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Effectiveness and safety of sofosbuvir/ledipasvir ± ribavirin treatment in liver and/or renal transplant patients with chronic hepatitis C: A single-center experience

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Abstract

Objective: Successful treatment is possible with novel direct-acting oral antiviral agents in solid organ transplant patients with hepatitis C. In this study, the effectiveness and safety of sofosbuvir/ledipasvir ± ribavirin treatment in liver and/or renal transplant patients with chronic hepatitis C were evaluated.

Materials and methods: A total of 23 liver and/or renal transplant patients who received sofosbuvir/ledipasvir ± ribavirin for chronic hepatitis C over 12 or 24 weeks were enrolled in the study. The treatment response, clinical and laboratory adverse effects, and effect on immunosuppressive drug levels were assessed.

Results: A total of 12 patients had undergone renal transplantation and 11 had undergone liver transplantation. All of the renal transplant patients and 91% of liver transplant patients had genotype 1. In total, 10 renal transplant patients and 4 liver transplant patients had treatment experience. Two renal transplant patients and one liver transplant patient had compensated cirrhosis. Nine renal transplant patients were on tacrolimus, and two were on cyclosporine; all of the liver transplant patients were on tacrolimus-based immunosuppressive therapy. While hepatitis C RNA was negative in 75% of renal transplant patients and 91% of liver transplant patients at week 4, it was negative in all of the patients at the end of treatment and 12 weeks after treatment. Significantly reduced hemoglobin levels were observed in patients administered ribavirin during treatment ($p = 0.01$). There were no significant differences between the baseline and treatment period values of mean creatinine, estimated glomerular filtration rate, bilirubin, and tacrolimus levels. There were no adverse effects leading to treatment discontinuation.

Conclusion: Sofosbuvir/ledipasvir ± ribavirin is quite safe and effective in hepatitis C treatment after liver and/or renal transplantation.

Keywords

Chronic hepatitis C, liver transplantation, renal transplantation, sofosbuvir/ledipasvir, ribavirin

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Introduction

Chronic hepatitis C (HCV) infection is a major risk factor for liver cirrhosis and hepatocellular carcinoma (HCC) and is one of the leading reasons for liver transplantation. Post-transplantation recurrence is inevitable in patients in whom HCV is not eradicated prior to transplantation, and this is related to significant graft loss and mortality.[1] HCV frequency is 5%–15% in renal transplant recipients, and HCV is a major risk factor for proteinuria, transplant glomerulopathy, post-transplant diabetes mellitus, chronic rejection, graft loss, and mortality in these patients.[2,3] Administration of pegylated interferon (Peg-IFN) and ribavirin (RBV), which were used in HCV treatment in the past, was limited in patients with post-liver transplant recurrence because of adverse effects,

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and 25%–33% sustained viral response rates were achieved.[4,5] In the case of renal transplant recipients, interferon-based treatments were not used because of increased allograft dysfunction and rejection risk.[6] Although treatment response rates were partially increased after the protease inhibitors boceprevir and telaprevir became available, later guidelines suggested the disuse of these drugs in transplant patients because of intolerance and serious immunosuppressive drug interactions seen particularly in transplant patients.[7] Since 2013, nonstructural protein 5B (NS5B) polymerase inhibitors, protease inhibitors, and nonstructural protein 5A (NS5A) inhibitors have been introduced, and various combinations of these with or without RBV have become a milestone in HCV treatment, including post-transplant patients. In many studies comprising real life data, it was reported that concomitant administration of the NS5B polymerase inhibitor sofosbuvir (SOF) with the NS5A inhibitor ledipasvir (LDV), together with or without RBV, is quite efficient and safe for HCV treatment after liver and renal transplantation.

In this study, the effectiveness of treatment, clinical and laboratory adverse effects, and effect on immunosuppressive drug levels were evaluated in patients treated with SOF/LDV ± RBV for HCV after liver and/or renal transplantation.

Methods

Patient selection

A total of 25 liver and/or renal transplant patients with chronic HCV who were followed up at Akdeniz University Medical Faculty Organ Transplantation Center and Gastroenterology Outpatient Clinic and treated with interferon-free direct-acting antiviral agents between July 2016 and September 2017 were designated for the study.

