ORIGINAL ARTICLE

CONTENTS

Virological and antifibrotic efficacy of antiviral treatment for hepatitis B+C in HIV-positive patients

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ABSTRACT

Aim: To study and compare the efficacy of different regimens of combination antiviral therapy for hepatitis C and B in achieving a sustained virological response in patients with HIV/HBV/HCV coinfection and their impact on the degree of liver fibrosis.

Materials and Methods: We examined 113 HIV-infected adult patients with HBV/HCV coinfection who were registered at the Municipal Non-profit Enterprise "Infectious Diseases Center of the Ivano-Frankivsk Regional Council" between 2017 and 2019. The efficacy of HBV AVT was assessed by the achievement of undetectable HBV DNA levels in plasma at the baseline of the surveillance and again 1 year later. Continuous variables were expressed as a median and interquartile range (Q1-Q3). Categorical variables were described as frequencies. Group differences in categorical variables were assessed with Pearson's Chi-square and post-hoc Pearson's Chi-square tests, and in continuous variables, the Kruskal-Wallis' test was used. Wilcoxon signed-rank test was used to compare two dependent groups.

Results: The treatment regimens with two direct-acting antivirals (sofosbuvir/ledipasvir, sofosbuvir+daclatasvir, sofosbuvir/velpatasvir and sofosbuvir/ledipasvir and ribavirin resulted in 100 % sustained virologic response. The efficacy of the pegylated interferon, sofosbuvir, and ribavirin regimen was lower, with sustained virologic response achieved in 86.2 % of patients. The lowest efficacy was observed with the sofosbuvir and ribavirin regimen – sustained virologic response achieved in 75.0 % of patients. Primary HBV resistance to tenofovir/emtricitabine was identified in 1.76 % of patients in the entire cohort. Among patients in the group treated with combined antiviral therapy for HBV and HCV using tenofovir/emtricitabine and direct-acting antivirals with or without ribavirin, the incidence of liver fibrosis F3-F4, as assessed by point-shear wave elastography, decreased from 20 % to 2.5 % ($p<0,05$) after one year of follow-up.

Conclusions: In patients with HIV/HBV/HCV coinfection, interferon-free regimens that include two direct-acting antivirals, either alone or in combination with ribavirin, demonstrated 100 % virologic efficacy and the most beneficial effects on the liver reducing the degree of liver fibrosis.

KEY WORDS: human immunodeficiency virus, hepatitis B, hepatitis C, antiviral agents, liver fibrosis

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INTRODUCTION

Hepatitis B (HBV) and hepatitis C (HCV) coinfection are common among HIV-positive people due to identical modes of transmission, with a prevalence of 50.3 %. Among these cases, HIV/HCV coinfection accounts for 35.4 %, HIV/HBV for 8.4 %, and HIV/HBV/HCV for 5 % [1]. According to estimates from the pre-war period (2021) *(Volosevich et al., 2021),* 5 % of the total population in Ukraine was infected with HCV (2,107,660 people), while HBV cases were recorded in 1.5 % of the population (632,298). Among people who live with HIV, HIV/HCV coinfection has been reported in 2.4 % of their total population. This includes 82.4 % of injecting drug users (IDUs), 6.4 % of men who have sex with men (MSM), and 4.0 % of HIV-positive pregnant women [2]. Overall, among HIV-positive persons under surveillance, 29,946 were diagnosed with HCV, 5,640 with HBV, and 3,004 with HBV/HCV coinfection [3, 4].

The risk of HCV infection or reinfection in HIV-positive individuals is 6 times higher than in the general population. These patients demonstrate an increased incidence of liver fibrosis, progression of liver failure, and, ultimately, death [5, 6]. End-stage liver disease is most common in patients with HIV/HBV/HCV coinfection, less frequent in those with HIV/HBV and HIV/HCV coinfections, and occasionally observed in HIV mono-infection due to alcohol consumption, non-alcoholic fatty liver disease, and, to some extent, due to the toxicity of certain drugs used in ART [7]. Consequently, the risk of death is 1.6 times higher in patients with HIV/HBV and HIV/HCV coinfections and 2.29 times higher in those with HIV/HBV/HCV coinfection compared to patients with HIV mono-infection [8].

