

# Difficulties with interferon treatment in former intravenous drug users

## ABSTRACT

**Objectives:** Intravenous drug use accounts for most of the new hepatitis C infections worldwide. Although there is an urgent need for antiviral treatment of infected intravenous drug users (IDUs), several factors compromise their treatment including lack of treatment adherence and high dropout rate. The aim of this study was to compare antiviral treatment-related problems among former IDUs to HCV-infected patients without a history of IDU. **Methods:** This was a retrospective chart review of HCV-infected IDUs who received combined antiviral therapy at the Hepatology Outpatient Clinic of Szent László Hospital between 1 January 2006 and 31 December 2008. A control group of interferon treated patients with no history of IDU matched for age and sex was selected. **Results:** Dropout rate was significantly higher in the IDU group ( $p = 0.016$ ). Treatment response at the 12th week of treatment was significantly better in the IDU group ( $p = 0.004$ ). Significantly more IDUs underwent antiviral treatment while in prison ( $p = 0.008$ ). **Conclusions:** In this study higher dropout rate was found among IDUs. IDUs had a better response rate to antiviral therapy compared to controls. More attention should be paid to factors that worsen treatment adherence of IDUs - particularly lack of abstinence - in order to increase the effectiveness of antiviral therapy.

**Keywords:** psychiatry; hepatitis C; substance-related disorders.

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## INTRODUCTION

In several European countries the prevalence of hepatitis C virus (HCV) infection in intravenous drug users (IDUs) is above 70%.<sup>1-3</sup> In Hungary until 2006 only limited data from health service providers were available.<sup>4-6</sup> Hungarian surveys reported 10-30% HCV prevalence rates in IDUs. Starting in 2006, the annual screening of IDUs covering specialized outpatient clinics and needle/syringe programs (NSP) using 'dried blood spot' techniques yielded a national prevalence of about 25%, though in Budapest the prevalence was considerably higher, 36% and in one NSP it even reached 70%.<sup>7</sup>

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.<sup>8,9</sup> There is no generally accepted recommendation concerning the antiviral treatment of active IDUs. Some authors ar-

gue that active IDU is a contraindication for combination therapy, partly due to their poor treatment adherence and partly to the increased likelihood of re-infection.<sup>10</sup> Others regard treatment necessary for harm-reduction and preventing further spreading of infection.<sup>11</sup> There is growing evidence that even in active IDUs the benefit of antiviral treatment exceeds the risks of side effects and re-infection.<sup>12</sup> Both active and former IDUs have a significantly higher dropout rate compared to HCV-infected patients without a history of illicit drug use.<sup>13,14</sup> In Budapest, the Hepatology Outpatient Clinic of Szent László Hospital plays a key role in the examination and antiviral treatment of HCV positive IDUs.

The aim of this study was to compare antiviral treatment-related problems among HCV-infected patients with and without a history of illicit drug use in the period between 2006 and 2008.

## Authors

Gábor Gazdag<sup>1</sup>  
Gergely Horváth<sup>2</sup>  
Olga Szabó<sup>3</sup>  
Gabor S Ungvari<sup>4</sup>

<sup>1</sup>MD, PhD, Consultation-Liaison Psychiatric Service, Szent István and Szent László Hospitals, Hungary  
<sup>2</sup>MSc, Drug Focal Point, National Center for Epidemiology, Hungary  
<sup>3</sup>MD, Hepatology Outpatient Clinic, Szent István and Szent László Hospitals, Hungary  
<sup>4</sup>MD, PhD, Graylands Hospital, Hungary

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## Correspondence to:

Gabor Gazdag,  
Consultation-Liaison  
Psychiatric Service,  
Szent István and Szent  
László Hospitals,  
Gyáli út 5-7., Budapest,  
1097 Hungary  
Phone/fax:  
00-36-1-455-8125  
gazdag@lamb.hu

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## METHODS

This was a retrospective chart review of HCV-infected IDUs who received combined antiviral therapy at the Hepatology Outpatient Clinic of Szent László Hospital between 1 January 2006 and 31 December 2008. A control group of interferon-treated patients without a history of drug use matched for age and sex was selected. The following treatment outcomes were analyzed: HCV-PCR results, dropout rate, treatment response, and psychiatric complications. The percentage of patients receiving antiviral therapy while in prison was also recorded.

For statistical analysis the SPSS 10.0 package (Statistical Package for Social Sciences, Chicago, IL, USA) was used. Descriptive data were presented with means and standard deviations. Binomial data were compared with the chi-square test; if the value in a cell was less than five, the Fisher exact test was applied. Statistical significance was set at 0.05.

## 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 36 of them (28%; 29 men and 7 women) received antiviral treatment for chronic hepatitis C. The mean ages of the sample and the control group were  $34.44 \pm 8.85$  and  $34.56 \pm 8.85$ , respectively. Ten of the 36 IDUs dropped out during treatment (Table 1). Table 2 shows the comparison between IDUs and controls with respect to treatment. Two IDU patients were on methadone maintenance, another two on buprenorphin+naloxon maintenance while undergoing antiviral treatment; none of these four IDUs dropped out. Abstinence was ascertained in 7 of the 36 IDU subjects by psychiatric evaluation. Another five cases were assessed by a psychiatrist (GG) to monitor their ongoing psychiatric treatment or to treat the side effects due to the antiviral therapy.