Inclusion criteria. Patients were included in the study if they were

- Aged 18 years and older;
- Treatment naive or experienced chronic hepatitis C infection after liver and/or renal transplantation;
- Genotype 1 and 4 HCV;
- Treated with SOF/LDV ± RBV.

Exclusion criteria. Patients were excluded from the study if they were

- Aged younger than 18 years;
- Genotype 2 and 3 HCV;
- Treated with another regimen other than SOF/LDV ± RBV.

One liver transplant patient with genotype 3 on SOF + RBV combination and another renal transplant patient on ombitasvir/paritaprevir/ritonavir and dasabuvir combination (OBV/PTV/r + DSV) were excluded from the study. As a result, data from 23 patients who were treated with SOF 400 mg/LDV 90 mg ± RBV (1000 mg/day for <75 kg body weight; 1200 mg/day for ⩾75 kg body weight) for 12 weeks or 24 weeks according to genotype, treatment experience, and cirrhosis status were evaluated retrospectively.

Determination of effectiveness and safety of treatment

Treatment response and clinical and laboratory adverse effects were assessed by determining HCV RNA level at initiation of treatment, 4 weeks after the initiation of treatment, at the end of treatment, and 12 weeks after the end of treatment and by determining the mean hemoglobin, creatinine, estimated glomerular filtration rate (eGFR), total bilirubin, and immunosuppressive levels at initiation of treatment, 4 weeks after the initiation of the treatment, and at the end of the treatment. Virological response is defined as the absence of detectable HCV RNA (detection limit < 15 IU/mL) at 4 weeks after the initiation of treatment, at the end of treatment, and 12 weeks after treatment (sustained virologic response (SVR)12). The primary endpoint was the ratio of patients with SVR12.

Statistical analysis

Statistical analyses were carried out using IBM-SPSS version 20.0 for Mac OS (IBM Corp. Released 2011). Two-way analysis of variance (ANOVA) was used to evaluate the interaction between treatment and time, and one-factor repeated-measures ANOVA with the use of Bonferroni adjustment was used for comparisons against baseline for normally distributed data. A p value < 0.05 was used to assess the significance for all statistical analyses. The results are presented as mean ± standard deviation (SD) and median (minimum-maximum).

Results

Patient demographics

A total of 12 patients had undergone renal transplantation and 11 had undergone liver transplantation. Mean ages were 44.4 ± 11.1 years and 60.8 ± 6.2 years in patients with renal and liver transplantation, respectively. All renal transplant patients (75% 1b, 25% 1a) and 91% of liver transplant patients (64% 1b, 27% 1a) had genotype 1. Demographic characteristics, treatment experience, cirrhosis status, immunosuppressive drug regimens, and baseline clinical and laboratory findings of patients are presented in Table 1, and treatment distribution is presented in Figure 1.

Effectiveness and safety of treatment

HCV RNA was negative in 75% of renal transplant patients and 91% of liver transplant patients at 4 weeks after the initiation of

Table 1. Demographic, clinical, and laboratory features of HCV-positive kidney and liver transplant recipients.

	Kidney transplantation (n = 12)	Liver transplantation (n = 11)
Sex, n (%)		
Female	2 (17)	4 (36)
Male	10 (83)	7 (64)
Age, years (mean ± SD)	44.4 ± 11.1	60.8 ± 6.2
HCV genotype, n (%)		
Genotype 1		
1a	3 (25)	3 (27)
1b	9 (75)	7 (64)
Genotype 4		1 (9)
HCV RNA, IU/mL (median, min-max)	1,635,000 (263,000–11,200,000)	885,000 (47,600–4,400,000)
Previous therapy (n)		
Naive	1	7
Peg-IFN	10	1
Peg-IFN + RBV	–	3
Time from transplantation to treatment, months (median, min-max)	72 (24–240)	15 (3–144)
Cirrhosis (n)		
No	10	10
Yes (Compensated)	2	1
Main immunosuppressive (n)		
Tacrolimus	9	11
Cyclosporine-A	2	–
Other immunosuppressive (n)		
Prednisolone	9	2
Mycophenolate mofetil	6	4
Everolimus	1	1
Creatinine, mg/dL (mean ± SD)	1.16 ± 0.29	0.90 ± 0.36
eGFR, mL/min (mean ± SD)	68.5 ± 17.9	79.5 ± 26.6
Total bilirubin, mg/dL (mean ± SD)	0.75 ± 0.28	1.25 ± 0.31

HCV: hepatitis C; SD: standard deviation; Peg-IFN: pegylated interferon; RBV: ribavirin; eGFR: estimated glomerular filtration rate.

