Barriers to antiviral treatment in hepatitis C infected intravenous drug users

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Background: Nowadays intravenous drug use is the main source of hepatitis C transmission, but only a small proportion of those who acquired infection via intravenous drug use receive antiviral treatment. **Aim:** to assess the barriers of access to antiviral treatment of infected intravenous drug users. **Methods:** A retrospective chart review was carried out in a hepatology outpatient clinic including all hepatitis C infected intravenous drug users in a 3-year period. **Results:** Only one-third of the infected former intravenous drug users received antiviral treatment. The main barrier to antiviral treatment was the lack of abstinence. Former intravenous drug users in prison or in long-term drug rehabilitation institutes were more likely to enter antiviral treatment. **Conclusions:** The low proportion of patients entering antiviral treatment calls the attention to further improving the pre-treatment management of this patient population. Special attention should be paid to the maintenance of abstinence.

Keywords: antiviral treatment, barriers, drug addiction, hepatitis C infection

Since 1991, intravenous drug use has been the main cause of hepatitis C infection in the United States and Europe [1]. In several European countries the prevalence of hepatitis C virus (HCV) infection in intravenous drug users (IDUs) is above 70% [2-4]. Starting in 2006, the annual screening of IDUs in Hungary using the 'dried blood spot' technique in specialized outpatient clinics and needle/syringe programs (NSP) yielded a national prevalence of about 25%, though in Budapest the prevalence was considerably higher, 36% and in one NSP it even reached 70% [5]. The most effective current therapy of HCV infection is pegylated interferon and ribavirin combination that could achieve sustained treatment response in 50-60% of the cases [6,7]. However, only a small proportion of those who acquired infection via intravenous drug use receive antiviral treatment [8].

The aim of this study was to assess the barriers of access to antiviral treatment of HCV infected IDUs who attended the largest Hepatology Outpatient Centre in Budapest.

MATERIALS AND METHODS

This is a retrospective chart review of IDUs who attended the Hepatology Outpatient Clinic of Szent László Hospital between 1 January 2006 and 31 December 2008 and had hepatitis C infection. The following variables were analysed: liver function tests (LFT), HCV-PCR status, treatment adherence and contraindications to antiviral treatment. The numbers of patients who were in prison or received substitution therapy were also recorded. The study protocol was approved by the Institutional Review Board of Szent László Hospital.

For statistical analysis the SPSS 10.0 package (Statistical Package for Social Sciences, Chicago, IL, USA) was used. Descriptive data were presented with percentages or means and standard deviations. Two-sample t-test was used to compare mean age of the groups.

RESULTS

Of the 6,759 patients who attended the Hepatology Outpatient Clinic between 1 January 2006 and 31 December 2008, 123 had a history of IDU and 39 (32%) of them received antiviral treatment. There were 30 men and 9 women; their mean age was 34.03±8.76 years. Six patients had symptoms of acute hepatitis infection and entered inpatient treatment. Acute liver inflammation was caused by hepatitis C and hepatitis B in 4 and 2 cases, respectively. Twelve IDU patients (10%) recovered from HCV infection; they had positive viral serology and negative HCV-PCR.

Twenty-eight patients (23%; 17 men and 11 women; mean age: 27.68±6.05 years) had carrier status characterized by normal LFT, positive viral serology, and positive HCV-PCR) relating to hepatitis C and B in 27 and one case, respectively. In the hepatitis C carriers, 6 patients followed through with control examinations while 22 patients terminated their care after 3.35±2.66 attendances. The possible reasons for terminating follow-up are shown in Table 1.

Altogether 44 patients (36%; 40 men, 4 women; mean age: 28.86±6.22 years) did not enter antiviral treatment although they would have needed it. These patients attended the hepatology centre 2.51±1.65 times. Hindrances to treatment that could be assessed from the documentation are shown in Table 2. In 22 cases (20 men, 2 women; mean age: 27.45±6.35 years) the possible reasons for termination follow-up were not clearly stated; these patients visited the centre 2.45±1.71 times.

Eight (57%) of the 14 imprisoned patients, and 6 (33%) of the 18 patients who were on methadone or buprenorphine+naloxone substitution therapy received antiviral treatment. The mean age of patients on antiviral medication was significantly higher than that of virus carrier patients' (p=0.002) or that of patients who did not start the treatment (p=0.009).

DISCUSSION

This was the first retrospective study conducted in Hungary that explored the barriers to the access to antiviral treatment in hepatitis C infected IDUs.

Of the 123 patients who attended the Hepatology Centre of Szent László Hospital in the 3-year study period, only 67% were found to be infected with hepatitis C and in need of antiviral treatment. This rate is lower than the one reported (76%) from England [8] or from Spain (75%) [9]. The divergence of the findings can be explained partly by ethnic and genetic differences between the patient populations [10], and partly by the different genotypes of hepatitis C virus in the samples [11,12]. In addition, over the study period guidelines for viral hepatitis were changed in Hungary: liver biopsy was omitted from the list of mandatory examinations in the treatment guidelines for viral hepatitis [13]. It is possible, that some patients with normal liver functions might have been categorised as virus carriers when a liver biopsy could have revealed mild, early inflammation. Further, the fact that there was only one patient in the early stage cirrhosis in the study population could be attributed to the lower age (30 versus 40 years) of the sample than in the English study [8].