Direct-acting antivirals (DAAs) used in the treatment of HCV have not only enabled the full recovery of patients but also significantly impacted the prevalence

of the disease, potentially leading to the eradication of the pathogen within the population. In this regard, the World Health Organization (WHO) has approved a strategy to combat HCV by 2030 through maximum population coverage with screening and treatment [9]. Drugs from the groups of RNA-dependent polymerase inhibitors (anti-NS5B), protease inhibitors (PI, anti-NS3/4A), and NS5A inhibitors are highly effective in improving patient prognosis both in the short and long-term [10]. New interferon-free regimens achieve a sustained virologic response (SVR) in over 95 % of patients, causing fewer side effects than interferon therapy [11]. DAAs are effective not only in inducing SVR but also in preventing the development of hepatocellular carcinoma, liver cirrhosis, and unfavorable outcomes [12]. Patients with HIV/HCV, HBV/HCV coinfections and decompensated cirrhosis constitute a so-called special group, as their treatment outcomes may differ from the expectations and, therefore, require careful monitoring [13].

According to the updated recommendations of the American Association for the Study of Liver Diseases (AASLD) and the Infectious Diseases Society of America (IDSA), patients who have not previously been treated for HIV and HCV coinfection, regardless of cirrhosis status, are suitable candidates for DAA therapy, as supported by the results of a phase 4 MINMON clinical trial conducted by *Solomon et al.* in 2022 [14, 15].

For individuals with HIV/HBV coinfection, the U.S. Department of Health and Human Services Panel on Antiretroviral Guidelines for Adults and Adolescents recommends prescribing an ART regimen containing the nucleoside reverse transcriptase inhibitors tenofovir disoproxil fumarate (TDF) and emtricitabine (FTC) or lamivudine (3TC), regardless of CD4+ T-cell count or HBV-related factors such as HBV DNA levels or elevated alanine aminotransferase activity [16]. The use of combination ART is associated with a reduction in FIB-4 score and a lower incidence of liver fibrosis in patients with HIV/HBV coinfection. Its effect on the reversal of liver fibrosis may persist for up to a decade [17].

A systematic review and meta-analysis indicate that HCV treatment with DAAs is associated with a more significant regression of liver fibrosis compared to interferon-based therapy. Additionally, among patients with initially severe fibrosis and cirrhosis (>9.5 kPa), 47 % achieved a reduction in liver stiffness after treatment (<9.5 kPa) [18]. The study by *Lledó GM et al. (2018)* demonstrates that HCV eradication with DAA therapy leads to a reduction in non-invasive markers of liver fibrosis (APRI, FIB-4, and transient elastography) at the time of achieving SVR. This effect is more pronounced in patients with initially advanced fibrosis and cirrhosis. Additionally, the presence of HIV coinfection does not affect the dynamics of liver fibrosis regression [19].

The results of the above studies demonstrate regression of liver fibrosis after achieving SVR for HCV, as well as the positive effects of ART on the reversal of fibrosis in patients with HIV/HBV coinfection. However, there is insufficient data on the effects of antiviral therapy used simultaneously against C and B viruses in patients with HIV/HBV/HCV coinfection, particularly on viral replication and the features of the liver parenchyma morphology.

AIM

To study and compare the efficacy of different regimens of combination antiviral therapy for hepatitis C and B in achieving a sustained virological response in patients with HIV/HBV/HCV coinfection and their impact on the degree of liver fibrosis.

MATERIALS AND METHODS

RETROSPECTIVE STUDY

We examined 113 HIV-infected adult patients with HBV/HCV coinfection who were registered at the Municipal Non-profit Enterprise "Infectious Diseases Center of the Ivano-Frankivsk Regional Council" between 2017 and 2019. Group 1 consisted of 44 patients who did not receive HCV antiviral therapy (AVT). Other patients, who received a 12-week HCV AVT, were divided into the following groups according to the treatment regimen: Group 2 – 29 patients who received pegylated interferon, sofosbuvir, and ribavirin (Peg IFN+SOF+RBV); Group 3 – 40 patients who received interferon-free DAA regimens with or without ribavirin: sofosbuvir and ribavirin (SOF+RBV) – 8 patients, sofosbuvir/ledipasvir and ribavirin (SOF/LDV+RBV) – 8 patients, combination of 2 DAAs (sofosbuvir/ledipasvir (SOF/LDV), sofosbuvir and daclatasvir (SOF+DCV) and sofosbuvir/velpatasvir (SOF/VEL)) – 24 patients. All patients who received HCV AVT had not been previously exposed to this treatment.

Patients were examined per the unified clinical protocol for primary, secondary (specialized), and tertiary (highly specialized) medical care "HCV infection in adults" (Order of the Ministry of Health of Ukraine No. 729 dated July 18, 2016).

All patients received antiretroviral therapy (ART) with nucleoside reverse transcriptase inhibitors, tenofovir and emtricitabine (TDF/FTC), both of which are active against HBV, and dolutegravir (DTG) – a TLD regimen. (Clinical protocol on the use of antiretroviral drugs for treating and preventing of HIV infection

(Order of the Ministry of Health of Ukraine No. 1292 dated June 5, 2019)).