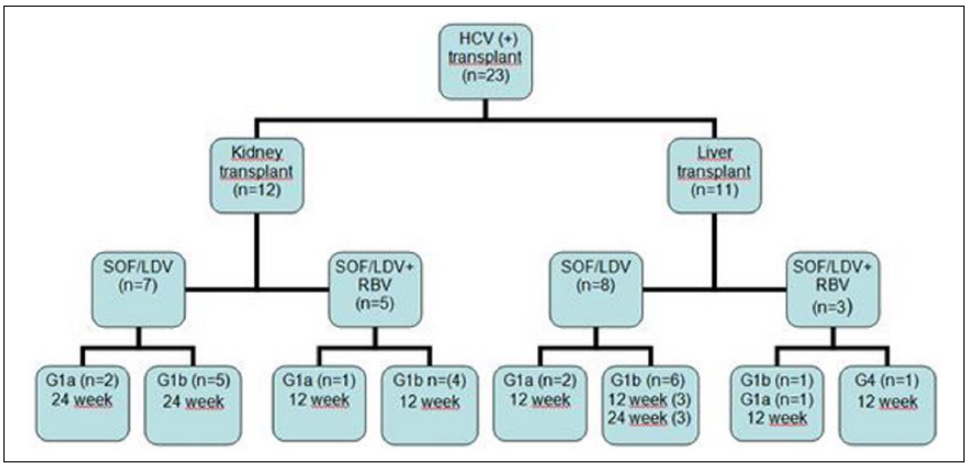

Figure 1. Distribution of patients according to treatment and HCV genotype.

treatment. Two patients (both treatment-experienced, one genotype 1a and one genotype 1b) in the renal transplantation group and one patient (genotype 1b, treatment-experienced and compensated cirrhotic) in the liver transplantation group had positive HCV RNA at 4 weeks after the initiation of treatment. HCV RNA was negative in all patients at the end of treatment and 12 weeks after treatment (Figure 2).

While there was a significant decrease in hemoglobin levels in patients who received RBV in both groups, there was no difference in the group not receiving RBV (Figure 3). No

significant difference was seen in mean creatinine, eGFR, bilirubin, or tacrolimus levels (Table 2). There was no difference leading to dose adjustment for serum cyclosporine and everolimus levels in two renal transplant patients receiving cyclosporine and one patient in each group receiving everolimus. There were no adverse effects leading to permanent discontinuation. The most common adverse effect was malaise (21%). Hemoglobin levels below 10 g/dL were observed in two patients treated with RBV and one patient without RBV. The dose was reduced in patients treated with RBV. Treatment was continued in the patient without RBV, and no progression was seen in the hemoglobin decrease. In one liver transplant patient with a baseline creatinine level of 1.5 mg/dL and an eGFR value of 45 mL/min, the creatinine level increased to 2.3 mg/dL during treatment, but since the eGFR level was above 30 mL/min, treatment continued, and the creatinine level decreased to 1.3 mg/dL after treatment. In another liver transplant patient with compensated cirrhosis with a baseline bilirubin level of 1.4 mg/dL, the bilirubin level increased to 2.7 mg/dL at 4 weeks after the initiation of treatment but the treatment continued. The bilirubin level decreased to 1.2 mg/dL at follow-up. Clinical and laboratory adverse effects are presented in Table 3.

