

Effects of Recent IV Drug Use and Severity of Psychiatric Symptoms to Antiviral Treatment in People Who Inject Drugs

Damar Yoluyla Madde Kullananlarda Son Dönemde IV Madde Kullanımının ve Psikiyatrik Belirti Şiddetinin Antiviral Tedaviye Etkisi

Sercan Karabulut ¹ 

1. Ataturk State Hospital, Antalya

Abstract

Objective: People who inject drugs have major contribution to a rise in hepatitis C virus (HCV) infections. Despite efficacy and safety of direct-acting antiviral (DAA) therapies, patients may have difficulties to receive treatment. In this study we aimed to examine the effect of clinical variables in substance users to access to antiviral treatment and the treatment rate.

Method: In this retrospective study, we examined the files of 5586 patients who admitted to Outpatient Treatment Center (OTC) between July 2020-April 2021 and files of 121 patients with positive Anti-HCV results were included. All patients had been routinely assessed by Addiction Profile Index (API) and Adult Attention Deficit Hyperactivity Disorder Self-Rating Scale (ASRS)..

Results: Of 121 patients, the most used substance was opiate. Because of the insurance restrictions, DAA treatment might be prescribed in only tertiary referral hospitals. All patients had been referred to a tertiary referral hospital. The mean duration from Anti-HCV testing to treatment was 190.3 days. Actively iv substance users were more likely to use substances every day (81.5 % vs 41.5%), start using the current substance at younger age (19.1 vs 20.9), have higher total API scores, have higher depression (4.7 vs 3.7), anxiety subscale scores, and ASRS-A scores (11.3 vs 8.3). Actively iv substance users were no more likely to have longer Anti-HCV – treatment duration (100.4 ve 254.5) and have worse treatment completion rates (% 100 vs 67.7).

Conclusion: According to research findings, young adults' expectations to obtain social status and social conformity through the acquisition of a product may affect spending time for online shopping and they may lose control of the use of credit cards..

Keywords: Hepatitis c, substance, intravenous, opiate

Öz

Amaç: Damar içi madde kullanan kişilerin hepatit C virüsü (HCV) enfeksiyonlarındaki artışa büyük katkısı vardır. Doğrudan etkili antiviral (DEA) tedavilerin etkinliği ve güvenliğine rağmen, hastalar tedaviye ulaşmakta zorluk çekebilirler. Bu çalışmada madde kullanıcılarında klinik değişkenlerin antiviral tedaviye erişim ve tedavi oranlarına etkisini incelemeyi amaçladık.

Yöntem: Bu retrospektif çalışmada Temmuz 2020-Nisan 2021 tarihleri arasında Ayaktan Arındırma Merkezi'ne (AAM) başvuran 5586 hastanın dosyası tarandı, Anti-HCV pozitif çıkan 121 hastanın dosyası incelenmiş ve eksik veri bulunan dosyalar dahil edilmemiştir. Tüm hastaların geçmişte Bağımlılık Profil İndeksi (BAPİ) ve Yetişkin Dikkat Eksikliği Hiperaktivite Bozukluğu Kendini Değerlendirme Ölçeği (ASRS) sonuçları rutin olarak mevcuttu.

Bulgular: Hastaların en çok kullandığı madde opiyatti. Sigorta kısıtlamaları nedeniyle, DEA tedavisi yalnızca üçüncü basamak hastanelerde reçete edilebildiğinden, çalışmaya alınan tüm hastalar üçüncü basamak bir hastaneye sevk edilmişti. Anti-HCV tarama testinden antiviral tedaviye kadar geçen ortalama süre 190,3 gündü. Aktif iv madde kullanıcılarının her gün madde kullanma oranı daha yüksek (%81,5 e %41,5), mevcut maddeyi daha genç yaşta

Correspondence / Yazışma Adresi: Sercan Karabulut, Addiction Center, Ataturk State Hospital, Antalya, Türkiye.

E-mail: drs_karabulut@hotmail.com

Received /Gönderilme tarihi: 24.04.2022 Accepted /Kabul tarihi: 22.06.2022

kullanmaya başlama oranları (%19,1 e %20,9) ve toplam BAPİ puanları daha yüksek, depresyon (4,7 e 3,7, $p=0,022$), anksiyete alt ölçek puanları ve ASRS-A puanları daha yüksekti (11,3 e 8,3). Aktif iv madde kullanıcılarını ile hayat boyu iv kullanıcıları karşılaştırıldığında, Anti-HCV testi – tedavi süresi (100,4 ve 254,5) ve antiviral tedaviyi tamamlama oranları açısından fark yoktu (%100 e %67,7).

