Research Article

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Frequency of HBV, HCV and HIV Infections and Determination of HCV Genotype Distribution in People who Inject Drugs

Damaryolu ile Madde Kullanımı Olan Kişilerde HBV, HCV ve HIV Enfeksiyonlarının Sıklığı ve HCV Genotip Dağılımının Belirlenmesi

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ABSTRACT

Objectives: The aim of this study was to determine the frequency of blood-borne infections [hepatitis B virus (HBV), HCV, and human immunodeficiency virus (HIV)] and the genotype distribution retrospectively in people who inject drugs (PWID).
Materials and Methods: A total of 150 PWID were investigated retrospectively. HBV, HCV, HIV serologies and viral load information were recorded.
Results: The mean age was 27.0±4.89 and 13 (8.7%) patients were female. One hundred and twenty six (84.0%) patients had shared injectors at least once in their lives. Anti-HCV positivity was detected in 91 (60.6%) of 150 patients, hepatitis B surface antigen positivity in 3 (2.0%) and anti-HIV positivity in 1 patient. HCV-RNA was detected in 61 of the patients with anti-HCV positivity and 48 (67.6%) of them were positive for HCV-RNA. Genotype was studied in 38 patients with HCV-RNA positivity. Genotype 1a was detected in 20 patients, genotype 3a in 12 patients, genotype 4c/d in 5 patients and 2b in 1 patient.
Conclusion: In PWID, HCV infection was found to be in high ratio in PWIDs and the most common HCV genotype was 1a. It was concluded that injector sharing caused infectious diseases in PWID and that some HCV genotypes were dominant in these patients. Genotype determination will be a guide for individualized treatments in these patients.
Keywords: Hepatitis C virus, genotype, people who inject drugs

ÖZ

Amaç: Bu çalışmanın amacı, damar içi madde kullanıcılarında (DİMK) kan yoluyla bulaşan enfeksiyonların [hepatit B virüs (HBV), HCV ve insan bağışıklık yetmezliği virüsü (HIV)] sıklığını ve genotip dağılımını geriye dönük olarak belirlemektir.
Gereç ve Yöntemler: Geriye dönük olarak toplam 150 DİMK incelendi. HBV, HCV, HIV serolojileri ve viral yük bilgileri kaydedildi.
Bulgular: Ortalama yaş 27,0±4,89 olup, 13 (%8,7) hasta kadındı. Yüz yirmi altı (%84,0) hasta hayatında en az bir kez enjektör paylaşmıştı. Yüz elli hastanın 91'inde (%60,6) anti-HCV pozitifliği, 3'ünde (%2,0) hepatit B yüzey antijen pozitifliği ve 1 hastada anti-HIV pozitifliği saptandı. Anti-HCV pozitifliği olan hastaların 61'inde HCV-RNA tespit edildi ve bunların 48'inde (%67,6) HCV-RNA pozitifti. Genotip tayini, 38 HCV-RNA pozitif hastada yapıldı. Yirmi hastada genotip 1a, 12 hastada genotip 3a, 5 hastada genotip 4c/d ve sadece bir hastada genotip 2b tespit edildi.
Sonuç: DİMK'de HCV enfeksiyonu yüksek oranda bulundu ve en yaygın HCV genotipi 1a olarak tespit edildi. Enjektör paylaşımının DİMK'de bulaşıcı hastalıklara neden olduğu ve bu hastalarda bazı HCV genotiplerinin baskın olduğu sonucuna varıldı. Genotip tespiti, bu hastalarda bireyselleştirilmiş tedavilerin planlanmasında yol gösterici olacaktır.
Anahtar Kelimeler: Hepatit C virüsü, genotip, damar içi madde kullanıcıları

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Introduction

Blood-borne pathogens are microorganisms, such as bacteria and viruses, that can cause disease in humans. These pathogens are transported through the blood. There are many blood-borne pathogens such as malaria, syphilis, brucellosis, hepatitis B virus (HBV), HCV and human immunodeficiency virus (HIV). Studies show that less than half of people who inject drugs (PWID) use a sterile syringe (46.9%) and 38.5-61% of them share syringe/needle or drug solutions with someone else over the past 6 months (1,2).

Due to the common use of contaminated needles and injection equipment, PWID are an important risk group for HCV infection (3,4,5). HCV seropositivity rate increases to 50-90% in PWID (6). In a study conducted in the UK, 428 PWID under the age of 30 were found to encountered 4% HIV and 44% HCV in the initial evaluation (7). In a systematic review of 11 studies from five European Union Countries, the proportion of undiagnosed HCV infections among those using intravenous drug varies between 24-76% (8).