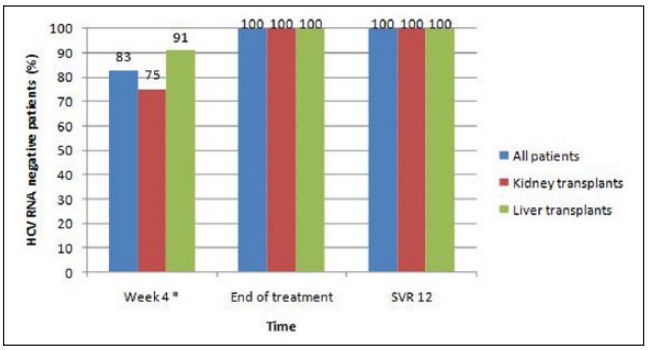

Figure 2. Response to therapy. (*Patients without virologic response at week 4: (1) kidney transplant, genotype 1b, treatment experienced; (2) kidney transplant, genotype 1a, treatment experienced; (3) liver transplant, genotype 1b, treatment experienced, compensated cirrhosis.)

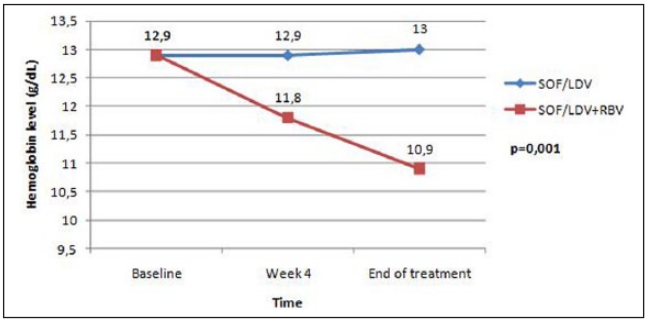

Figure 3. Mean hemoglobin levels during treatment.

Discussion

Successful treatment of chronic HCV infection in all patients became possible after the introduction of various combinations of direct-acting oral antiviral agents, although there are partial variations related to genotype, treatment experience, and cirrhosis status. Post-transplant patients with HCV infections are special and difficult-to-treat populations. Liver disease associated with HCV infection progresses more rapidly in transplant recipients. So, more severe fibrosis may be an unfavorable factor for these patients. This situation can affect the effectiveness and tolerability of therapy. SOF/LDV and RBV treatment was reported to be effective for post-transplant recurrent genotype 1 or 4 HCV in the earlier SOLAR-1 and SOLAR-2 trials. The SVR12 rates were reported as 96% in those without cirrhosis, 96% in those with Child-Pugh A cirrhosis, 85% in those with Child-Pugh B, and 60% in those with Child-Pugh C decompensated cirrhosis.[8,9] In addition, interactions with immunosuppressive drugs should be

Table 2. Mean serum creatinine, eGFR, total bilirubin, and tacrolimus levels during therapy.

Variables	Time	Kidney transplant	Liver transplant	p value
Serum creatinine, mg/dL (mean ± SD)	Baseline	1.17 ± 0.10	0.9 ± 0.10	0.387
	Week 4	1.16 ± 0.10	0.91 ± 0.10	
	End of therapy	1.16 ± 0.13	1 ± 0.13	
eGFR, mL/min (mean ± SD)	Baseline	68.58 ± 6.5	79.55 ± 6.79	0.197
	Week 4	71.92 ± 6.84	78.36 ± 7.14	
	End of therapy	72.67 ± 6.78	75.91 ± 7.08	
Serum total bilirubin, mg/dL (mean ± SD)	Baseline	0.75 ± 0.28	1.25 ± 0.31	0.672
	Week 4	0.69 ± 0.15	0.98 ± 0.16	
	End of therapy	0.57 ± 0.14	0.84 ± 0.15	
Tacrolimus level, ng/mL (mean ± SD)	Baseline	4.82 ± 0.71	6.08 ± 0.64	0.726
	Week 4	5.33 ± 0.65	6.53 ± 0.59	
	End of therapy	4.89 ± 0.54	5.65 ± 0.49	

SD: standard deviation; eGFR: estimated glomerular filtration rate.

Table 3. Side effects in all patients.