Sonuç: Yüksek tedavi oranlarını gösteren kapsamlı verilere rağmen, iv madde kullanıcıları için tedavi oranları kabul edilebilir olmaktan uzak görünmektedir. Aktif damar içi madde kullanan kişileri ayırtıran faktörlerin analizi iv kullanımı sonlandırmak açısından önem taşısa da, antiviral tedavi kararı geciktirilmemelidir.

Anahtar kelimeler: Hepatit C, madde, intravenöz opiyat

Introduction

Cumulative data on the efficacy and safety of direct antiviral therapies caused an increase in studies on HCV elimination (1). Evaluating the new case increase and estimated prevalence, 23 % of new HCV infections were detected in patients with substance use disorder. In many different studies in Europe, the rate of Anti-HCV positivity in IV drug users has been reported between 13.8-90 % (2). It is estimated that 10 million patients with substance use disorder have chronic HCV infection (3). This indicates that people who inject drugs (PWID) are a key population for HCV treatment, to reduce both the disease burden and infection transmission. Direct-acting antiviral (DAA) therapies are safe, efficacious and have shorter regimens than previous medications, increasing suitability for community settings. Cure, defined as elimination of virus 12 weeks post-treatment, was as high as 95 % in clinical trials (4).

As shown in previous studies, sharing injection equipment, incarceration, getting tattoos in unhygienic conditions and unprotected sexual behaviors increase the risk in PWIDs (5). The WHO has defined international targets toward the elimination of hepatitis C by 2030 (6). Strategies that includes HCV (clinical evaluation and available resources evaluation); events or awareness campaigns for HCV; national register of disease for HCV; legal framework, particularly in terms of discrimination of HCV patients; national policy to address prevention of HCV infection; “Safe health” measures for screening and treatment of surgical instruments, equipment and supplies; general population screening; free and anonymous HCV testing, targeting high-risk populations; availability of social support for HCV patients (7).

In this population, diagnosis and treatment process has some difficulties, thus outcomes may be compelling for clinicians. In a study conducted in Australia, it was seen that 46 % of the anti- HCV positive patients were screened for viral load, 31 % could see the treatment provider specialist, and only 8% could reach the treatment (8). Although positive changes in treatment rates are predicted in centers where reflex testing (simultaneous HCV RNA testing in the same sample is performed if the Anti-HCV test is positive) is available, real-life data show several challenges (9). Several studies indicate different barriers for HCV infection care continuum among PWID, including refusal to engage with healthcare workers due to stigma associated with drug use, mistrust of the healthcare system, low level of perception about the need for treatment, and concerns about waiting periods and drug withdrawal (10, 11). In a study conducted in Georgia, the main barriers of linkage to HCV viremia testing among PWID were a lack of information about further steps after receiving a positive HCV antibody test and unawareness about the availability of free diagnosis and treatment (12).

To the best of our knowledge, this is the first study which investigated psychiatric symptoms including severity of substance use disorder and impulsivity associated with attention deficit hyperactivity disorder concomitantly in PWIDs. The aim of the present study was to better understand the effect of clinical variables to antiviral treatment access. We also aimed to examine the treatment rate in PWIDs. In addition, while longer time to take treatment may be correlated with less treatment compliance, assessing Anti-HCV test - treatment durations becomes more evident. It was hypothesized that, consistent with research conducted in other countries, treatment rate and access durations may not be related with recent iv drug use. Considering prejudices about active IV drug users which may be a potential obstacle to antiviral treatment in Turkey; it is important to define the characteristics of these patients and antiviral treatment access durations. It is also important to define the treatment rates to bring a new perspective to antiviral treatment trends.

Methods

Participants

The study was conducted in outpatient treatment clinic (OTC) in Ataturk State Hospital, Antalya. OTC is the largest specialized center for substance use disorders in Antalya, with 30 inpatient beds. In this retrospective study, inclusion criteria were age older than 18, positive Anti-HCV result and use of any illicit substance. Candidates whose file included missing data (sociodemographic variables, anti-HCV, HCV-RNA test results, missing scale scores, uncertain/unknown duration to test or treatment data), who have any mental retardation, cognitive impairment or comorbid psychotic disorder history were excluded. The minimum sample size calculation was performed with G-Power 3.1.9.7 program. The sample population was determined as a minimum of 84 with a probability of 95 %, a margin of error of 5 %, and an effect size of 80 %.

