Research Article

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Direct-acting Antiviral Agents in Patients with Chronic Hepatitis C: Real-life Data

Kronik Hepatit C Hastalarında Direkt Etkili Antiviral Ajanlar: Gerçek Yaşam Verileri

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ABSTRACT

Objectives: In the treatment of chronic hepatitis C (CHC), very high rates of sustained virological response (SVR) have been obtained with direct-acting antivirals. In this study, we aimed to evaluate the efficacy and safety of therapies containing ledipasvir + sofosbuvir (Led + Sof), Sof, paritaprevir/ritonavir/ombitasvir + dasabuvir (PrOD) and PrO.

Materials and Methods: Three hundred patients with CHC, who received Led + Sof, Sof, PrOD or PrO treatment were included in the study.

Results: One hundred two (34%) of the patients were treatment-naive patients and 198 (66%) had undergone treatment. Cirrhosis was present in 70 (23.3%) of the patients. Thirty-five (11.7%) of the patients were with genotype 1a, 261 (87%) were with genotype 1b, 1 (0.3%) was with genotype 2a, 2 (0.7%) were with 3a and 1 (0.3%) was with genotype 4a. While the rate of SVR was 98% in patients receiving Led +Sof ± ribavirin (R), it was 100% in patients receiving PrOD ± R. Cirrhosis was found to be the only factor affecting SVR. An adverse event was observed in 60 (40.5%) of patients using PrOD or PrOD + R, and in 68 (44.7%) of those using Led + Sof or Led + Sof + R.

Conclusion: In CHC patients, PrOD and Led + Sof treatments are effective and reliable treatments and shows promise.

Keywords: Chronic hepatitis C, direct-acting antiviral agents, real-life data

ÖZ

Amaç: Kronik hepatit C (KHC) tedavisinde direkt etkili antiviraller ile çok yüksek kalıcı virolojik yanıt (KVY) oranları elde edilmiştir. Bu çalışmada, hastalarda ledipasvir + sofosbuvir (Led + Sof), Sof, paritaprevir/ritonavir/ombitasvir + dasabuvir (PrOD) ve PrO içeren tedavilerin etkinliğinin ve güvenilirliğinin değerlendirilmesi amaçlanmıştır.

Gereç ve Yöntemler: Çalışmaya KHC'li Led + Sof, Sof, PrOD veya PrO tedavisi alan 300 hasta alındı.

Bulgular: Hastaların 102'si (%34) naif hasta, 198'i (%66) tedavi deneyimliydi. Hastaların 70'inde (%23,3) siroz mevcuttu. Hastaların 35'i (%11,7) genotip 1a, 261'i (%87) genotip 1b, 1'i (%0,3) genotip 2a, 2'si (%0,7) 3a ve 1'i (%0,3) genotip 4a olarak saptandı. Led + Sof ± ribavirin (R) alan hastalarda KVY oranı %98 saptanırken, PrOD ± R alan hastalarda %100 saptandı. Siroz, KVY'yi etkileyen tek faktör olarak saptandı. PrOD veya PrOD+R kullanan hastaların 60'ında (%40,5), Led + Sof veya Led + Sof + R kullanan hastaların 68'inde (%44,7) herhangi bir advers olay görüldü.

Sonuç: KHC hastalarında, PrOD ve Led + Sof tedavileri, etkin ve güvenilir tedaviler olup, umut vadetmektedir.

Anahtar Kelimeler: Kronik hepatit C, direkt etkili antiviral ajanlar, gerçek yaşam verileri

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Introduction

The prevalence of hepatitis C virus (HCV) infection in the world is around 3%. This indicates that an estimated 170-180 million people are infected with HCV. Of all HCV cases, 42.2% are with genotype 1, 30.1% are with genotype 3, 9.1% are with genotype 2, 8.3% are with genotype 4, 5.4% are with genotype 6, and less than 1% are with genotype 5 (1). In terms of the HCV cases in Turkey, 66.7 to 100% of the patients are with genotype 1b , 3.45 to 33.7% are with genotype 1a and 3.7% are with genotype 4 (2).