The viral load (VL) of HCV RNA and HBV DNA in the blood plasma of patients was determined using quantitative real-time polymerase chain reaction (PCR) using the Rotor-Gene 6000 system (Corbett Research Pty Limited, Australia) with a lower limit of quantification (LLOQ) of 150 IU/mL.

The stage of liver fibrosis was determined using two non-invasive methods of investigation: the APRI index and point-shear wave elastography (pSWE) of the liver. The APRI (AST to Platelet Ratio Index) was calculated as AST / upper limit of normal AST (40 U/L) / platelet count in 1 μL of blood) × 100. Liver fibrosis was categorized as absent or minimal if the APRI value was <0.5, moderate or significant if the value was 0.5–1.5, and severe fibrosis or cirrhosis if the value was ≥1.5 [20].

Liver pSWE elastography was performed using an ACUSON S3000 ultrasound system (Siemens, Germany). The stiffness of the liver parenchyma was measured as the shear rate of the ultrasound wave (m/sec) passing through the tissue. The stages of liver fibrosis were classified based on pSWE results as follows: F0 (no fibrosis) – 0.87-1.23 m/sec, F1 (mild) – 1.23-1.37 m/sec, F2 (significant) – 1.37-1.68 m/sec, F3 (advanced) – 1.68-2.0 m/sec, F4 (cirrhosis) – >2.0 m/sec [21].

The APRI and liver pSWE indices in group 1 patients who received ART but not HCV AVT were determined twice with a 1-year interval. For patients in groups 2 and 3 who received both ART and HCV AVT, the study was also conducted twice: once before starting HCV treatment and again 1 year later, i.e., 9 months after completing AVT.

The effectiveness of HCV AVT was evaluated based on the achievement of a rapid virologic response (RVR) at week 4 of treatment and a sustained virologic response (SVR12) at 12 weeks after the AVT completion.

The efficacy of HBV AVT was assessed by the achievement of undetectable HBV DNA levels in plasma at the baseline of the surveillance and again 1 year later.

STATISTICS

Continuous variables were expressed as a median and interquartile range (Q1-Q3). Categorical variables were described as frequencies. Group differences in categorical variables were assessed with Pearson's Chi-square and post-hoc Pearson's Chi-square tests, and in continuous variables, the Kruskal-Wallis' test was used. Wilcoxon signed-rank test was used to compare two dependent groups. The proportion of patients with SVR12 and the two-sided exact 95 % confidence interval (95 % CI) were calculated using the Clopper-Pearson method. Differences were judged as significant if the p-value was less than 0.05. Statistical analysis of data was performed using the Microsoft Excel Statistical Package for Microsoft 365 MSO (setup 2801 of version 16.0.14332.20204) (64-bit version). License ID: EWW_1c997d34-53bc-44a6-89a1-90707b6e2997_a3409c5e83bd296b20.

The study design was approved by the Ethics Committee of the Ivano-Frankivsk National Medical University (Protocol № 109/19 dated May 29, 2019)

RESULTS

The mean age of patients across all three groups was 42.60±0.60 years. In each group, the majority were men – 90 (79.6 %), with a predominant contingent of individuals diagnosed with mental and behavioral disorders due to opioid use – 84 (74.3 %). The routes of HIV infection included parenteral transmission through intravenous drug use – 74.3 % and sexual transmission – 25.7 %. The proportion of patients with stage 1-2 HIV infection was 21.8 %, while those with stage 3-4 accounted for 78.2 %. Patients were categorized according to the degree of immune deficiency as follows: 46.90 % exhibited profound immune deficiency (CD4+ T cells/mm^3 <350), 26.55 % had moderate immune deficiency (CD4+ T cells/mm^3 350-499), and 26.55 % showed no immune deficiency (CD4+ T cells/mm^3> 500) (Table 1).

At the beginning of the study, the average HCV RNA levels in blood plasma were $5.9\times10^6\pm1.5\times10^6$ IU/mL in group 1, $3.8\times10^6\pm1.8\times10^6$ IU/mL in group 2, and $4.1\times10^6\pm1.3\times10^6$ IU/mL in group 3. The HCV genotype was determined in 83 patients: genotype 1 was identified in 37 patients (44.58 %), and genotype 3 in 42 patients (46, 98 %) (Table 1).

The APRI value ≥1.5, indicative of severe fibrosis, was found in 13.64 % of patients in group 1, 6.9 % in group 2, and 7.5 % in group 3, with no statistically significant difference between the groups (p>0.05). The median APRI value was 0.49 in group 1 and 0.45 in groups 2 and 3. The median pSWE value at baseline was 1.53 m/sec in group 1, whereas advanced liver fibrosis corresponding to METAVIR stage F3-F4 was detected in 31.82 % of patients, which was 2.3 times higher than the proportion detected using APRI (13.64 %, p<0.05). In group 2, the median pSWE value was 1.46 m/sec, and F3-F4 liver fibrosis was identified in 17.24 % of patients, which is 2.5 higher than according to APRI (6.9 %, p<0.05). In group 3, the baseline median pSWE value was 1.45 m/sec, and F3-F4 liver fibrosis was found in 20.0 %, which is 2.7 higher than according to APRI (7.5 %, p<0.05).

