to control this epidemic must include a systematic strategy to address this group. The development of such programs may be quite complex, but the ultimate benefit...is certainly worth the effort.'

The spread of injection drug use (IDU) has led to an explosive epidemic of hepatitis C virus (HCV) infection in many urban populations. Of the estimated 123 million prevalent cases in the world, more than 50% occur in IDUs, with over 75% of incident infections being associated with this high-risk behavior, representing over 200,000 new cases each year in the USA alone [1]. Only 20% of these patients or fewer will clear their viremia spontaneously (usually within the first year following infection), with the remainder progressing to chronic disease and serving as a reservoir for the further spread of infection [2].

Pharmacological advances have led to the development of HCV treatment regimens with improved efficacy, resulting in a virological cure in 50% of patients receiving once-weekly pegylated interferon (PEG-IFN) in combination with twice-daily ribavirin for 24–48 weeks, a figure that exceeds 80% (with only 24 weeks of treatment) in a subgroup of individuals carrying HCV genotype 2 or 3 infection [3]. In the past, clinical guidelines have excluded IDUs from being considered for therapy unless they had been free of IDU for at least 6 months. This approach is still in place in many centers, despite the fact that guidelines promoted by the National Institutes of Health in 2002 advocate the broader consideration of active IDUs on an individual basis [101]. Concerns over patient motivation and adherence, medical and psychiatric comorbidity, reinfection due to recurrent risk behaviors, and the lack of infrastructure to ensure long-term access to care, have all been raised as obstacles to the initiation of HCV treatment in this population [4].

Preliminary reports from some centers have confirmed that many IDUs may be likely to consider treatment if this is coupled with a comprehensive approach to their medical and psychiatric requirements (including a systematic addiction treatment program) within existing infrastructures [5]. How do we move forward from these positive, anecdotal reports to a more systematic approach to meet the needs of the millions of IDUs living with this condition, not to mention the hundreds of thousands that will become infected in the next year?

The first simple measure is to raise awareness in the affected population. A recent study has demonstrated that as many as 80% of infected IDUs would be motivated to receive treatment if it were made available to them [6]. This desire may well extend to a broader population of IDUs of unknown HCV status, who, upon being informed of the availability of a potentially curative treatment, would come forward to be tested.

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In fact, in our own center we were able to determine that 64% of our population was infected with HCV and that 45% of these carried genotype 2 or 3 infection [7]. This was a pleasant surprise, as it indicates that a significant minority of our patient population could receive a 24-week treatment course with a high expected cure rate. We think this information will help us engage even larger numbers of individuals in care. Our results should also provide the impetus for other centers to conduct systematic surveys of their patient populations to help plan for the implementation of treatment programs.

The second measure is to develop pilot programs for the treatment of HCV in selected individuals in a way that will maximize the probability of success and allow the identification of necessary criteria for their scale-up. In our center, HCV-infected IDUs who were

viremic, noncirrhotic, with alanine transferase (ALT) levels more than 1.5-times the upper limit of normal (ULN) and in whom there was a reasonable expectation of adherence to therapy were offered 24–48 weeks (based on HCV genotype) of combination therapy with ribavirin along with IFN- α 2b (1.5 μ g/kg three-times weekly) replaced by PEG-IFN- α 2b (1.5 μ g/kg once weekly) as it became available [8]. Staff administered all injections under direct observation. In total, 37 patients (31 males) received therapy with IFN- α 2b (12 patients) or PEG-IFN- α 2b (25 patients), 20 with genotype 2 or 3 infection (54%). The mean baseline age, body weight, ALT and duration of infection were 42 years, 83 kg, 170 U/l and 13 years. Only 11 patients discontinued therapy early (30%). Overall end-of-treatment response was 70% (26 out of 37), 85% (17 out of 20) in subjects with genotype 2 or 3 infection. Overall the 16 patients receiving the entire course of PEG-IFN-based therapy had a maximal virological response. Pretreatment drug abstinence and illicit drug use during treatment did not have a significant impact on response rates, as long as interventions were available to prevent the drug use from becoming regular. It is quite encouraging to see that a number of pilot studies in Australia, Europe and the USA [5] have already generated results similar to our own. Further study is required to evaluate the sustained virological responses in larger numbers of individuals, but our results certainly suggest that, in the right setting, response rates in IDUs can approach those reported in clinical trials of combination therapy for HCV infection. The key will be to identify systematically which components of the program will be needed to ensure its success, a concept that will likely vary according to the center and its specific population.

Finally, it will be important that these programs be implemented within research protocols to ensure their rigorous design and evaluation.

An important concern remains the risk of reinfection with HCV after treatment. If this were high, it could rapidly negate the benefit of any therapeutic interventions.

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We have already begun to compare the incidence of HCV infection in those having spontaneously cleared their viremia with those who were documented to be previously uninfected [7]. HCV reinfection was documented in 14 out of 152 (9.2%) individuals or an incidence rate of 1.8 cases per 100 person-years. In contrast, new infections were documented in 172 out of 926 (18.6%) individuals, at a much higher rate of 8.1 cases per 100 person-years. These data are consistent with those generated in a cohort of IDUs in Baltimore, MD, USA [9]. Although we have not yet identified the mechanism of the protective effect of prior infection, we will be able to design studies to establish this as well as to see if the reduced rate of reinfection extends to those who have cleared infection while on treatment compared with those who have spontaneously cleared viremia. In the meantime, these data reassure us that we should continue to develop our treatment programs while these questions are being addressed.

As IDUs constitute the bulk of the HCV epidemic in developed countries, it is quite clear that any comprehensive approach to control this epidemic must include a systematic strategy to address this group. The development of such programs may be quite complex, but the ultimate benefit (for the treated population and for society as a whole) is certainly worth the effort.

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