HCV infection is a slowly progressive, insidious disease. The natural course of HCV infection differs among individuals. This difference is due to many factors that concern both virus and host (3). Clinical significance of liver disease associated with HCV involves the fact that 50-85% of the disease becomes chronic after acute infection and that cirrhosis develops in 2-20% of chronic cases after 20-30 years as well as presence of 1-4% risk for developing hepatocellular carcinoma (HCC) per year in cases with cirrhosis (4).

The primary goal of treatment in chronic hepatitis C (CHC) infection is to prevent liver necroinflammation, fibrosis, cirrhosis, HCC and extrahepatic findings by accomplishing eradication of HCV. Thus, the need for liver transplantation, morbidity and mortality is reduced (5,6). Permanent response was confirmed in more than 98% of patients with negative HCV-RNA in serum during long-term follow-up studies in the 24th week following the completion of the treatment (7). Even in patients with advanced fibrosis, significant reductions in liver-related deaths and hepatic decompensation can be observed after successful treatment (8,9,10). In patients responding to treatment, a decrease in the incidence of HCC has been detected (11). It has been shown that life expectancy is prolonged in patients with advanced fibrosis and liver cirrhosis if SVR is achieved (12).

In this study, we aimed to evaluate the efficacy and safety of therapies containing ledipasvir/sofosbuvir (Led + Sof), Sof, paritaprevir/ritonavir/ombitasvir + dasabuvir (PrOD) and PrO.

Materials and Methods

Patients

Three hundred patients who admitted to Gaziantep University Faculty of Medicine Hospital, Hepatology and Infection Outpatient Clinic between June 2016 and December 2017 with a diagnosis of CHC and received Led + Sof, Sof, PrOD or PrO treatment were retrospectively included in the study.

The study was carried out in accordance with principles of the Helsinki Declaration of 1975 as revised in 2008, and with the approval number 08/05/2017/187 of the Gaziantep University Faculty of Medicine Clinical Research Ethics Committee. All patients provided written consent and study entry with all clinical investigations conducted according to the principles expressed in the Declaration of Helsinki.

Methods

Age, gender, body mass index (BMI) of patients, previous treatment experiences, responses to previous treatment, presence of cirrhosis, Child-Pugh score, HCV genotype, concomitant disease status, fibrosis staging of liver biopsies, treatment regimen, duration of treatment regimen, pre-treatment HCV-RNA level, complete blood count, biochemical parameters, international normalized ratio (INR) level and alpha fetoprotein (AFP) level were examined. HCV-RNA, complete blood count, biochemical parameters, INR level, AFP level, and side effects that occurred during treatment were evaluated on the 4th and 8th weeks of treatment, end of treatment and 12th week after treatment. The efficacy and safety of treatments with direct-acting antiviral agents (DAA) were investigated. Patients were divided into two subgroups; those receiving PrOD or PrO and those receiving Led + Sof or Sof.

Laboratory Testing

Anti-HCV test is a two-step immunoassay and chemiluminescent microparticle immunoassay technique (Architect i1000, Abbott, USA) was studied. HCV-RNA measurement was performed using COBAS® AmpliPrep/COBAS® TaqMan® HCV Quantitative v2.0 (Roche Molecular Diagnostics, USA) commercial kits according to the manufacturer's instructions. HCV-RNA genotyping was performed with sequence primers in the PyroMark Q24 device.

Statistical Analysis

The compliance of the numerical data to the normal distribution was tested with the Shapiro-Wilk test. Student's t-test was used to compare variables that comply with normal distribution in 2 groups. The paired sample t-test was used to compare measurements of normally distributed dependent variables. The relationship between categorical variables was tested by chi-square test. SPSS 22.0 (SPSS Inc., Chicago, IL, USA) package program was used in the analysis. A p-value ≤0.05 was considered statistically significant.

