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# HCV treatment in HIV/HCV co-infected patients
## A single center, observational study

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ΑΡΧΕΙΑ ΕΛΛΗΝΙΚΗΣ ΙΑΤΡΙΚΗΣ 2019, 36(6):787–791

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Θεραπεία της ηπατίτιδας C σε ασθενείς με HIV/HCV συλλοίμωξη. Μελέτη ενός κέντρου

*Περίληψη στο τέλος του άρθρου*

OBJECTIVE **To investigate the effectiveness of direct acting antiviral drugs (DAAs) in HIV/HCV co-infected patients and to document treatment-associated problems.** METHOD **All HIV/HCV co-infected patients attending the HIV unit of the "Laiko" University Hospital in Athens, Greece, from 1.1.2015 to 31.12.2017 were screened for this study. Inclusion criteria were HIV/HCV co-infection and age 18–85 years. A diagnosis of poor prognosis cancer was an exclusion criterion. Transient elastography (TE) was performed at study entry and laboratory tests were conducted at baseline and every 3 months until the end of follow up. HCV treatment was administered according to national guidelines. All the patients were followed up for 6 months after sustained virological response (SVR) and treatment-related and HIV-related complications were noted.** RESULTS **A total of 28 patients with HIV/HCV coinfection were treated during the study period, 25 of which were male. Abnormal serum levels of transaminases were recorded in 21 patients at study entry. The median TE value was 7.6 kilopaskal (KPa), with 11 patients being classified as Metavir F0–F1 fibrosis, 6 F2, 8 F3 and 3 F4 according to TE. Thirteen patients had HCV genotype 1, 7 genotype 3, 4 genotype 2 and 4 genotype 4. Stage C HIV infection according to CDC staging was identified in 5 patients. SVR for HCV infection was achieved in 26 of the 28 patients treated (93%). Before the initiation of DAAs, 9 patients required a change in HIV-antiretroviral treatment (ARV), due to drug-drug interactions. No patient had a worsening of HIV-related serum markers during HCV-treatment and follow up.** CONCLUSIONS **DAAs treatment in HIV/HCV co-infected patients results in high SVR rates, with no significant side effects. ARV modification, when needed, allows HCV eradication with no adverse HIV-related effects.**

**Key words**

Direct-acting antiviral drugs (DAA)
HCV
HCV/HIV coinfection
HIV

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More than 2,000,000 individuals worldwide are living with chronic hepatitis C (HCV) and human immunodeficiency virus (HIV) co-infection.[1] Since the advent of antiretroviral therapy (ART), HIV-infected patients have had a significant increase in life expectancy.[2] HCV-related liver disease, however, continues to be a leading cause of morbidity and mortality in HIV-infected patients, since HIV/HCV co-infection leads to a higher HCV viral load,[3] a faster rate of progression to liver fibrosis and cirrhosis, increased risk of hepatic decompensation and hepatocellular carcinoma (HCC) and increased risk of drug-related hepatotoxicity.[4–6]

Although successful treatment of HCV infection with pegylated interferon and ribavirin (pegIFN/RBV) led to a decrease in liver-specific and all-cause mortality in the past,[7,8] the rate of eradication of HCV infection was low among HIV/HCV co-infected patients,[9] due to poor tolerability of dual therapy[9] and low percentages of sustained virological response (SVR) in the patients treated.[10,11] The addition of telaprevir (TPV) or boceprevir (BOC), the first-generation HCV NS3/4A protease inhibitors for HCV treatment, led to higher SVR rates,[12,13] at the cost of significant side effects,[14] and several drug-drug interactions with the concomitant ART.[15,16]

Treatment of patients with HIV/HCV co-infection, using a variety of potent, better tolerated, all oral, direct acting antiviral drugs (DAAS) has been shown to achieve SVR rates of up to 95%, in clinical trial settings.[17–28] In a few "real world" studies conducted on DAAs in HIV/HCV co-infected patients, the SVR rates were near 90%, somewhat less than that in "drug studies".[29–36] However, drug-drug interactions

of DAAs with ART may occur, leading to ART modification in some patients, before the initiation of DAA-treatment.[37]

We conducted a study in a tertiary university hospital in Athens, Greece, aimed at investigating the effectiveness of DAAs in HIV/HCV co-infected patients, and documenting treatment-associated problems.