Assessments had been done by the same psychiatrist (SK) and files were under private protection in the clinic. All 5586 patients' files who had admitted to OTC between July 2020 – April 2021 were screened. 133 patients were anti-HCV positive. 12 of the patient files had missing data and were excluded. Thus 121 Anti-HCV positive patients' files were included and assessed. Data on socio-demographics, substance use within last month, HCV-RNA viral load, genotypes and duration to treatment were collected by using a structured data form.

This study protocol was reviewed and approved by the Ethics Committee of Antalya Research and Training Hospital, approval number 14/10/2021, 16/11. All subjects were contacted by the author and written informed consent was obtained from all participants. The research was conducted ethically in accordance with the World Medical Association Declaration of Helsinki.

Procedure

In Turkey, direct-acting antivirals may be prescribed by only infectious diseases or gastroenterology specialists in only tertiary referral hospitals. State hospitals in where the patients diagnosed with hepatitis C must be referred to tertiary referral hospitals to receive treatment. In addition to this, a drug use report should be signed by the specialist and the HCV-RNA load and genotype class also should be noted in the report. As a routine process, all patients in the clinic had been screened with Anti-HCV test. Since our OTC was a secondary-care clinic, patients that tested Anti-HCV positive, had been referred to Antalya Research and Training Hospital. All patients of which files were screened, had been referred to tertiary center. Rates of patients which admitted to the tertiary center, were tested for viral load, genotype, and received the treatment were calculated.

Measures

While all patients applying OTC had been screened with ASRS for ADHD symptoms and ASI for addiction severity, all results in files were thoroughly noted.

Adult Attention Deficit Hyperactivity Disorder Self-Rating Scale (ASRS)

The ASRS includes 18 questions about frequency of recent DSM-IV Criterion A symptoms of adult ADHD. There are two sections; section A contains six questions, section B contains remaining twelve questions. The ASRS screener consists of six out of these 18 questions that were selected based on stepwise logistic regression to optimize concordance with the clinical classification (κ , 0.76 v. 0.58). The clinical calibration of the ASRS was carried out by re-interviewing a quota subsample of 154 respondents from the US National Comorbidity Survey Replication (13). In the study by Doğan et al., the scale had Cronbach alpha of 0.88, with calculated values of 0.82 for attention deficit and 0.78 for hyperactivity/impulsivity subdimensions (14).

Table 1. Sociodemographic characteristics

Sex	n	%	Income Status (per month)	n	%
Male	107	88.4	< 2500 Turkish Liras (low)	66	55.3
Female	14	11.6	2500 – 5000 Turkish Liras (middle)	40	33.1
Current job position			> 5000 Turkish Liras (high)	14	11.6
Unemployed	82	67.7	Nicotine use		
Worker	39	32.3	Regular smoker	120	99.1
Marital Status			Non-smoker	1	0.9
Single	75	62	Number of substance used within last month		
In a relationship	26	21.5	1 substance	66	54.5
Separated/Divorced	20	16.5	≥ 2 substances	55	44.5
Admission			Admission Status		
Voluntary	111	91.7	First admission	7	5.8
Compulsory	4	3.3	Multiple admissions	114	94.2
By family/friend	3	2.5	Injecting equipment use		
Environment			Lifetime	105	86.8
Urban areas	97	80.1	Last one month	63	52.1
Rural areas	24	19.9	None	11	9.1
Psychotic symptoms (hallucinations, delusions or disorganized behaviors)			Syringe/needle sharing		
Life time	37	30.6	Yes	82	67.8
Recently (within last month)	16	13.2	None	34	28.1
None	84	69.4	Missing	5	
Suicide attempt			Tattoo/piercing		
Yes	37	30.6	Yes	81	66.9
None	79	65.3	None	40	33.1
Contagious diseases			Parole/probation history		
Anti-HIV positive	0	0	Yes	64	41.3
HBV screening positive	1	0.9	None	31	20
Syphilis screening positive	4	3.3	Self-mutilative behaviors		
Risky sexual behaviors			Yes	59	48.8
Yes	16	13.2	None	62	52.2
None	82	67.8	Incarceration history		
Missing	23	19	Yes	86	71.1
			None	35	28.9

HBV= Hepatitis B Virus, HIV= Human Immunodeficiency Virus

Addiction Profile Index (API)

Addiction Profile Index (API) is a self-report questionnaire that consists of 37 items and 5 subscales. The subscales measure the characteristics of substance use, dependency diagnosis, the effect of substance use on the person's life, craving and the motivation for quitting using substances. The scale was developed by Ögel et al. in 2012 with 345 alcohol and/or substance abusers who participated to the study (15). Cronbach alpha coefficient for the whole questionnaire was 0.89 and for subscales of the questionnaire ranged from 0.63 to 0.86. Item- total item correlation coefficient was between 0.42-0.89. For whole questionnaire Spearman Brown split-half method coefficient was found 0.83. API-clinical form is also a self-report

questionnaire, which consists of additional 21 items that measures depression, anxiety, anger management deficiency, safety behavior deficiency, sensation seeking behavior and impulsivity.