Results

Three hundred patients were included in this study. Ninety-seven (32.3%) of the patients were male and 203 (67.7%) were female. Thirty-five (11.7%) of the patients were with genotype 1a, 261 (87%) were with genotype 1b, 1 (0.3%) was with genotype 2a, 2 (0.7%) were with genotype 3a and 1 (0.3%) was with genotype 4a. The number of patients with cirrhosis was 70 (23.3%). In terms of previous treatment experiences; 102 (34%) of the patients were naive, 185 (61.7%) received peginterferon alpha (Peg-IFN α) + ribavirin and 13 (4.5%) received Peg-IFN α + ribavirin + first generation protease inhibitor (PI). Ninety-four of the patients (31.3%) had at least one additional disease. Fifty patients (16.7%) had diabetes, 16 (5.3%) had chronic renal failure (CRF), 35 (11.7%) had hypertension (HT) and 3 (1%) had hepatitis B virus (HBV) infection. The number of liver transplant patients was 10 (3.3%). In terms of the DAA regimens received by patients; 12 patients (4%) were given Led + Sof for 12 weeks, 112 (37.3%) patients received Led + Sof for 24 weeks, 27 (9%) patients received Led + Sof + R for 12 weeks, 1 (0.3%) patient received Sof for 12 weeks, 139 (46.3%) patients received PrOD for 12 weeks, 8 (2.7%) patients received PrOD + R for 12 weeks and 1 (0.3%) patient received PrO + R for 12 weeks. Ribavirin could not be administered to one patient with genotype 2a who received the Sof regimen because the hemoglobin (Hb) value of that patient was 8.6 g/dL. The demographic characteristics of the patients are shown in Table 1.

Table 1. Demographic and clinical characteristics of the patients	
Patients	**n (%)**
Age	61.65±9.76
Diagnosis year	9.32±3.92
BMI, (kg/m^2)	27.72±4.22
Gender, female	203 (67.7)
Genotype	
1A	35 (11.7)
1B	261 (87)
2A	1 (0.3)
3A	2 (0.7)
4A	1 (0.3)
Cirrhosis	70 (23.3)
Child Pugh	
A	35 (50)
B	26 (37.1)
C	9 (12.9)
Treatment experience	
Naive	102 (34)
Peg-IFN + R	185 (61.7)
Peg-IFN + R + PI	13 (4.3)
Treatment response	
Relapse	158 (52.7)
Partial response	4 (1.3)
Unresponsive	31 (10.3)
Stop treatment due to side effects	6 (2)
Additional disease	
CRF	16 (5.3)
DM	50 (16.7)
HT	35 (11.7)
HBV	3 (1)
Liver transplantation	10 (3.3)
DAAs	
Led + Sof 12 week	12 (4)
Led + Sof 24 week	112 (37.3)
Led + Sof + R 12 week	27 (9)
Sof 12 week	1 (0.3)
PrOD 12 week	139 (46.3)
PrOD + R 12 week	8 (2.7)
PrO + R 12 week	1 (0.3)
Fibrosis	
F1-2	32 (23.8)
F3-4	67 (50)
F5-6	35 (26.2)

BMI: Body mass index, Peg-IFN + R: Peginterferon + ribavirin, Peg-IFN + R + PI: Peginterferon + ribavirin + protease inhibitor, CRF: Chronic renal failure, DM: Diabetes mellitus, HT: Hypertension, HBV: Hepatitis B virus, DAAs: Direct-acting antiviral agents, Led + Sof: Ledipasvir + sofosbuvir, PrOD: Paritaprevir/ritonavir/ombitasvir + dasabuvir