Among PWID, the prevalence of hepatitis B surface antigen (HBsAg) carriers ranges from 5% to 10% in 21 countries and exceeds 10% in 10 countries (9). The prevalence of hepatitis B infection was found to be 0.8% in a study in Bosnia and Herzegovina, but it was found to be as high as 21.5% in another study in China (10,11). In a study conducted in 2077 patients using intravenous drug in Germany, HIV seroprevalence was found to be 0-9.1% compared to cities (12).

There are six genotypes of HCV. Determination of HCV genotypes is important in the treatment and course of the disease. HCV genotype distribution was investigated in different groups in the world geography. In the general population, genotype 1 is the most common in North America, Northern and Southern Europe, Japan, and Eastern Europe including our country (13,14,15). Genotype 3 is common in PWID in the Middle East and North Africa (16); In a Chinese study, genotype 3b and genotype 6a were more common (17). In our country, the most common genotype was found to be 1a in HCV-infected adolescents using intravenous drug (18,19).

The aim of this study is to investigate the sociodemographic characteristics of PWID who applied to Akdeniz University Alcohol and Substance Addiction Research and Application Center (AMBAUM) and to determine the frequency of blood-borne infections (HBV, HCV, and HIV) in this patient group. We also aimed to determine genotype distribution in patients with HCV infection.

Materials and Methods

This study was planned retrospectively in PWID who applied to AMBAUM between August 2017 and March 2018. Age, sex, education, heroin use, age of initiation of heroin use, drug use other than heroin, possible blood-borne agent serology and HCV genotype distribution were evaluated in PWID. Anti-HBs, anti-HCV and anti-HIV antibodies were analysed by EIA method (Advia Centaur HP, Siemens Healthcare Diagnostics, USA). HCV-RNA determination was performed by a commercial real time-polymerase chain reaction (RT-PCR) test (COBAS AmpliPrep/COBAS TaqMan HCV, Roche Diagnostics, Roche Molecular Systems, Pleasanton, CA). A commercial reverse hybridization (line probe-based assay; GEN-C RT-PCR, Italy) was carried out for HCV genotyping. The ethics committee approval of the study was given by Akdeniz University Faculty of Medicine Clinical Research Ethics Committee (approval number: 352, date: 30/07/2018).

Statistical Analysis

The data obtained in the study were analyzed by a computer using SPSS 20 software package program. Mean ± standard deviation was used for descriptive continuous variables and number and percentage were used for median categorical variables. The suitability of continuous variables to normal distribution was examined by Shapiro-Wilk test. The difference in percentages of categorical variables was analyzed by Pearson chi-square test, if more than 20% of expected frequencies were less than 5, Fisher's exact test was used. Due to lack of parametric test assumptions, difference between two independent group averages was analyzed by Mann-Whitney U test. Spearman's rho correlation analysis was used to determine the relationship between the two variables. When comparing continuous data of three or more groups, One-Way ANOVA was used when parametric test assumptions were met, and where parametric test assumptions were not met, Kruskal-Wallis test was used. α=0.05 error margin (or 95% significance level) was used to determine differences in the analyzes.

Results

A total of 150 patients with intravenous drug use were included in the study. The mean age of the patients was 27.0±4.89 and the sociodemographic characteristics including gender, education, and clinical characteristics such as smoking, cannabis, cocaine and stimulant use in addition to heroin are shown in Table 1.

Table 1. Sociodemographic characteristics and use of substances other than heroin

	(n=150)	%
Gender		
Female	13	8.7%
Male	137	91.3%
Education status		
Primary school	15	10.0%
Middle school	101	67.3%
High school	23	15.3%
University	11	7.3%
Smoking		
Yes	142	94.7%
No	8	5.3%
Cannabis use		
Yes	106	70.7%
No	44	29.3%
Cocain use		
Yes	95	63.3%
No	55	36.7%
Use of stimulant		
Yes	72	48.0%
No	78	52.0%