The regimens containing two DAAs were associated with a high rate of RVR: SOF/LDV – 85.7 %, SOF+DCV – 90.0 %, and SOF/VEL and SOF/LDV+RBV – 100.0 %. These regimens achieved SVR12 in 100.0 % of patients (Table 2).

Table 1. Baseline demographic and clinical characteristics of patients with HIV/HBV/HCV coinfection

	Group 1 No HCV AVT, n=44	Group 2 Peg IFN+SOF+RBV 12 weeks, n=29	Group 3 DAA±RBV 12 weeks, n=40	p
Age, M±m	43.7±1.1	41.0±1.1	42.5±0.9	
Sex: n, %				
Men	32 (72.7)	23 (79.3)	35 (87.5)	p>0.05
Women	12 (27.3)	6 (20.7)	5 (12.5)	
HIV transmission route: n, %				
Sexual	11 (25.0)	8 (27.6)	10 (25.0)	p>0.05
Parenteral	33 (75.0)	21 (72.4)	30 (75.0)	
Stage of HIV infection: n, %				
1	1 (2.3)	3 (10.3)	1 (2.5)	p>0.05
2	5 (11.4)	6 (20.7)	8 (20.0)	
3	6 (13.6)	5 (17.2)	7 (17.5)	
4	32 (72.7)	14 (48.3)	22 (55.0)	
CD4+ T cell count / mm^3, n (%)				
<350	15 (34.10)	13 (44.83)	25 (62.50)	p_1 >0.05 p_2=0.028 p_3 >0.05
350-499	20 (45.45)	5 (17.24)	5 (12.50)	p_1= 0.019 p_2= 0.003 p_3 >0.05
>500	9 (20.45)	11 (37.93)	10 (25.00)	p>0.05
RNA HCV viral load, IU/mL, M±m	$5.9x10^6$±$1.5x10^6$	$3.8x10^6$±$1.8x10^6$	$4.1x10^6$±$1.3x10^6$	p>0.05
HCV genotype, n (%)				
1	14 (31.8)	12 (41.4)	11 (27.5)	p>0.05
2	0 (0.0)	0 (0.0)	5 (12.5)	
3	13 (29.6)	8 (27.6)	18 (45)	
3a	0 (0.0)	3 (10.3)	0 (0.0)	
Unknown	17 (38.6)	6 (20.7)	6 (15)	
DNA HBV qualitative test, n (%)				
detected	3 (6.82)	1 (3.45)	2 (5.00)	p>0.05
DNA HBV viral load, IU/mL, M±m	$2.4x10^7$±$2.3x10^7$	$8.5x10^7$	$1.3*10^2$±$1.2*10^2$	p>0.05

Notes: Group differences in categorical variables were assessed with Pearson's Chi-square and post-hoc Pearson's Chi-square tests; in continuous variables, the Kruskal-Wallis' test was used

p – statistical significance of differences among the comparison groups;

p_1 – statistical significance of differences between the 2nd and 1st group;

p_2 – statistical significance of differences between the 3d and 1st group;

p_3 – statistical significance of differences between the 3d and 2nd group

Source: compiled by the authors of this study

The efficacy of the Peg IFN+SOF+RBV regimen was slightly lower, with RVR and SVR12 achieved in 86.2 % of patients (95 % CI: 68.3-96.1). The lowest efficacy was observed with the SOF+RBV regimen – RVR and SVR12 achieved in 75.0 % of patients (95 % CI: 34.9-96.8) (Table 2). Virologic failure occurred in patients with HCV genotype 1 (3 patients – 10.3 %) and 3 (1 patient – 3.4 %), who exhibited resistance to these treatment regimens. No significant difference in achieving RVR and SVR12 was observed between the groups treated with PegIFN+-SOF+RBV and SOF+RBV (p>0.05). However, when comparing the DAA±RBV and Peg IFN+SOF+RBV groups, a statistically significant difference in achieving SVR12 was identified (100.0 % vs. 86.2 %, respectively, p<0.05).