The mean baseline HCV-RNA levels of the patients were 1,854,026±2,577,916 IU/mL. The mean baseline AFP levels were 10±16.1 ng/mL. The mean baseline alanine transaminase (ALT) and aspartate transaminase (AST) levels were 53.5±35 U/L and 58±38.6 U/L, respectively. The mean baseline total bilirubin (TB) level was 1±0.9 mg/dL. The mean baseline albumin level was 3.9±0.5 g/dL, whereas the mean baseline INR level was 1.1±0.5. The mean baseline of creatinine was 1±0.7 mg/dL. The mean baseline complete blood count parameters were as follows; white blood cell (WBC): 6.80±2.79x10^3/µL, neutrophil: 3.74±1.70x10^3/µL, lymphocyte: 2.06±1.00x10^3/µL, Hb: 13.6±2 g/dL and platelet (PLT): 194.77±88.14x10^3/µL (Table 2).

Patients were divided into two groups in this study. Those who received Led + Sof for 12 weeks, Led + Sof for 24 weeks, Led + Sof + R for 12 weeks and Sof for 12 weeks were defined as Led + Sof ± R group, while those who received PrOD for 12 weeks, PrOD + R for 12 weeks and PrO + R for 12 weeks were defined as PrOD ± R group. Led + Sof ± R group consisted of 152 patients whereas PrOD ± R consisted of 148 patients. When the virological response between the groups were assessed, there was no significant difference in the evaluation of the 4th, 8th, end of treatment and 12th week of SVR. In the 4th week of treatment, HCV-RNA was negative in 135 (88.8%) of patients receiving Led + Sof ± R and in 133 (89.8%) of patients receiving PrOD ± R. In the 8th week of treatment, HCV-RNA was negative in 150 (98.7%) of patients receiving Led + Sof ± R and 146 (98.6%) of patients receiving PrOD ± R. At the end of treatment, HCV-RNA was negative in all patients in both groups. While relapse was detected in 3 of the patients who received Led + Sof ± R at 12th weeks, HCV-RNA negativity persisted in all patients who received PrOD ± R (Figure 1).

Two of the patients who had relapse received Led + Sof for 24 weeks and one received Led + Sof for 12 weeks. Two of the patients were male and one was female. Patient 1 was 54 years old, patient 2 was aged 61, and patient 3 was aged 41. When the genotype was examined, patient 1 was with 1b, patient 2 was with 1a and patient 3 was with 3a. Patient 1's HCV-RNA level was

Table 2. Initial laboratory characteristics of the patients	
HCV-RNA (IU/mL)	1854026±2577916
AFP (ng/mL)	10±16.1
ALT (U/L)	53.5±35
AST (U/L)	58±38.6
Total bilirubin (mg/dL)	1±0.9
Albumin (g/dL)	3.9±0.5
INR	1.1±0.5
Creatinine (mg/dL)	1±0.7
WBC (×10^3/µL)	6.80±2.79
Neutrophil (×10^3/µL)	3.74±1.70
Lymphocyte (×10^3/µL)	2.06±1.00
Hemoglobin (g/dL)	13.6±2
Thrombocyte (×10^3/µL)	194.77±88.14

HCV: Hepatitis C virus, AFP: Alpha fetoprotein, ALT: Alanine transaminase, AST: Aspartate transaminase, WBC: White blood cell, INR: International normalized ratio

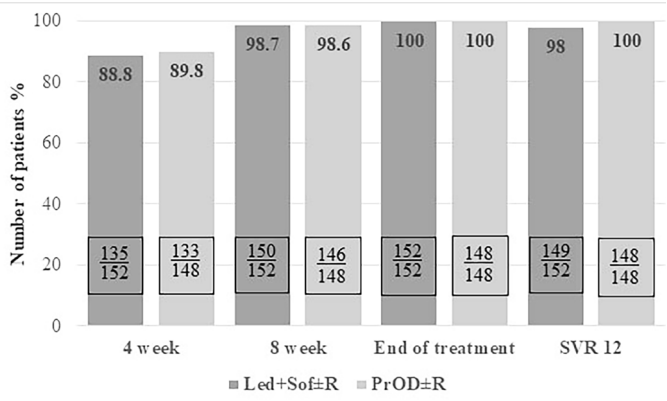

Figure 1. Response to treatment rates

Led + Sof: Ledipasvir + sofosbuvir, SVR: Sustained viral response, PrOD: Paritaprevir/ritonavir/ombitasvir + dasabuvir