The mean age at onset of drug use was 19.04±3.85 years, the amount of use was 2.12±1.79 gram/day and the mean drug use time was 7.71±3.95 years. The number of drug users in the last 1 month was 122 (81.9%). The number of patients using drug intravenously in the last 1 month was 113 (75.8%). In addition, 84.0% (126) of the patients reported that they shared injectors at least once in their lives. The number of patients admitted to any treatment clinic before admission to our clinic was 104 (69.3%). Thirty-six patients reported that they had never received treatment at a substance abuse center before. Hepatitis markers and HCV genotype distribution were shown in Table 2. Anti-HCV positivity was detected in 91 (60.6%) of 150 patients with intravenous drug use. HCV-RNA was studied in 61 patients with anti-HCV positivity. HCV-RNA was positive in 48 (67.6%) of these patients. Genotype was determined in patients with HCV-RNA positivity. In some patients, genotype detection could not be performed due to the low number of HCV-RNA copies or the patient not coming back to the control. Genotype was detected in 38 patients. Genotype 1a in 20 patients, genotype 3a in 12 patients, genotype 4c/d in five patients and 2b in one patient were detected. No statistically significant difference was found between serum HCV-RNA levels and the mean age of the patients according to genotype distribution (p=0.332, p=0.457) (Table 2). In addition, the mean age of patients with anti-HCV positive and anti-HCV negative was 28 and 25.53, respectively. The mean age of anti-HCV positive patients was higher and it was found to be statistically significant compared to anti-HCV negative patients (p=0.03).

Of the 91 patients with anti-HCV positivity, 67 (73.6%) who were regularly followed up were consulted to the infectious diseases outpatient clinic. However, only 38 (56.7%) of these patients applied to the related unit. Of the 48 patients with positive HCV-RNA levels, 23 patients (47.91%) received treatment. The remaining patients did not apply, so treatment could not be given.

The prevalence of HBV seropositivity was 2.0% (3/150). HCV co-infection was not detected in three patients. Seventeen (11.3%) of the 150 patients developed immunity to HBV either naturally or by vaccination. HBV-DNA was found high in two of the HBsAg positive patients, the levels were $3x10^5$ and $98x10^7$ copies/mL. The other one's HBV-DNA value was negative. Treatment could not be given because none of them admitted to us again.

Anti-HIV seropositivity was detected in 1 of 150 patients. As a result of detailed examination, false seropositivity was found in this patient.

Discussion

In our study, in PWID, genotype 1a was found to be the most common in patients who came to AMBAUM from Antalya and the surrounding provinces, and genotype 3a was detected in the second frequency. The distribution of HCV genotypes in the world generally varies according to geographical regions (20). In a study conducted in China, genotype 1b was dominant in the general population, whereas genotype 6a was the most common in PWID (11). 1b and 2a/2c have been identified among HCV genotypes in PWID in Korea (21). In studies conducted in Italy and Brazil, genotypes 1 and 3 were similarly detected at a higher rate (22,23). In Romania, non-1b genotypes were detected in 54.8% of cases; The most common of these are 1a and 3a (24). In South Africa the most common HCV genotype was genotype 1a in PWID (73%, 270/368) (25). In our country, the number of studies on the detection of HCV genotype in PWID is limited. Similar to our study, 1a was found to be the most common genotype in studies İstanbul and Mersin regions (18,19). In a study conducted in Çukurova region, 52 (58.6%) of 87 patients had genotype 3 (26). As a result of the comparisons, although the regional variability is seen among PWID in our country, the most common genotype is 1a.

In our study, HCV-RNA was detectable in 52.3% (48/91) of the patients with anti-HCV positivity. In a Korean study, 154 patients had anti-HCV positivity and HCV-RNA was found 98.1% (151/154) in patients who were anti-HCV positive. In 151 patients with detectable serum HCV-RNA, 90 (59.6%) patients showed high levels of viremia (HCV-RNA level above 400,000 IU/mL) (21). In Italy, HCV-RNA was found in 68.3% of patients who were anti-HCV positive. High levels of viremia (HCV-RNA level above 600,000 IU/mL) were found in approximately 50% of these patients (22). In Romania, active HCV viral replication was detected in 104 patients (80%) (24). In studies among PWID, In Myanmar HCV prevalence was 68-76% and in South Africa HCV seroprevalence was 55% (513/937) (25,27). A meta-analyse suggest that based on 118 HCV antibody prevalence measures, the pooled mean prevalence in PWID for all Middle East and North Africa was 49.3% (28).