	Patients (n, %)
Treatment discontinuation	0
Most common side effects	
Weakness	5 (21)
Headache	2 (8)
Dizziness	1 (4)
Nausea	1 (4)
Constipation	1 (4)
Laboratory abnormality (grade 2)	
Hemoglobin decrease[a]	3 (13)
Creatinine increase[b]	1 (4)
Bilirubin increase[c]	1 (4)

RBV: ribavirin; eGFR: estimated glomerular filtration rate.
[a]In two patients treated with RBV and in one patient without RBV.
[b]In a liver transplant patient (baseline creatinine: 1.5 mg/dL, eGFR: 45 mL/min). Creatinine increased at the 2.4 mg/dL; however, eGFR remained > 30 mL/min and treatment was continued.
[c]In a liver transplant patient who has compensated cirrhosis, bilirubin increased at the 3.5 mg/dL and treatment was continued.

considered in the treatment choice for these patients. In the following years, various combinations of direct-acting antiviral agents were found to be effective and safe in these patient groups in numerous studies. In the European Association for the Study of the Liver (EASL) guidelines, SOF/LDV or SOF and daclatasvir (DCV) combination with or without RBV are suggested for the treatment of post-liver transplant recurrent HCV genotype 1, 4, 5, and 6 for 12 weeks, and, in cases in which RBV cannot be administered, the duration of treatment should be 24 weeks. SOF and velpatasvir (VEL) combination is also suggested as another treatment choice in these patients. SOF/LDV, SOF and DCV, or SOF and VEL combinations are suggested in solid organ transplantations other than liver.[10] Protease inhibitor–containing regimens are not considered appropriate for transplant patients, because of drug–drug interactions and requirement of dose modification and close monitoring for calcineurin inhibitors.[10]

Direct-acting oral antiviral agents (only SOF, SOF/LDV, and OBV/PTV/r + DSV) for treatment of chronic HCV infection were approved from July 2016 in our country. According to the payment rules from Social Security Institution of Turkey, treatment options for genotype 1 and 4 post-transplant patients are SOF/LDV with or without RBV for 12 weeks in non-cirrhotic patients and SOF/LDV for 12 weeks with RBV or 24 weeks without RBV in compensated and decompensated cirrhotic patients, or OBV/PTV/r + DSV with RBV for 24 weeks. We generally do not prefer OBV/PTV/r + DSV treatment for transplant patients who use calcineurin inhibitors, because of the drug-interaction problem. Although we generally prefer 12-week therapy with RBV or 24 weeks without RBV in treatment-experienced and cirrhotic patients, the choice of RBV combination and treatment duration may vary from physician to physician. In our study, we evaluated the effectiveness, adverse effects, and effect on immunosuppressive drug levels of SOF/LDV ± RBV treatment for 12 or 24 weeks in our post-liver and/or renal transplant patients with HCV infection. There are many studies in the literature, which evaluated SOF/LDV treatment in transplant recipients with HCV infection.

Kwok et al.[11] evaluated SOF/LDV ± RBV treatment over 8, 12, and 24 weeks in 204 post-liver transplant patients with chronic HCV in a multicenter study. The majority of patients was genotype 1 (69% 1a, 23% 1b), 9% were concomitant renal transplant recipients, and almost half were treatment-experienced. The majority of patients were on tacrolimus, and dose adjustment was required in 32% during the treatment period. Although the end of treatment virological response was reported as 100% and SVR12 as 98% in patients treated with RBV, these ratios were reported as 99% and 96%, respectively, in patients without RBV. Treatment failure was observed in seven patients—one of these patients had treatment incompliance and the others had comorbidities such as HIV infection, HCC existence, or combined renal and liver transplantation. Treatment was discontinued in four patients (two with RBV, two without RBV) because of adverse effects. Adverse effects were reported as major depressive episode leading to treatment incompliance (one patient), increased bilirubin and transaminase (one patient), intolerable neurological symptoms including headache (one patient), and feeling sick after the treatment (one patient). Also, treatment-unrelated death was observed in four patients. Excluding the adverse events stated above, the most common reported adverse effect was constitutional symptoms such as malaise and fatigue. Grade 3–4 biochemical and hematological abnormalities were reported in 9% of patients. Mild acute cellular rejection was seen in one patient during the treatment, which was treated with an increased dose of immunosuppressive agent. No hepatic decompensation was observed in any patients.