Statistical Analysis

Descriptive statistics were used to characterize the study population with respect to demographics and infection risks. Differences in demographic and substance use characteristics between actively and lifetime iv drug users were compared using chi-squared, independent t and Mann-Whitney U tests. Duration of Anti HCV – HCV RNA viral load test, Anti HCV- genotype test, Anti-HCV – DAA treatment, HCV-RNA – DAA treatment were measured at day period and compared between two groups. All tests were two-sided with significance set at $p < 0.05$. All statistical analyses were performed with SPSS (version 26.0, IBM).

Table 2 Descriptive statistical overview

Variables	n	Mean	SD
Age	121	30.9	6.6
Duration of schooling (year)	121	9.1	2.9
Number of substances used within last month	121	1.5	0.6
Amount of cigarettes smoked (pack/year)	121	15.6	11.2
Total hospitalization	109	2.5	3.1
Total completed inpatient treatment	107	1.7	2.1
Amount of outpatient admission	94	2.4	2.7
Duration from previous treatment to last admission (month)	55	20.6	31.4
Age of first use of current substance	121	24.6	5.9
Duration of iv drug use (month)	35	27.1	21.7
Suicide attempts	116	0.7	1.6
API total score	109	13.1	3.2
API substance use subscale score	109	2.5	1.5
API dependency diagnosis subscale score	109	16.4	4.6
API the effect of substance use on the person's life subscale score	109	30.3	7.7
API craving subscale score	109	9.6	4
API motivation for quitting using substances subscale score	109	10.9	2
API depression subscale score	109	4.2	2.1
API anxiety subscale score	109	2.6	1.7
API anger management deficiency subscale score	109	3	1.8
API safety behavior deficiency subscale score	109	4.9	2.4
API sensation seeking behavior subscale score	109	1.9	1.4
API impulsivity subscale score	109	2.8	1.4
ASRS-A subscale score	74	9.8	4.6
ASRS-B subscale score	74	21.1	9.1

SD=standard deviation, API=Addiction Profile Index, ASRS= Adult ADHD Self-report Scale

Results

Between July 2020 – April 2021, 121 patients (88.4 % men) were enrolled meeting the study criteria. Of patients, 75 were single, 26 were in relationship, 20 were separated or divorced. 91.7 % of cases were voluntary, % 80.1 were living in urban areas. Over the half of patients were in low-income group (55.3 %). 54.5 % of patients were using single substance. Mainly used substance was opiate (97.5 %). Within two or more substance user group, second most used substance was cocaine (78 %). Majority of patients were regular cigarette users. 86.8 % of patients were lifetime iv drug user, 52.1 % of patients had used iv drug

in last month. Rate of sharing of needles or syringes was 67.8 %. 30.6 % had suicide attempts. 48.8 % of patients had self-mutilative behaviors (cutting, burning, sticking oneself with needles, and severe scratching), 66.9 % had piercing or tattoo. Risky sexual behavior (having multiple sexual partners, sexual intercourse with commercial sex workers, unprotected sexual intercourse) was determined in 13.2 % of patients. 67.9 % of patients had imprisonment history, 57.8 % had parole or probation in the past. Table 1 shows the data of sociodemographic characteristics.

Table 3 Rate overview of viral load, genotype tests and treatment

HCV-RNA test rates	n	%	Genotype	n	%
Total test	92	76	1a	1	4.2
Viral load negative	24	19.8	1b	10	41.6
Viral load positive	68	56.1	3	11	45.8
Treatment received			4	1	4.2
Yes	5	7.3			
No	63	92.7			

HCV=Hepatitis C Virus

The mean age of participants was 30.9 ± 6.6 . The mean duration of schooling was 9.1 ± 2.9 years. Of smoker patients, mean level of used cigarettes was 15.6 ± 11.2 pack/years. The mean of total hospitalizations was 2.5 ± 3.1 , of admissions to OTC was 2.4 ± 2.7 . Most of patients were diagnosed with opiate use disorder (52.9 %). The mean age of first use of current substance was 19.9 ± 4.7 years. The mean duration of iv substance use was 27.1 ± 21.7 months. API score mean was 13.1 ± 3.2 , ASRS-A score mean was 9.7 ± 4.8 , ASRS-B score mean was 21.1 ± 9.1 . Table 2 shows the descriptive statistical overview.