Table 2. Hepatitis markers, HCV genotype distribution

Viral marker	n	%	HCV-RNA count (median) (IU/mL)
Anti-HCV positive	91	60.6	-
HCV-RNA positive*	48	67.6	-
HCV genotype**			
1a	20	52.6	$9.5x10^5$
2b	1	2.6	$43.3x10^5$
3a	12	31.6	$1.48x10^5$
4c/d	5	13.2	$1.9x10^5$
HBsAg positive	3	2.0	-
Anti-HBs positive	17	11.3	-

*Measured at detectable level in anti-HCV positive patients. **In patients with genotype determination.
HCV: Hepatitis C virus, RNA: Ribonucleic acid, HBsAg: Hepatitis B surface antigen, anti-HBs: Hepatitis B surface antibody

According to these results, we can say that HCV has high viremia levels in PWID. In addition, in our study, genotype 4c/d was found to be 13.2% among all genotypes. Kandemir and Gültekin. (18) found this rate to be 6.3%, and it was observed that genotype 4 could not be detected in two other studies on genotype determination in our country (19,26). According to these results, genotype 4 may be increasing between PWID. Considering that the mean age of this patient group is lower than the general population; genotype 4 may be highly prevalent in the general population in the near future. In addition, it is thought that one of the most important reasons for this genotype to be seen at a higher rate in PWID compared to other genotypes is the injector sharing of the patients. A study in Korea reported that 51.3% of patients shared injectors (21). In Romania, the injector sharing rate was 86.9%, which is similar to our study (24). Injector sharing is one of the most powerful predictors for increasing the likelihood of HCV (29).

Seven (8.7%) of the patients who participated in our study were female and this rate was higher than other studies conducted in our country (19,26). This data makes us think that the incidence of intravenous drug use and blood-borne infectious diseases is increasing among women in our country.

HBV markers (HBsAg, HBcAb, HBeAb and HBV-DNA) were found to be significantly higher in PWID than in the general population but HBsAb positivity in PWID was lower than in the general population (21). While the prevalence of HBV in PWID is 6.2% in our country, this rate is 5.9% in those who have injected intravenously within the last 30 days (29). We observed that these rates were lower in the province of Antalya (the prevalence of HBsAg positivity was 2.0% and immunity to HBV was 11.3%). In addition, HCV co-infection was not detected in any of HBsAg positive patients. With this result, it can be said that HBV and HCV coinfections between PWID are low.

HIV is expected to be seen at higher rates among PWID (12). While anti-HIV positivity was found in 3.1% in Italy (22), 80.8% of 130 patients with HCV in Romania were found to be HIV-infected (24). In contrast to these studies, anti-HIV seropositivity was detected in only 1 out of 150 patients in our study. Detailed investigations of this patient revealed false seropositivity. HIV infection is very rare among PWID in our country with a prevalence of 0.34% (29). These results show that HIV is still not common among PWID in our country.

Patients with intravenous drug use who were found to be HCV positive were referred to ınfectious diseases outpatient clinic, but only 56.7% of them went to related unit and most patients did not come to the check examination. This suggests that most patients choose to refuse treatment after learning about HCV positivity. This low treatment compliance can be considered as an important factor in the spread of infections in PWID.

In HCV infected PWID group, the rate of reinfection is high despite the treatment. Among PWID treated for hepatitis C were reported higher rates of re-infection than existing estimates (30). In our study, only 47.91% of patients with positive HCV-RNA levels received HCV therapy. The reason for this low rate was that patients did not apply for HCV treatment. These data highlight the importance of substance use therapy in PWID patients, along with HCV therapy. Thus, compliance of patients to HCV treatment can be increased.

Study Limitations

Our study has limitations such as low number of patients, being a retrospective study, being performed in a single center and low number of patients applying to the infection department.

Conclusion

Our study reveals the frequency and HCV genotype distribution of blood-borne pathogens in PWID. The most common genotype in patients was 1a and 3a was the second most common genotype. HCV infection is an important health problem among PWID. Determining HCV genotype distribution among PWID will be a guide for future individualized treatments. In addition, it is important that our study is the first study conducted in Antalya region and it is one of the limited number of studies in our country.

Ethics

Ethics Committee Approval: The ethics committee approval of the study was given by Akdeniz University Faculty of Medicine Clinical Research Ethics Committee (approval number: 352, date: 30/07/2018).

Informed Consent: Retrospective xstudy.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: H.K., D.İ., Design: H.K., D.İ., Data Collection or Processing: Ö.Ö., D.Ç., G.Ö., Analysis or Interpretation: H.K., D.İ., Ö.Ö., A.E., D.Ç., G.Ö., Literature Search: H.K., D.İ., Ö.Ö., A.E., D.Ç., G.Ö., Writing: D.Ç., G.Ö.

Conflict of Interest: The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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