In another multicenter study performed by Ueda et al.,[12] 54 post-liver transplant patients with genotype 1b chronic HCV infection were treated with SOF/LDV without RBV over 12 weeks. In total, 70% of patients were treatment-experienced, and 31% had received direct-acting antiviral agent previously. At the end of the treatment, virologic response rate was reported as 52% at 4 weeks, and end treatment response and SVR12 ratio were 98%. One death was reported in a patient with bacterial pneumonia that developed at 4 weeks after the initiation of the treatment. The patient died due to multiorgan failure despite treatment discontinuation. SVR12 ratio was reported as 100% in intention-to-treat analysis after excluding this patient. There were patients with duodenal ulcer bleeding, alveolar hemorrhage, pleural effusion, and herpes zoster, but these were not directly related to treatment. In this study, the majority of patients were using tacrolimus-based immunosuppressive agents, and no drug interactions were reported. Similarly,

Pillai et al.[13] reported the ratio of SVR12 as 95.9% in genotype 1 post-liver transplant patients treated with SOF/LDV without RBV. In this study, it was stated that SVR ratio was not different according to age, gender, viral load, genotype, or creatinine level, and the only positive predictor of SVR insufficiency was viral load at week 8.

Recently, a meta-analysis comprising 12 studies including totally 994 post-liver transplant patients treated with SOF/LDV ± RBV for genotype 1 infection was reported by Liao et al.[14] SVR12 ratio was found as 94.9% and 95.1% in patients with and without RBV treatment, respectively. It was reported that SVR ratio did not differ with 12 or 24 weeks treatment, but the response was better in non-cirrhotic patients. The most common reported adverse effects were anemia, fatigue, headache, nausea, and diarrhea in this meta-analysis.

In a study by Fernández et al.,[15] which was performed in 103 renal transplant patients treated with direct-acting oral antiviral agents for chronic HCV, HCV RNA negativity was reported to be 59% at 4 weeks after the initiation of treatment and 98% at the end of treatment, and SVR12 ratio was 98%. The majority of these patients were genotype 1 (83%), and 57% of them were administered SOF/LDV with or without RBV. There was no difference in treatment response in patients treated with or without RBV, treated over 12 or 24 weeks, or between cirrhotic and non-cirrhotic patients. Grade 2 and 3 anemia were observed in 33% of patients treated with RBV, and this ratio was significantly higher than that without RBV. Grade 2 and 3 increased bilirubin levels were seen in 4% of patients. Dose reduction was made in 62.6% of tacrolimus-receiving patients, 50% of cyclosporine-receiving patients, and in 33% of everolimus-receiving patients, with similar ratios between various treatment regimens. There were no reported adverse effects leading to treatment discontinuation, but acute renal failure was seen in seven patients treated with SOF/LDV. Five of these were accepted as unrelated to treatment (related to sepsis in two patients, hepatorenal syndrome in two patients, and diarrhea in one patient), and two were reported as the consequence of increased tacrolimus levels. Also, acute humoral rejection developed in a patient who had received SOF/LDV and was treated by increased immunosuppressive dose. None of the patients required renal replacement therapy, and no problems were reported in three patients with eGFR < 30 mL/min and receiving SOF-based treatment.

Lubetzky et al.[16] assessed the data from 31 patients retrospectively in their study which evaluated the direct-acting oral antiviral agents in post-transplant HCV treatment. It was found that 24 of the patients had undergone renal transplantation, 5 combined renal and liver transplantation, and 2 liver transplantations after renal transplantation. In total, 90% of patients used the combination of calcineurin inhibitor, mycophenolate mofetil, and prednisolone; 28 were genotype 1, and 21 patients were administered SOF/LDV + RBV. Virological response rate was reported as 93.5% at 4 weeks after the initiation of the treatment and 100% at the end of treatment, and the SVR12 ratio was reported as 97%. Tacrolimus level was stable in the majority of the patients; only two patients had dose increment as the drug level fell under 4 ng/mL. When all cohorts were considered, there was no significant difference in eGFR and proteinuria levels, but proteinuria increased in six patients. There were no adverse effects leading to discontinuation or hospitalization.