Table 4 Descriptive overview of viral load, genotype and duration from tests to treatment

	n	Mean	SD
HCV-RNA copy number	92	763271.4	1857165.6
Duration of Anti-HCV - HCV-RNA test (day)	95	36.8	84.4
Duration of Anti-HCV - genotype test (day)	24	105.7	161.6
Duration of Anti-HCV test – treatment (day)	12	190.3	237.4
Duration of HCV-RNA test – treatment (day)	12	96.8	120.7

SD=Standard deviation, HCV=Hepatitis C Virus

Of 121 patients, 12 % had DAA treatment, 50 % of the group completed the treatment. All patients had been referred to Antalya Research and Training Hospital, Clinic of Infectious Diseases. Of patients referred, 92 (76 %) applied for viral load test. 26 % (24) of patients had negative viral load. Mean of HCV RNA viral load was $763271.47 \pm 1857165.689$ copies/ml. 5 patients were on DAA medication (7.3 %). Among HCV infected patients, frequency of genotypes 1b and 3 were similar (41.6 % vs 45.8 %). Table 3 shows the rate overview of viral load, genotype tests and treatment. The mean duration of Anti-HCV - HCV-RNA viral load test was 36.8 days, Anti-HCV – genotype test was 105.7 days, Anti-HCV – treatment was 190.3 days. Table 4 shows descriptive overview of viral load, genotype and duration from tests to treatment.

Patients that actively inject drugs were compared with lifetime iv drug users. Active users were in lower income group although the difference was insignificant ($p=0.051$), the rate of daily substance use was higher ($p<0.001$), the rate of two or more recent substance use was higher ($p=0.009$). Of substance recently used, first use age was lower in active iv drug user group (19.1 vs 20.9, $p=0.04$), API – substance use subscale and dependency diagnosis subscale mean scores were higher (2.8 vs 2.2, $p=0.04$; 17.5 vs 15.2, $p=0.007$, respectively). In addition, craving and the effect of substance use on the person's life subscale mean scores were higher (11 vs 8.1, $p<0.001$; 32.2 vs 28.2, $p=0.008$, respectively), total API score was higher ($p=0.001$). Consistently with previous findings, depression and anxiety subscale mean scores were higher in actively injecting drug group (4.7 vs 3.7, $p=0.02$; 3 vs 2.2, $p=0.006$, respectively). ASRS-A mean scores

were higher significantly, even although ASRS-B mean scores were higher, the difference showed no significance (11.3 vs 8.3, $p=0.005$; 23 vs 19.2, $p=0.07$, respectively).

Table 5 Statistical overview of demographic and clinical dimensions, separately for active and lifetime substance users

	Actively iv substance users n (%)		Lifetime iv substance users n (%)		p	
Sex						
Male	59 (89.3)		48 (87.2)			
Female	7 (10.7)		7 (12.8)		0.780	
Income						
High	5 (7.9)		9 (17)			
Middle	18 (28.6)		22 (41.5)		0.051	
Low	40 (63.5)		22 (41.5)			
Use frequency						
Every day	53 (81.5)		22 (41.5)			
Other	12 (18.5)		31 (58.5)		<0.001	
Previous antiviral treatment						
Completed	2 (33.3)		5 (62.5)		0.208	
Uncompleted	4 (67.7)		3 (37.5)			
Current antiviral treatment						
Completed	2 (100)		2 (67.7)		0.649	
Uncompleted	0 (0)		1 (33.3)			
	mean $\pm$ SD		mean $\pm$ SD			
First use age of current substance	19.1 $\pm$ 3.1		20.9 $\pm$ 6.1		0.04	
Duration of Anti-HCV test – treatment (day)	100.4 $\pm$ 87.5		254.5 $\pm$ 294.4		0.288	
API substance use subscale scores	2.85 $\pm$ 1.57		2.25 $\pm$ 1.53		0.04	
API dependency diagnosis subscale scores	17.5 $\pm$ 3.7		15.2 $\pm$ 5.2		0.007	
API craving subscale scores	11 $\pm$ 3.2		8.1 $\pm$ 4.3		< 0.001	
API the effect of substance use on the person's life subscale scores	32.2 $\pm$ 5.9		28.2 $\pm$ 8.9		0.008	
API depression subscale scores	4.7 $\pm$ 2.2		3.7 $\pm$ 2		0.022	
ASRS-A subscale scores	11.3 $\pm$ 4.5		8.3 $\pm$ 4.3		0.005	
ASRS-B subscale scores	23 $\pm$ 8.3		19.2 $\pm$ 9.7		0.07	
	n	MR	n	MR	U	p
Number of substances used	66	67.88	55	52.75	2269	0.008
API total scores	57	65.04	52	44	2054	0.001
API anxiety subscale scores	57	62.87	52	46.38	1930.5	0.006