## MATERIAL AND METHOD

This study included patients attending the HIV unit of the "Laiko" University Hospital in Athens, Greece, from 1.1.2015 to 31.12.2017. The inclusion criteria were HIV/HCV co-infection and an age of 18 to 85 years. A diagnosis of poor prognosis cancer was an exclusion criterion, as HCV treatment is contraindicated in these patients.

Antiviral treatment was chosen according to national guidelines. Where ART change was required, it was carried out under consultation with the HIV unit. The medical history of each patient was acquired from both interview and the patients' health records. Transient elastography (TE) was performed at study entry and laboratory tests were conducted at baseline and every 3 months until the end of follow up. Patients not achieving SVR were re-treated according to national guidelines.

All patients were followed up for 6 months after the end of HCV treatment in order to find out if ARV modification, when necessary, led to worsening of HIV status, in terms of higher viral load or lower CD4 count.

The study was reviewed and approved by the ethics committee of the "Laiko" University Hospital and written informed consent was obtained from all the enrolled patients. All study procedures were in agreement with the Declaration of Helsinki (Edinburgh, 2000).

## RESULTS

A total of 28 patients were treated with DAAs during the study period, 25 of which were male. Their median age was 40 years (range 29–57 years) and their median body mass index (BMI) 24.4 (range 21–34.3). The laboratory findings of the patients are shown in table 1. The serum transaminase levels at study entry were abnormal in the vast majority of patients (21/28, 75%), but the platelet count and serum total bilirubin were normal in all patients. The median HCV RNA viral load at study entry was 4,200,000 IU/mL (range 120,000–8,400,000) and the median value of TE was 7.6 kilopaskal (KPa). According to the TE results, 11 patients had a score equivalent to a Metavir fibrosis score of F0–F1, 6 patients F2, 8 F3 and 3 F4. Fibrosis-4 (FIB-4) and AST to platelet ratio index (APRI) scores were 1.32 and 0.95, respectively, with 3 patients according to FIB-4 and 4 according to APRI being classified as patients with severe liver fibrosis. The most common HCV genotype was genotype 1 (13 patients, 47%), while genotype 3 was found in 7 patients, genotype 2 in 4 and genotype 4 in 4 patients (fig. 1). No patient was HBV co-infected. The median duration of the HCV and HIV infection at study entry are listed in table 1.

Intravenous drug use was the cause of HIV infection in 23 (82%) patients, of which 6 were still using drugs intravenously, and sexual transmission in 5 patients. Five patients (18%) had clinical AIDS (stage C) according to CDC staging (38), 17 were at stage A and 6 at stage B. The median CD4 count at study entry was 559 cells/mm$^3$ (range 11 1,357) and no patient had a detectable HIV viral load (tab. 1). All patients were receiving ART, mainly abacavir/

**Table 1.** Laboratory results of patients with HIV/HCV co-infection at study entry (D0) and at sustained virological response (SVR), and duration of HIV and HCV infection (n=28).

| | D0 | SVR | p value |
|---|---|---|---|
| AST (IU/mL) (median, range) | 50 (21–161) | 18.5 (14–25) | 0.0141 |
| ALT (IU/mL) (median, range) | 58 (25–301) | 14 (5–21) | 0.0298 |
| γGT (IU/mL) (median, range) | 50 (30–120) | 20 (13–67) | 0.0198 |
| ALP (IU/mL) (median, range) | 72 (19–173) | 64 (45–112) | 0.2716 |
| TBil (mg/dL) (median, range) | 0.55 (0.2–1.06) | 0.57 (0.24–0.63) | 0.4905 |
| PLTs (K/μL) (median, range) | 172 (129–361) | 199 (154–226) | 0.6942 |
| CD4 (median, range) | 559 (11–1357) | 528 (332–1562) | 0.317 |
| Undetectable HIV viral load (no of patients) | 19 | 18 | n/a |
| HCV duration (months) | 95 (24–252) | | |
| HIV duration (months) | 70 (24–304) | | |