*Table 1. Reasons for termination of antiviral therapy in intravenous drug users*

Case	Sex	Age	Time of termination	HCV-PCR 3 <sup>rd</sup> month	Reason for termination of therapy
1	Male	26	1 <sup>st</sup> month		THC+IF- induced psychosis (hospitalization)
2	Male	43	1 <sup>st</sup> month		Thrombopenia
3	Male	27	7 <sup>st</sup> month		Unknown. Released from prison?
4	Male	26	3 <sup>rd</sup> month		Disappeared. Released from prison?
5	Female	51	8 <sup>th</sup> month	Negative	Hypothyreosis
6	Male	19	6 <sup>th</sup> month	Negative	Disappeared (side effects: itching, loss of appetite)
7	Male	29	7 <sup>th</sup> month		Disappeared. Released?
8	Male	41	1 <sup>st</sup> month		Disappeared. Released from prison? Psychiatric condition deteriorated?
9	Male	40	8 <sup>th</sup> month		Refused to continue. Released from prison?
10	Female	34	9 <sup>th</sup> month	Negative	Diffuse pain, weight loss, indigestion.

*Table 2. Comparison of the outcome of combined antiviral therapy between intravenous drug users and controls*

	IDUs	Control group	Statistics
HCV-PCR at 12 <sup>th</sup> week	28	29	p = 1.000
Negative HCV-PCR at 12 <sup>th</sup> week	18	9	p = 0.004
Negative HCV-PCR at 24 <sup>th</sup> week	22	17	p = 0.125
Rapid responder	2	1	p = 1.000
Prolonged therapy	1	4	p = 0.250
Dropout	10	3	p = 0.016
Termination due to ineffectiveness	3	8	p = 0.063
Therapy while in prison	10	2	p = 0.008
Psychiatric complications	5	8	p = 0.250

## DISCUSSION

It is estimated that there are at least 2000 IDUs in Budapest,<sup>15</sup> and at least 700 of them could be infected with HCV. Yet, only 123 (18%) sought treatment in these three years at the Hepatology Outpatient Clinic of Szent László Hospital. This low proportion clearly indicates the need for increasing the efforts to better identify HCV-infected IDUs, a rather difficult task.<sup>16</sup>

In this study, IDU patients prematurely terminated treatment more frequently ( $p = 0.016$ ) than the control group; in three cases due to somatic and in one due to psychiatric complications (Table 1). Five patients dropped out for unknown reasons; four received antiviral combination therapy while in prison, while the fifth patient reported itching and loss of appetite. Similar dropout rate (31%) was found by Seal *et al.*,<sup>17</sup> and the corresponding figure was even higher (43%) in a German report<sup>13</sup> than the 28% seen in this study. A possible explanation for the lower dropout rate could be that in our hepatology center only 28% of the HCV-infected IDU patients received antiviral treatment, as opposed to 89% in Schaefer *et al.*'s study which included non-IDU patients as well. All four patients in substitution therapy adhered to treatment and three became HCV-PCR negative by week 12. By the end of the study period, however, only one completed the treatment successfully.

In the group of IDUs, 50% and 63% became HCV-PCR negative by the 12<sup>th</sup> and 24<sup>th</sup> week, respectively. At the 12th week the IDU group showed significantly better response to treatment than the control group ( $p = 0.004$ ) indicating a more rapid treatment response by IDUs; however, this difference disappeared by the 24<sup>th</sup> week. IDUs' better antiviral treatment response is also supported by the finding that fewer cases of IDUs needed prolonged (up to 18 months) treatment and rapid response was more frequent, though these differences did not reach statistical significance.

The response rate of IDUs at week 24 in this study was rather high (63% were HCV-PCR negative) in comparison to other studies.<sup>13,18</sup> This could be explained by the possibility of having more frequent genotypes 2 and 3 in the sample of IDUs,<sup>19</sup> as patients with these two genotypes respond better to antiviral treatment than genotypes 1 and 4.<sup>20</sup>

The need for psychiatric evaluation were significantly more often<sup>13</sup> in the group of IDUs, although the evaluation mainly aimed at confirming abstinence. Serious psychiatric problems resulting in termination of treatment were restricted to the IDU group. In one case, tetrahydrocannabinol (THC) abuse during antiviral therapy led to psychosis; another patient who had been on psychiatric treatment discontinued antiviral

therapy after one month. Schaefer *et al.*<sup>13</sup> found similar reasons for treatment termination among IDUs. Though psychiatric complications were observed slightly more frequently in the control group compared to IDUs (8 vs. 5), psychiatric evaluation was requested for only one case and no patient dropped out from interferon therapy because of psychiatric reasons. In four cases the treating physicians recommended short-term anxiolytic treatment.

The results of this study should be interpreted with caution due to the relatively small sample size and the inaccuracies inherent to retrospective chart reviews.

## CONCLUSION

In this study, higher dropout rate was found among IDUs who otherwise had a better response to antiviral therapy compared to controls. More attention should be paid to factors that worsen treatment adherence of IDUs – particularly lack of abstinence – in order to increase the effectiveness of antiviral therapy.

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