SD= standard deviation, API= Addiction Profile Index, ASRS = Adult ADHD Self-Report Scale, HCV=Hepatitis C Virus, MR= mean ranking

Patients with history of DAA treatment were compared in terms of treatment completion. Actively iv drug user group showed similar results with lifetime group (33.3 % vs 62.5 %, $p=0.208$). At the same time, both

groups were no different in terms of duration of test to treatment, either (254.5 vs 100.4, $p=0.288$). Within the patients that completed DAA treatment, both groups' proportions were similar to each other (100 % vs 67.7 %, $p=0.649$). Table 5 shows the statistical overview of demographic and clinical dimensions, separately for active and lifetime iv drug users.

Discussion

To best of our knowledge, this study presents first detailed findings of anti-HCV positive patients on interdisciplinary journey in terms of treatment durations. Important majority of the patient group included opiate users. In addition, within multiple substance user group, the proportion of patients who use opiates and cocaine together seemed to be remarkable. Findings in this study which points out mostly iv opiate users as a prominent group in active iv substance users in Turkey, were consistent with previous studies. Given that opiate and stimulant use disorder comorbidity was shown to be associated with reinfection, two or more substance user subpopulation need to be prioritized (16, 17).

Unfortunately in Turkey, there is limited data about patients injecting drugs with chronic HCV infection. In a longitudinal follow-up study from Spain, the proportion of HCV-RNA viral load positivity was found 69.3 % in patients that tested Anti-HCV positive. Of patients, 19.1 % were reported to receive DAA treatment. In our treatment center, lack of infection disease services and need to referral as a local limitation may be related with lower rates. Although in European studies, main genotype has been reported as 1b; in our study genotype 3 was found mostly similar to other findings in Turkey (18, 19, 20).

As expected, considering the low rates and times of patients reaching treatment, the analysis of factors that complicate treatment becomes more valuable. One of the important difficulties in patients' access to treatment could be that the provider sees active iv drug use as a reason to delay the initiation of treatment. Our study presents that patients who actively use iv drugs started using drugs at an earlier age, had higher addiction severity scores, used substances more frequently, and had more depression and anxiety symptoms. However in our study, it was observed that these factors did not cause a significant change in the time to receive treatment in patients who actively use iv drugs. They were at the same level as those who have not used recently, and the treatment completion rates were similar. However, due to low numbers of patients completing the antiviral therapy, retention rate results should be interpreted with caution. Studies examining concomitant antiviral and opiate agonist therapy have shown that active IV substance use during the initiation of treatment does not affect sustained viral response rates. Considering the role of HCV treatment in motivating the patient to abstinence and harm reduction programs, the importance of starting the antiviral treatment becomes clearer (21, 22, 23, 24). In a recent study, re-infection rates after direct-acting antiviral treatment were reported as 1.22 %. Considering all the literature together, it has been reported that it is not recommended to limit HCV treatment, and it is cost-effective to start treatment as soon as detected (17, 25).

It has been reported in the previous studies that stigmatization, homelessness, financial inadequacies and insurance problems related to substance users also create significant barriers to access to antiviral treatment (26). Consistent with previous studies, a significant part of the patients in our study had financial problems and unemployment. Therefore in our sample, there were health insurance problems. These factors may have contributed to the low rate of access to treatment (22).

The rate of comorbid ADHD in patients with substance use disorder has been reported between 15-25 % (27). Many theories have been suggested for the role of ADHD in patients with substance use disorder, such as self-medication, attention deficits, and executive dysfunction (28). In our study, high ADHD self-report scale scores were found in consistency with the literature. It suggests that higher ASRS scores may be related with more frequent iv drug use by the deterioration in executive functions.