In accord with earlier findings [14,15], the most frequent barrier to cooperation with pre-treatment examinations and antiviral treatment was ongoing drug abuse. In 43% of the cases this was the reason for missing medical examinations, and in 27% of the virus carrier cases for terminating follow-up. Ongoing psychiatric disorders led to the cessation of the examination in 2 (10%) cases of the HCV carriers. There were no psychiatric disorders in the group of patients with advanced liver disease, but in 2 cases (5%) epilepsy, a contraindication of antiviral therapy, precluded antiviral treatment [13]. In the group of virus carriers and patients with advanced liver conditions 1 case each had subnormal intelligence that hampered pre-treatment examinations. From the group of virus carriers two patients dropped-out before liver biopsy and 1 left before Fibroscan examination raising the possibility that phobic anxiety triggered by these examinations [16,17] resulted in drop-out. Providing information about the interventions and intensive counselling could have decreased the risk of the refusal of consent to the examination in these cases [18].

The low number (2.45 - 3.35 occasions) of doctor-patient encounters before the eventual drop-out – in addition to a number of other reasons – could be explained by patients' low motivation level. The first 2-3 occasions were usually sufficient only for the most necessary examinations to evaluate patients' current conditions. More than half of the patients dropped out after this initial phase so a comprehensive management plan could not be drawn up.

In accord with the results of an Australian study [19] and a meta-analysis [20], the mean age of the 39 patients who entered antiviral treatment was significantly higher than that of the virus carriers or that of those with advanced liver conditions. The mean age of 34 years of patients receiving antiviral treatment in

Table 1. Possible reasons for terminating medical follow-up in virus carriers (n=22)

Reason for termination	Number of patients	
Lack of abstinence	**6**	Amphetamine: 2
		Other: 4
Poor treatment adherence (low IQ)	1	
Psychiatric disorder	**2**	Personality disorder: 1
		Depression: 1
Fear from examination	**3**	Before Fibroscan: 1
		Before liver biopsy: 2
Reason unclear	12 (methadone maintenance: 4)	

Table 2. Possible hindrances to antiviral treatment in patients in need of antiviral treatment (n=44)

Reason for termination	Number of patients	
Lack of abstinence	**19**	Cocaine: 1
		Methadon: 1
		Cannabis: 3
		Amphetamine: 1
		Alcohol: 2
		Other: 11
Poor treatment adherence (low IQ)	1	
Neurological contraindication (epilepsy)	2	
Interruption of examinations	22 (methadone substitution: 5)	

this study is identical with the figure reported earlier [15]. Patients without IDU belong to a considerably higher age group that those with a history of IDU [15].

In this study, 18 of the 123 HCV positive patients took part in methadone or buprenorphine+naloxone maintenance therapy; 6 (33%) of them entered antiviral treatment. The figure of 33% does not differ significantly from the 32% access rate of the 39 patients of the total sample of 123 who received combination therapy. This shows that good treatment adherence of patients in methadone maintenance therapy [15] does not confer an advantage in accessing antiviral treatment. In the group of patients in long-time drug rehabilitation institutes, the proportion (57%) of those who entered antiviral therapy was substantially higher than the 32% in the whole sample. This finding is in line with the findings of studies conducted in prison settings [21,22].

The main limitation of the study is its retrospective nature. The documentation was not systematically collected in the medical notes, therefore the information ranged from the patchy to the sufficiently detailed.

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A hepatitisz C fertőzött intravénás szerhasználók antivirális kezelésének akadályai

Napjainkban az intravénás kábítószer-használat a hepatitisz C fertőzés terjedésének leggyakoribb oka, ugyanakkor azok közül, akik intravénás szerhasználat útján fertőződtek meg, csak kevesen jutnak el az antivirális kezelésig. **Célkitűzés:** az intravénás szerhasználók antivirális kezeléshez való hozzáférését akadályozó tényezők felmérése. **Módszer:** a Szent László Kórház Hepatológiai Ambulanciáján a vizsgált 3 éves időszakban megfordult összes hepatitisz-fertőzött intravénás kábítószer-használó orvosi dokumentációjának retrospektív elemzését végeztük. **Eredmények:** a korábbi intravénás szerhasználóknak csak egyharmada részesült antivirális kezelésben. Az antivirális kezelés leggyakoribb akadálya az absztinencia hiánya volt. A börtönben, vagy hosszú távú rehabilitációt végző intézetben lévő korábbi intravénás szerhasználóknak nagyobb esélyük volt hozzájutni az antivirális kezeléshez. **Következtetések:** az antivirális kezelésbe kerülő korábbi intravénás szerhasználók alacsony aránya a kezelésre való előkészítés javításának szükségességére hívja fel a figyelmet. Ezen belül is kiemelt jelentőségű az absztinencia fenntartása.

Kulcsszavak: antivirális kezelés, akadályok, intravénás kábítószer-használat, hepatitisz-fertőzés