HCV: Hepatitis C virus, HIV: Human immunodeficiency virus, AST: Aspartate transaminase, ALT: Alanine transaminase, γGT: Gamma glutamyl transferase, ALP: Alkaline phosphatase, TBil: Total bilirubin , PLTs: Platelets

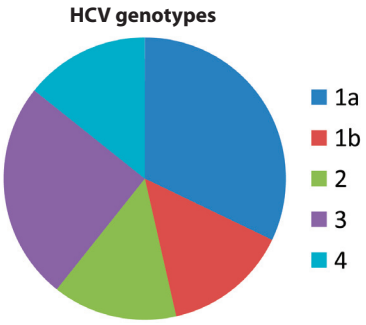


**Figure 1.** The hepatitis C virus (HCV) genotypes of the study patients with HIV/HCV co-infection (n=28).

lamivudine/raltegravir or efavirenz/emricitabine/tenofovir disoproxil fumarate.

For the HCV infection, the majority of the patients in our study received sofosbuvir-based treatment regimens (22/28 78.5%) (tab. 2). Of the 28 patients treated, 26 (93%) achieved SVR. One patient stopped treatment after 3 weeks due to a relapse in drug use, and one patient failed to achieve SVR and was retreated for a longer period with the addition of ribavirin, achieving, this time, SVR. Nine patients (32.1%) had their ART modified, before the initiation of DAAs, because of drug-drug interactions.

**Table 2.** Anti-HCV treatment regimens used in patients with combined HIV/HCV infection (n=28).

| Regimen | Patients (no) | Percentage (%) |
|---|---|---|
| Sofosbuvir/daclatasvir | 3 | 10.7 |
| Sofosbuvir/ledipasvir | 10 | 35.7 |
| Sofosbuvir/velpatasvir | 9 | 32.2 |
| Grazoprevir/elbasvir | 4 | 14.3 |
| Ombitasvir/paritaprevir/ritonavir | 2 | 7.1 |

HCV: Hepatitis C virus, HIV: Human immunodeficiency virus

As shown in table 1, the levels of serum transaminases and gamma glutamyl-transferase (γGT) were significantly lower after completion of HCV infection treatment while the serum levels of alkaline phosphatase (ALP) and total bilirubin showed no change. No patient showed worsening of HIV infection in terms of number of CD4 cells or positivity of HIV viral load during the 6 months of follow up.

## DISCUSSION

Treatment of HCV in HIV/HCV co-infected patients was a major problem up in the interferon era, but in the DAAs era, clinical trials showed SVR rates of up to 95% for HCV infection in this subset of patients. In a review of 11 "real world" studies, SVR of the HCV infection was achieved in an average of 90% of treated HIV/HCV co-infected patients (39), a percentage close to that in HCV mono-infection.

In our "real world" study, the vast majority of patients achieved SVR for HCV infection; 26/28 receiving treatment (92.9%) and 26/27 completing it (96.3%) with no significant adverse effects. In 9 (32.1%) patients, ARV modification was required before the initiation of anti-HCV treatment due to drug-drug interactions, but all the changes proved to be safe as far as HIV infection is concerned, since no patient exhibited reduction of CD4 cells or increase of HIV viral load.

Overall, our study showed that HCV treatment of HIV/HCV co-infected patients, in the new era of DAAs, achieves high rates of SVR with few, if any, adverse effects. Moreover, ARV treatment can be safely modified before the initiation of DAA, in order to avoid drug-drug interaction, with no setback in the HIV status.