This study has a number of limitations. Firstly, a detailed analysis of past antiviral treatment could not be performed, as the patients' previous antiviral treatment data was insufficient. Secondly, since the number of patients who could reach the antiviral treatment is low, there were not enough samples to assess the re-

infection rates of the patients. Difficulties in patients' access to antiviral treatment may also be related to some other major psychiatric problems (29, 30). There was lack of data whether patients had major depressive disorder, anxiety disorder or personality disorder. There was also inefficient data about whether patients had any treatment history of ADHD in the past. Therefore, the inability to analyze these confounding factors seems to be an important limitation.

In the light of all these findings, various difficulties in the treatment process of patients prolong the duration of treatment journey. Necessary preventive actions including temporarily insurance regulations should be taken to solve the financial problem.

Co-location of antiviral treatment centers with OTCs may contribute to shorter treatment times. Stigmatization of active iv substance use as a barrier to the antiviral treatment, may cause disruptions in elimination targets and in preventing viral spread. Participation in antiviral treatment could increase motivation for substance use disorder treatment, thus it becomes even more important to treat patients when detected. Social support systems including families may play an important role in treatment retention and should be included to the treatment as much as possible.

In conclusion, factors differentiating people who recently use iv drugs such as start using substances at earlier age, polydrug use, higher total API and craving scores, impulsivity associated with attention deficit hyperactivity disorder may play an important role to prevent continuing iv drug use although treatment decision should not be postponed. Higher treatment access rates may contribute to the elimination of HCV target especially in special groups including PWIDs. Thus, further studies should investigate whether family role and stigmatization of active iv substance use effect on treatment rates with larger samples. It is also suggested that local treatment clinics and syringe-sharing programs may decrease the duration to antiviral treatment and additional research is needed.

References

1. Scott N, Doyle JS, Wilson DP, et al. Reaching hepatitis C virus elimination targets requires health system interventions to enhance the care cascade. *Int J Drug Policy* 2017; 47: 107-116.
2. Wiessing L, Ferri M, Grady B, et al. Hepatitis C virus infection epidemiology among people who inject drugs in Europe: a systematic review of data for scaling up treatment and prevention. *PLoS One* 2014; 9(7): e103345.
3. Iversen J, Grebely J, Catlett B, et al. Estimating the cascade of hepatitis C testing, care and treatment among people who inject drugs in Australia. *Int J Drug Policy* 2017; 47: 77-85.
4. Falade-Nwulia O, Suarez-Cuervo C, Nelson DR, et al. Oral direct-acting agent therapy for hepatitis C virus infection: a systematic review. *Ann Intern Med* 2017; 166(9): 637-648.
5. Grebely J, Applegate TL, Cunningham P, Feld JJ. Hepatitis C point-of-care diagnostics: in search of a single visit diagnosis. *Expert Rev Mol Diagn* 2017; 17: 1109-1115.
6. World Health Organization. Global Health Sector Strategy on Viral Hepatitis 2016-2021: Towards Ending Viral Hepatitis. Geneva: WHO, 2016.
7. Lopes H, Baptista-Leite R, Franco D, et al. Let's End HepC: Modelling public health epidemiological policies applied to hepatitis C in Spain. *Front Public Health* 2022; 9: 735572.
8. World Health Organization. Global Hepatitis Report, 2017. Geneva: WHO, 2017.
9. Hagan H, Pouget ER, Des Jarlais DC. A systematic review and meta-analysis of interventions to prevent hepatitis C virus infection in people who inject drugs. *J Infect Dis* 2011; 204(1): 74-83.
10. Mittal A, Kosinski KC, Stopka TJ. HCV treatment access among Latinos who inject drugs: qualitative findings from Boston, Massachusetts. *Harm Reduct J* 2019; 16: 1-9.
11. Versfeld A, McBride A, Scheibe A, Spearman CW. Motivations, facilitators and barriers to accessing hepatitis C treatment among people who inject drugs in two South African cities. *Harm Reduct J* 2020; 17(1): 39.
12. Butsashvili M, Abzianidze T, Kamkamidze G, et al. Barriers of linkage to HCV viremia testing among people who inject drugs in Georgia. *Subst Abuse Treat Prev Policy* 2022; 17(1): 23.
13. Kessler RC, Adler L, Ames M, et al. The World Health Organization Adult ADHD Self-Report Scale (ASRS): a short screening scale for use in the general population. *Psychol Med* 2015; 35(2): 245-256.
14. Doğan S, Öncü B, Varol-Saraçoğlu G, Küçüköğücü S. Validity and reliability of the Turkish version of the Adult ADHD Self-Report Scale. *Anadolu Psikiyatri Derg* 2009; 10: 78-87.