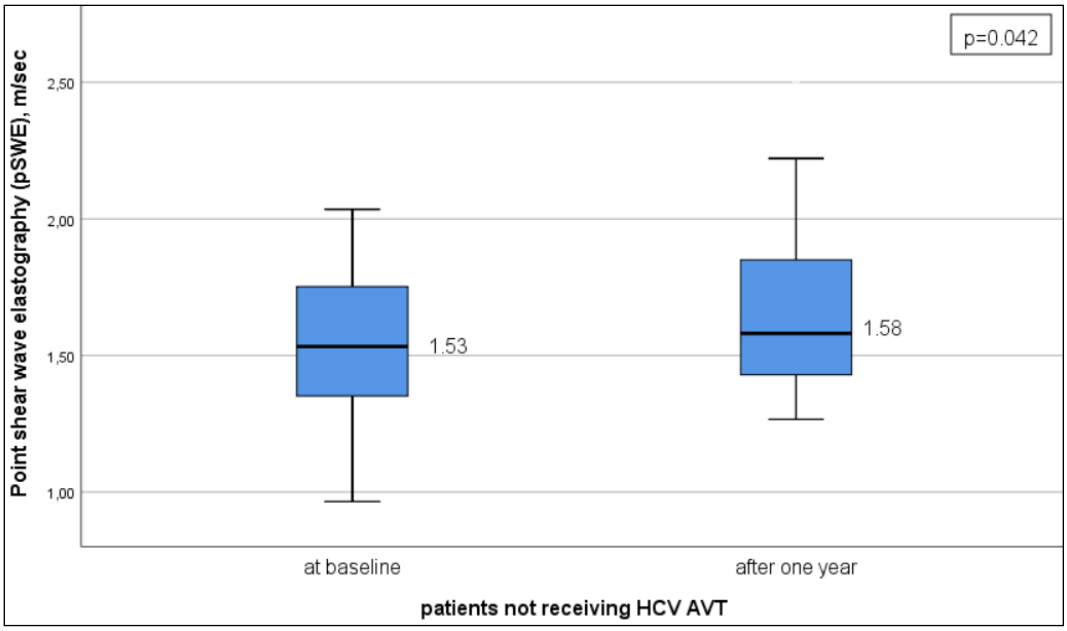

Fig. 1. Dynamics of median values of liver pSWE in patients not receiving HCV AVT
Picture taken by the authors

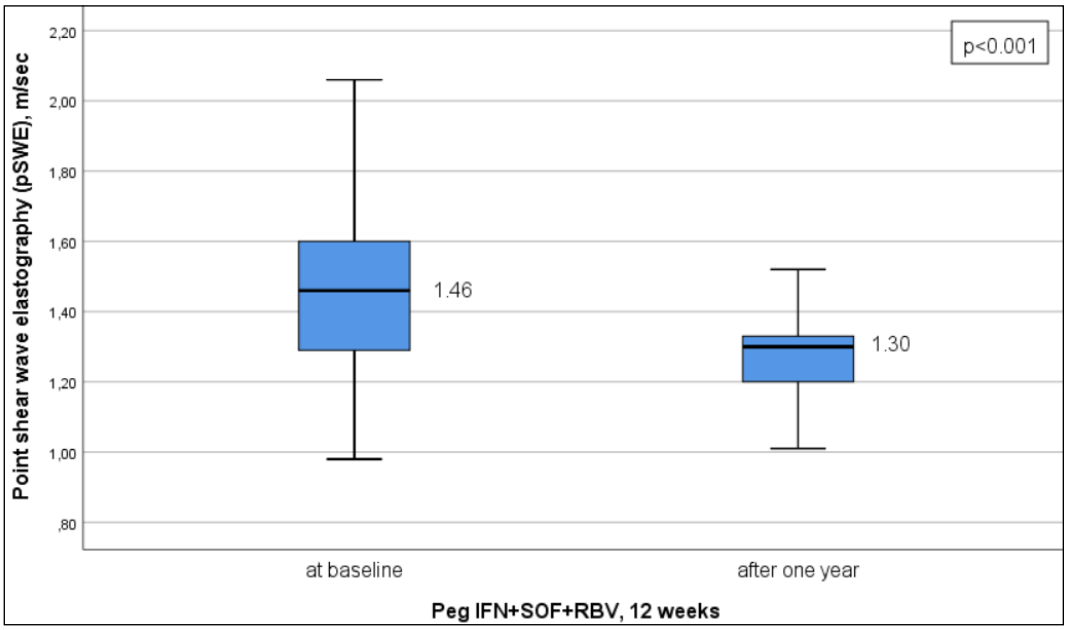

Fig. 2. Dynamics of median values of liver pSWE in patients receiving Peg IFN+SOF+RBV
Picture taken by the authors

All patients received TDF/FTC as part of ART for HBV suppression. However, not all patients reached the integration phase at baseline. HBV DNA remained detectable in 6 (5.3 %) patients: 3 from group 1, 1 from group 2, and 2 from group 3. At the beginning of the study, the average HBV DNA viral load was $2.6\times10^7\pm1.7\times10^7$ IU/mL and was accompanied by severe immune suppression (CD4+ <350 T cells/mm^3) and elevated ALT activity ranging from 49.3 to 60.9 U/L in 5 patients (83.3 %).