163,000 IU/mL, patient 2's was 1,200,000 IU/mL, and patient 3's was 1,700,000 IU/mL. Two patients had cirrhosis, while one did not. According to the Child-Pugh classification, patient 1 was B and patient 2 was C. One patient had received Peg-IFN α + ribavirin before, while the other two were naive. While patient 1 had HT and CRF, patient 2 and patient 3 had no additional disease.

Factors affecting SVR are examined in Table 3. These factors included age, gender, BMI, HCV-RNA level, genotype, presence of cirrhosis, previous treatment experience, CRF, diabetes mellitus, HT, HBV, newly received treatment and use of ribavirin. Among these, the only factor affecting SVR was the presence of cirrhosis and a significant relationship was found (p=0.013).

In treatment groups, the change between baseline TB levels and levels in the 4th week, 8th week of treatment end-of-treatment, and SVR 12th week were examined. There was a significant increase in TB levels in the 8th week of treatment in the PrOD group. However, there was a significant decrease in TB levels in the 12th week of SVR in both groups.

In treatment groups, the change between the baseline Hb levels and the 4th week, 8th week of treatment, end-of-treatment and SVR 12th week was examined.

The relationship between mean ALT, AST, TB, albumin, INR, PLT and Hb levels and SVR 12th week levels in all patients were examined. Significant decreases were observed in AST, ALT and TB levels in the 12th week of SVR, while significant increases were observed in albumin levels and PLT counts. No significant change was observed in Hb and INR Levels.

In terms of the side effects occurring in patients, the most common side effect in both groups was pruritus, insomnia and weakness. Side effects that would require discontinuation of treatment were seen in 2 (1%) patients. Both patients were in the group receiving PrOD ± R and the treatment was terminated at the 8th week due to the grade 3 TB elevation. HCV-RNA was negative in both patients at the 12th week of SVR. There was no significant difference between the groups in terms of itching, insomnia and weakness. Nausea was seen in 14 (9.2%) of patients receiving Led + Sof ± R, in 5 (3.4%) of patients receiving PrOD ± R and difference was statistically significant (p=0.038). Grade 2 anemia (Hb: 8-10 g/dL) occurred in 2 (1.3%) of patients receiving Led + Sof ± R and in 3 (2%) of patients receiving PrOD ± R, while grade 3 anemia (Hb: <8 g/dL) was not seen in either group and no significant relationship was found between the groups. Grade 2 TB elevation (1.5-3 fold increase) was seen in 3 (2%) of patients receiving Led + Sof ± R, and in 2 (1.4%) of patients receiving PrOD ± R. Grade 3 TB height (>3 times) was not seen in Led + Sof ± R group, it was seen in 2 (1.4%) of patients receiving PrOD ± R. There was no significant relationship between groups with regard to TB elevation (p=0.333) (Table 4).

Table 3. Evaluation of the factors affecting the sustained virological response

Patient characteristics	SVR, n (%)	p
Age group		
Over 65	117 (100)	0.084
Under 65	180 (98.4)	
Gender		
Male	95 (98)	0.221
Female	202 (99.3)	
BMI, (kg/m²)		
<25	69 (98.5)	0.801
25-30	156 (99.4)	
>30	72 (98.6)	
HCV-RNA (IU/mL)		
>800,000	166 (98.8)	0.705
<800,000	131 (99.2)	
Genotype		
1A	34 (97.1)	0.071
1B	260 (99.6)	
2A	1 (100)	
3A	1 (50)	
4A	1 (100)	
Treatment experience		
Naive	100 (99)	0.478
Peg-IFN + R	184 (99.4)	
Peg-IFN + R + PI	13 (100)	
Additional disease		
Cirrhosis	42 (97.1)	**0.013***
CRF	15 (93.7)	0.129
DM	50 (100)	0.294
HT	34 (97.1)	0.320
HBV	3 (100)	0.806
The use of ribavirin	36 (100)	0.380
Treatment regimen		
Led + Sof ± R	149 (98)	0.055
PrOD ± R	148 (100)	