Drug interactions, particularly with immunosuppressives, should be considered in the treatment choice in post-transplant patient groups. Calcineurin inhibitors (tacrolimus and cyclosporine) and mammalian target of rapamycin inhibitors (sirolimus and everolimus), which are used for immunosuppression after transplantation, are cytochrome (CYP) P450 isoenzymes 3A4 and the drug transporter P-glycoprotein (P-gp) substrates. Therefore, concomitant use with the inhibitors of these pathways can result in a significant increase in drug levels, and dose modification is necessary with close monitoring. SOF does not interact with CYP3A4 and P-gp, but there is a serious interaction with protease inhibitors (such as simeprevir and ritonavir-boosted paritaprevir). Increased concentration of everolimus can be seen as LDV inhibits P-gp to mild-to-moderate degree. Routine dose modification for calcineurin inhibitors is not suggested during SOF/LDV treatment, but caution should be exercised and drug levels should be monitored closely because of the potential interaction in everolimus-receiving patients.[10,17,18] Also, interaction with mycophenolate mofetil, azathioprine, and prednisolone is not expected in these patient groups. In the studies summarized above, no serious interaction with calcineurin inhibitors, mainly tacrolimus, was reported in either liver or renal transplant patients. In patients receiving everolimus, no interaction that caused drug interruption or treatment change was observed, although various dose modifications were performed.

There are also different SOF-based treatment options for HCV infection in transplant patients. Pungpapong et al.[19] investigated the 12 weeks SOF + Simeprevir (SMV) ± RBV treatment in liver transplant recipients with genotype 1 HCV infection. In this study, 60% of patients were genotype 1a, 30% had severe fibrosis, 7% had kidney transplant, and 91% of patients on tacrolimus-based immunosuppression. SVR12 was reported in 90% of patients. Anemia was observed in 72% of patients who received RBV. Drug-related pulmonary toxicity and respiratory failure leading to death was reported in one patient. Dumortier et al.[20] evaluated the effectiveness and safety of different SOF-based therapies in patients with severe fibrosis after liver transplantation. In this study, patients were mostly genotype 1 and mostly treated with SOF/DCV ± RBV. SVR12 rates were reported as 94% in patients with stage 3 fibrosis and 92% in stage 4 fibrosis. Most commonly reported adverse event was infection. In another study, fixed dose combination of SOF/VEL therapy for 12 weeks without RBV was given the liver transplant patients with chronic HCV. SVR12 rate was reported 96% in this study.[21] In a recent meta-analysis from Ferreira et al.,[22] 14 studies, which include liver transplant patients treated

with SOF/LDV ± RBV, SOF/DCV ± RBV, SOF + RBV, and SOF/SMV ± RBV, were evaluated. Although overall SVR12 rates were reported as approximately 91%, the meta-analysis showed that SOF/LDV ± RBV and SOF/DCV ± RBV regimens had the highest SVR12 rates (over 95%).

In our study, all of the renal transplant patients and all of the liver transplant patients excluding one patient with genotype 4 were genotype 1. End-of-treatment virological response and SVR12 ratios were 100% in both groups in patients treated SOF/LDV with RBV for 12 weeks or SOF/LDV without RBV for 12 or 24 weeks. There were no adverse effects leading to discontinuation of treatment. No significant changes in mean creatinine, eGFR, bilirubin, or tacrolimus levels occurred during the course of treatment. There were no significant changes that caused a significant dose modification in serum cyclosporine and everolimus levels in the two renal transplant patients treated with cyclosporine or one patient in each group who received everolimus.

There are some limitations of our study. Main limitations are small number of patients and retrospective design of study. As pointed out earlier, treatment options for genotype 1 and 4 post-transplant patients are SOF/LDV with or without RBV for 12 weeks in non-cirrhotic patients and SOF/LDV for 12 weeks with RBV or 24 weeks without RBV in compensated and decompensated cirrhotic patients in our country. Because of the retrospective design of study, the choice of RBV combination and treatment duration may vary from physician to physician. However, it was observed that this situation does not affect the effectiveness of treatment.

In conclusion, according to the large-scale literature data and the results of our study, SOF/LDV ± RBV is quite effective in liver and/or renal transplant patients with chronic HCV treatment, particularly in genotype 1. It can be said that administration of treatment without RBV will decrease anemia rates without changing the effectiveness. The treatment-related adverse effect rate is quite low. No serious interaction with immunosuppressive agents, mainly tacrolimus, was observed, but caution should be exercised and close monitoring of drug levels should be considered in patients receiving everolimus.

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Declaration of conflicting interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Ethical approval

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Informed consent

Written informed consent was waived by the Ethics Committee of Akdeniz University Faculty of Medicine.

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