After one year of follow-up, HBV replication persisted in four patients (3.5 %) despite regular ART. At the same time, all four patients exhibited minimal to moderate chronic hepatitis activity with ALT levels ranging from 47.5 to 240 U/L and continued to experience severe immune deficiency (CD4+ <350 T cells/mm^3). The causes of replication after one year of follow-up varied among the groups. In group 1 (patients not receiving HCV AVT), three patients had HBV replication at the beginning of the study. After one year, two of these patients achieved HBV suppression, while one patient exhibited viral replication. In this case, primary HBV resistance to TDF/FTC was likely present. Additionally, two patients

Table 2. Rapid virologic response and sustained virologic response when using different regimens of HCV antiviral treatment in patients with HIV/HBV/HCV coinfection

Treatment regimen, n (%)	RVR, n (%)	95% CI	SVR12, n (%)	95% CI	p
Peg IFN+SOF+RBV, n=29	25 (86.2)	68.3-96.1	25 (86.2)	68.3-96.1	> 0.05
SOF+RBV, n=8	6 (75.0)	34.9-96.8	6 (75.0)	34.9-96.8	> 0.05
SOF/LDV+RBV, n=8	8 (100.0)	63.1-100.0	8 (100.0)	63.1-100.0	> 0.05
SOF/LDV, n=7	6 (85.7)	42.1-99.6	7 (100.0)	59.0-100.0	> 0.05
SOF+DCV, n=10	9 (90.0)	55.5-99.7	10 (100.0)	69.2-100.0	> 0.05
SOF/VEL, n=7	7 (100.0)	59.0-100.0	7 (100.0)	59.0-100.0	> 0.05
Total of DAA±RBV, n=32	30 (93.7)	79.0-99.2	32 (100.0)	89.0-100.0	> 0.05

Note: p – statistical significance of the difference between RVR and SVR12
Source: compiled by the authors of this study

in this group (4.54 %) appeared to develop secondary resistance to TDF/FTC, as HBV DNA was undetectable at the beginning of the study but reappeared after one year at levels of 0.6×10^2 IU/mL and 3.0×10^3IU/mL, respectively. At the same time, these patients experienced a significant exacerbation of hepatitis activity, with ALT levels increased to 153.3-240 U/L compared to 54.3-60.9 U/L at baseline.

In group 2, consisting of patients treated with Peg IFN+SOF+RBV, HBV DNA was present in 1 patient both at the beginning of the study and one year later. However, the HBV DNA VL decreased by four orders of magnitude, from 8.5×10^7 IU/mL vs. 1.2×10^3 IU/mL, respectively. This reduction occurred alongside an increase in CD4+ T cell counts, from 183 to 389 T cells/mm^3. Primary viral resistance to TDF/FTC was also observed in this case.

In group 3, consisting of patients receiving DAA±RBV, HBV DNA was detected in 2 patients (with VL of 1.0×10 IU/mL and 2.5×10^2 IU/mL) at the beginning of the study. However, after one year, complete HBV suppression was observed with achieved higher immunity parameters (initial CD4+ count in these two patients were 440 and 97 T cells/mm^3, respectively, increasing to 520 and 348 T cells/mm^3, respectively, after one year).

Therefore, primary HBV resistance to TDF/FTC was observed in two patients across all groups under observation (1.76 %). Secondary resistance was noted in the remaining two patients but only in the group that did not receive HCV AVT (4.54 %).

In groups 2 and 3, where patients received combined HBV and HCV AVT, no HBV reactivation was observed with achieved HCV suppression.

After one year, in patients from group 1 who did not receive HCV AVT, the median pSWE increased to 1.58 m/sec compared to baseline measurements, which showed 1.53 m/sec (p=0.042) (Fig. 1). However, the proportion of patients with F3-F4 remained unchanged (40.91 % vs. 31.82 % at baseline, p>0.05) (Fig. 4). At the same time, the median APRI decreased to 0.40 compared to baseline values of 0.49 (p<0.001). Yet, the proportion of patients with F3-F4 by this indicator also remained unchanged (9.09 % vs. 13.82 % at baseline, p>0.05).

After one year of follow-up and 9 months after completion of HCV AVT, in patients from group 2 receiving Peg IFN+SOF+RBV, the median pSWE value decreased to 1.30 m/sec from 1.46 m/sec at baseline (p<0.001) (Fig. 2). However, the incidence of stages F3-F4 did not change significantly (10.34 % vs. 17.24 % at baseline, p>0.05) (Fig. 4). The median APRI decreased by half (0.23 vs. 0.45 before treatment (p<0.001)), and no patients exhibited advanced fibrosis (F3-F4).