## ΠΕΡΙΛΗΨΗ

**Θεραπεία της ηπατίτιδας C σε ασθενείς με HIV/HCV συλλοίμωξη. Μελέτη ενός κέντρου**

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**ΣΚΟΠΟΣ** Η διαπίστωση της αποτελεσματικότητας των νεότερων, από του στόματος, αντι-ιικών άμεσης δράσης (DAAs) και των επιπλοκών που συνεπάγεται η σχετική θεραπεία. **ΥΛΙΚΟ-ΜΕΘΟΔΟΣ** Όλοι οι ασθενείς με HIV/HCV συλλοίμωξη που παρακολουθήθηκαν από το Εξωτερικό Ιατρείο Λοιμώξεων της Παθολογικής Φυσιολογίας του Γενικού Νοσοκομείου «Λαϊκό» από 1.1.2015–31.12.2017 αξιολογήθηκαν για πιθανή ένταξη στη μελέτη. Κριτήρια εισόδου στη μελέτη ήταν η ύπαρξη HIV/HCV συλλοίμωξης και η ηλικία των 18–85 ετών. Ως κριτήριο αποκλεισμού θεωρήθηκε η

ύπαρξη καρκίνου με κακή πρόγνωση. Κατά την είσοδο του ασθενούς στη μελέτη διενεργείτο ελαστογραφία ήπατος και εργαστηριακός έλεγχος, με τον τελευταίο να επαναλαμβάνεται ανά τρίμηνο έως τη λήξη της παρακολούθησης. Η θεραπεία για την HCV λοίμωξη ακολουθούσε τις ελληνικές κατευθυντήριες οδηγίες. Η παρακολούθηση των ασθενών συνεχιζόταν έως και 6 μήνες μετά την κάθαρση του HCV, με καταγραφή πιθανών ανεπιθύμητων ενεργειών των DAAs, καθώς και επιπλοκών της HIV λοίμωξης. **ΑΠΟΤΕΛΕΣΜΑΤΑ** Στη μελέτη εντάχθηκαν 28 ασθενείς, 25 από τους οποίους ήταν άνδρες. Από τους ασθενείς της μελέτης 21 εμφάνιζαν αυξημένες τρανσαμινάσες κατά την ένταξή τους. Η διάμεση τιμή ελαστογραφίας ήταν 7,6 KPa, 11 ασθενείς εμφάνιζαν ίνωση F0–F1 κατά Metavir, 6 F2, 8 F3 και 3 F4. Από το σύνολο των ασθενών, 13 είχαν γονότυπο 1, 7 γονότυπο 3, 4 γονότυπο 2 και 4 γονότυπο 4. Πέντε ασθενείς είχαν HIV λοίμωξη σταδίου C κατά CDC. Μακροχρόνια ιολογική ανταπόκριση **(**SVR) εμφάνισαν 26 από τους 28 ασθενείς που έλαβαν θεραπεία (93%). Πριν από τη χορήγηση των DAAs, 9 ασθενείς χρειάστηκαν μετατροπή της αντιρετροϊκής τους θεραπείας, λόγω αλληλεπιδράσεων των φαρμάκων. Κανένας από τους ασθενείς δεν εμφάνισε επιδείνωση των δεικτών που σχετίζονται με τον HIV κατά τη διάρκεια της θεραπείας και κατά την παρακολούθηση. **ΣΥΜΠΕΡΑΣΜΑΤΑ** Η θεραπεία με DAAs στους ασθενείς με HIV/HCV συλλοίμωξη επιτυγχάνει υψηλά ποσοστά SVR, χωρίς σοβαρά ανεπιθύμητα συμβάματα. Η μετατροπή της αντιρετροϊκής θεραπείας, όταν αυτή χρειάζεται, επιτρέπει την εκρίζωση της ηπατίτιδας C, χωρίς επιβάρυνση της HIV λοίμωξης.

**Λέξεις ευρετηρίου:** Άμεσης δράσης αντι-ιικά (DAA), HIV/HCV συλλοίμωξη, Ιός ανθρώπινης επίκτητης ανοσοανεπάρκειας (HIV), Ιός ηπατίτιδας C (HCV)

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