15. Ögel K, Evren C, Karadağ F, Tamar Gürol D. Development, Validity and Reliability Study of Addiction Profile Index. *Türk Psikiyatri Derg* 2012; 23(4): 263-275.
16. Butler K, Day C, Dietze P, et al. The potential reach of opioid substitution settings to deliver HCV care to people who inject drugs in Australia. *J Subst Abuse Treat* 2015; 58: 90-94.
17. Akiyama MJ, Lipsey D, Heo M, et al. Low Hepatitis C reinfection following direct-acting antiviral therapy among people who inject drugs on opioid agonist therapy. *Clin Inf Dis* 2020; 70(12): 2695-2702.
18. Robaey G, Bielen R, Azar DG, et al. Global genotype distribution of hepatitis C viral infection among people who inject drugs. *J Hepatol* 2016; 65(6): 1094-1103.
19. Sanvisens A, Rivas I, Faure E, et al. Monitoring hepatitis C virus treatment rates in an opioid treatment program: A longitudinal study. *World J Gastroenterol* 2020; 26(38): 5874-5883.
20. Erman Daloğlu A, Parkan ÖM, Erdoğan A, et al. Distribution of hepatitis C virus genotypes among intravenous drug and non-drug user patients. *Mikrobiyol Bult* 2021; 55(1): 30-40.
21. Aspinall EJ, Corson S, Doyle JS, et al. Treatment of hepatitis C virus infection among people who are actively injecting drugs: a systematic review and meta-analysis. *Clin Infect Dis* 2015; 57 (Suppl 2): 80-89.
22. Trooskin SB, Dore G, Kostman J. We must do better: Addressing HCV treatment barriers in persons who inject drugs in the United States. *J Infect Dis* 2020; 222(S9): 773-781.
23. Rosenthal ES, Silk R, Mathur P, et al. Concurrent initiation of hepatitis c and opioid use disorder treatment in people who inject drugs. *Clin Infect Dis* 2020; 71(7): 1715-1722.
24. Akiyama MJ, Norton BL, Arnsten JH, et al. Intensive models of hepatitis C care for people who inject drugs receiving opioid agonist therapy: a randomized controlled trial. *Ann Intern Med* 2019; 170: 594-603.
25. Muller A, Vlahov D, Akiyama MJ, Kurth A. Hepatitis C reinfection in people who inject drugs in resource-limited countries: a systematic review and analysis. *Int J Environ Res Public Health* 2020; 17(14): 49-51.
26. Zeremski M, Zibbell JE, Martinez AD, et al. Hepatitis C Virus control among persons who inject drugs requires overcoming barriers to care. *World J Gastroenterol* 2013; 19: 7846-7851.
27. Wilens TE. Impact of ADHD and its treatment on substance abuse in adults. *J Clin Psychiatry* 2004; 65 (Suppl 3): 38-45.
28. Tapert SF, Baratta MV, Abrantes AM, Brown SA. Attention dysfunction predicts substance involvement in community youths. *J Am Acad Child Adolesc Psychiatry* 2020; 41(6): 680-686.
29. Fernández de Cañete Camacho JC, Mancebo Martínez A, García Mena MA, Moreno Planas JM. Influence of psychiatric disorders and opioid substitution therapy on hepatitis C treatment with direct-acting antivirals in people who inject drugs. *Gastroenterol Hepatol* 2022; 45(4): 265-273.
30. Pericot-Valverde I, Heo M, Niu J, et al. Relationship between depressive symptoms and adherence to direct-acting antivirals: Implications for Hepatitis C treatment among people who inject drugs on medications for opioid use disorder. *Drug Alcohol Depend* 2022; 14: 234.

Yazar Katkıları: Tüm yazarlar ICMJE'in bir yazarda bulunmasını önerdiği tüm ölçütleri karşılamışlardır

Etik Onay: Bu çalışma için ilgili Etik Kuruldan etik onay alınmıştır.

Hakem Değerlendirmesi: Dış bağımsız.

Çıkar Çatışması: Yazarlar çıkar çatışması olmadığını beyan etmişlerdir.

Finansal Destek: Yazarlar finansal destek beyan etmemişlerdir.

Author Contributions: All authors met criteria recommended by ICMJE for being an author

Ethical Approval: Ethical approval was obtained for this study from relevant Ethics Committee.

Peer-review: Externally peer-reviewed.

Conflict of Interest: The authors have declared that there is no conflict of interest.

Financial Disclosure: Authors declared no financial support