In group 3, consisting of patients who received 2 DAAs or 2 DAAs+RBV, the median pSWE value decreased to 1.31 m/sec at one year of follow-up and 9 months after completion of HCV AVT, compared with 1.45 m/sec before treatment (p<0.001) (Fig. 3). Based on pSWE results, the incidence of advanced F3-F4 liver fibrosis decreased to 2.5 % from 20.0 % before treatment (p<0.05) (Fig. 4). The median APRI also decreased almost twofold to 0.26 compared with the baseline value of 0.45 (p<0.001), with no patient in this group exhibiting APRI ≥1.5, which corresponds to severe fibrosis (0.0 %).

DISCUSSION

According to our study and the literature, pSWE values provide a more accurate reflection of fibrotic changes in the liver compared to APRI [22, 23]. The latter, while showing high specificity but low sensitivity, can only serve as an indicative tool for assessing the degree of fibrosis [24].

The treatment regimens with 2 DAAs (SOF/LDV, SOF/VEL, SOF+DCV) and the regimen, which includes ribavirin (SOF/LDV+RBV), resulted in 100 % SVR12. According to other published studies, such therapy for patients

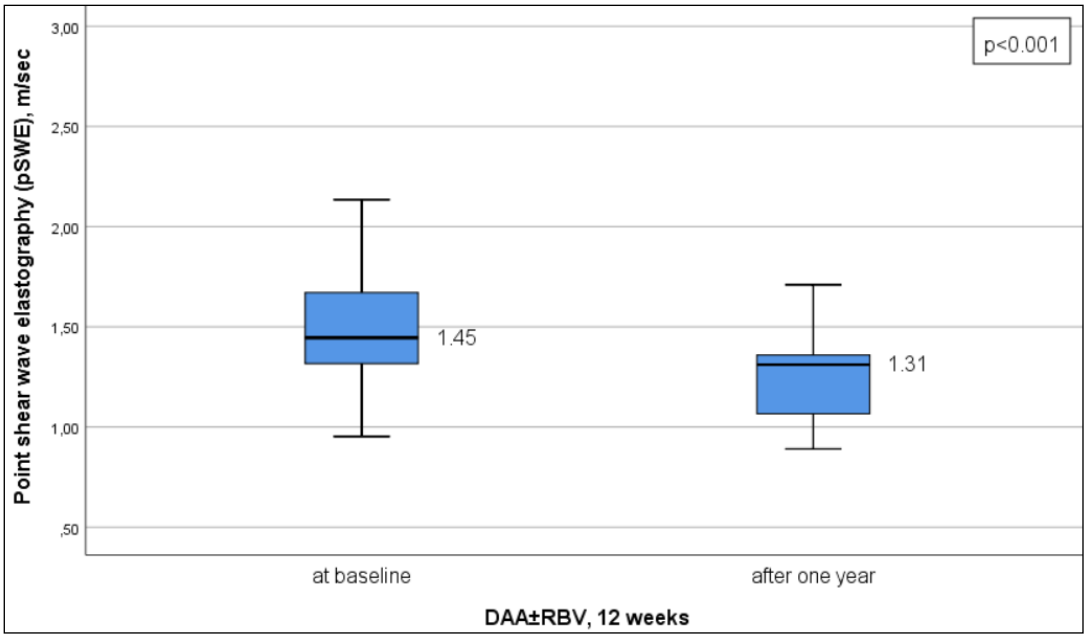

Fig. 3. Dynamics of median values of liver pSWE in patients receiving DAA±RBV
Picture taken by the authors

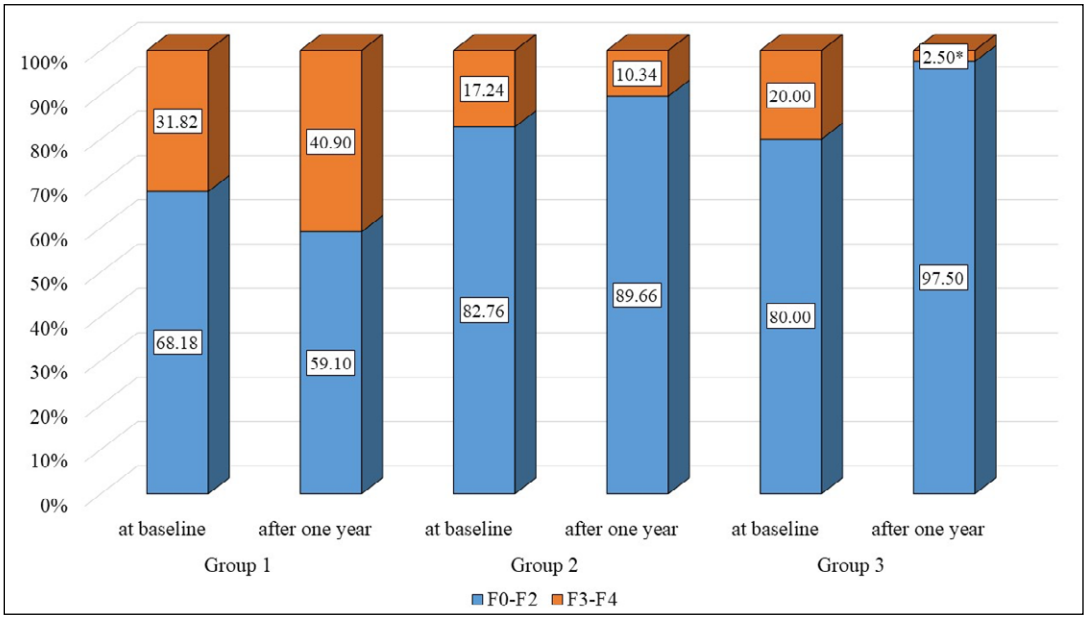

Fig. 4. Dynamics of liver fibrosis stages according to pSWE in patients with HIV/HBV/HCV coinfection
Notes:
Group 1 – patients not receiving HCV AVT;
Group 2 – patients receiving Peg IFN+SOF+RBV for 12 weeks;
Group 3 – patients receiving DAA±RBV for 12 weeks;
* – p <0.05
Picture taken by the authors

with HIV/HCV is effective, and its success rate reaches 93-100 %, depending on the drug regimen [25-27]. Two regimens were not effective enough: sofosbuvir with ribavirin alone (SVR12 was in 75 % of patients) and in combination with pegylated interferons (86.2 %).

At the end of one year of follow-up, HBV replication persisted in 4 (3.5 %) patients across different groups due to HBV resistance to TDF/FTC. Among these, two patients likely exhibited primary HBV resistance, while the other two developed secondary resistance. The latter occurred exclusively in the group receiving ART without concurrent HCV AVT.

While numerous reports in the literature describe HBV reactivation in the setting of HCV suppression, its

incidence in patients with HIV/HBV/HCV coinfection remains poorly understood [28]. In our study, no cases of HBV reactivation were observed in patients receiving combined HBV and HCV AVT. The single instance of HBV replication noted at the beginning and end of the study in the group treated with Peg IFN+SOF+RBV can be attributed to primary resistance to TDF/FTC. The absence of HBV reactivation in the presence of HCV suppression is associated with both the suppressive effect of TDF/FTC on the hepatitis B virus and immune reconstitution when receiving ART, as well as improvement of the functional and morphological state of the liver after combined antiviral therapy.

Interferon-free regimens that include two DAAs, either alone or in combination with ribavirin, demonstrated the most beneficial effects on the liver parenchyma in patients with HIV/HBV/HCV reducing the degree of fibrosis, with a significant decrease in the incidence of advanced fibrosis observed 9 months post-treatment (from 20 % to 2.5 %). Our findings align with those reported by authors who observed a reduction in liver stiffness and improvement in fibrosis indices after successful therapy with DAAs [29, 30].

The distinguished feature of the present study, compared to those previously mentioned, is the focus on HIV-infected individuals with coexisting hepatitis B+C who received combined suppressive therapy for chronic hepatitis B using TDF/FTC and chronic hepatitis C using 2 DAA drugs with or without ribavirin. This treatment is characterized by 100 % suppression of both viruses, effectively preventing hepatitis B virus reactivation except in cases of primary HBV resistance. Consequently, a significant reduction in the degree of liver fibrosis is achieved.

CONCLUSIONS

1. In HIV-infected individuals with chronic hepatitis B+C, HCV AVT regimens SOF/LDV, SOF/VEL, SOF+DCV, SOF/LDV+RBV demonstrated 100 % virologic efficacy. Regimens involving Peg IFN+SOF+RBV (86.2 %) and SOF+RBV (75.0 %) were comparatively less effective.
2. Among patients in the group treated with combined AVT for HBV and HCV using TDF/FTC and DAA±RBV, the incidence of liver fibrosis F3-F4, as assessed by pSWE, decreased from 20 % to 2.5 % ($p<0,05$) after one year of follow-up.
3. Primary HBV resistance to TDF/FTC was identified in 1.76 % of patients in the entire cohort. Secondary HBV resistance was observed in 4.54 % of patients who did not receive HCV AVT.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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