*: Statistically significant, SVR: Sustained viral response, BMI: Body mass index, Peg-IFN + R: Peginterferon + ribavirin, Peg-IFN + R + PI: Peginterferon + ribavirin + protease inhibitor, CRF: Chronic renal failure, DM: Diabetes mellitus, HT: Hypertension, HBV: Hepatitis B virus, Led + Sof: Ledipasvir + sofosbuvir, PrOD: Paritaprevir/ritonavir/ombitasvir + dasabuvir

Table 4. Adverse effects			
	Led + Sof ± R (n=152) (%)	**PrOD ± R (n=148) (%)**	**p**
Any adverse effects	68 (44.7)	60 (40.5)	0.463
Serious adverse effects	0 (0)	2 (1.4)	0.092
Itching	42 (27.6)	27 (18.2)	0.053
Insomnia	21 (13.8)	14 (9.5)	0.240
Weakness	19 (12.5)	21 (14.2)	0.667
Nausea	14 (9.2)	5 (3.4)	**0.038***
Headache	13 (8.6)	12 (8.1)	0.889
Anorexia	14 (9.2)	9 (6.1)	0.308
Anemia			
Grade 2	2 (1.3)	3 (2)	0.737
Grade 3	0 (0)	0 (0)	
Total bilirubin increase			
Grade 2	3 (2)	2 (1.4)	0.333
Grade 3	0 (0)	2 (1.4)	
*: Statistically significant, Led + Sof: Ledipasvir + sofosbuvir, PrOD: Paritaprevir/ritonavir/ombitasvir + dasabuvir			

Discussion

DAA are extremely important since they have very low rates of side effects as well as the SVR rates exceeding 95%.

While HCV-RNA was negative in all patients at the end of the treatment, the rates of 12th week of SVR were found to be 98% in the Led + Sof ± R group and 100% in the PrOD ± R group. The results of this study are consistent with studies previously performed in patients with CHC. In the study by Juanbeltz et al. (13), the 12th week rate of SVR was 97.3% in all patients. When we look at the factors that affect SVR in our study, it was found that only the presence of cirrhosis was effective. The high number of patients with cirrhosis in the Led + Sof ± R group may be the reason that the rate of SVR is not 100% in this group.

In a study by Colombo et al. (14) in patients with genotype 1b, the 12th week rate of SVR was 98.3% in the group who were with or without cirrhosis, naive or had previous treatment and received PrOD + R treatment. In the non-cirrhotic, naive or previously treated group receiving PrOD therapy, the 12th week rate of SVR was 99.3% (14).

In the LONESTAR study, the 12th week rate of SVR was 100% in the Led + Sof + R group and 95% in the Led + Sof group (15). In our study, it was 100% in the Led + Sof + R group and 97.6% in the Led + Sof group.

In a study by Calleja et al. (16) in patients with genotype 1b, the 12th week SVR rates were 91.7% in patients receiving Led + Sof for 8 weeks, 94.6% in patients receiving Led + Sof for 12 weeks, 98.0% in patients receiving PrOD for 12 weeks and 95.5% in patients receiving PrOD + R for 12 weeks (17). In our study, 12th week SVR rates were 98.2% for patients receiving Led + Sof for 24 weeks, and 91.7% for those using Led + Sof 12 weeks, while it was 100% in other regimes.

In the study by Calleja et al. (16), 12th week SVR rates were 95.8% in Led + Sof ± R group and 96.8% in PrOD ± R group. Another point highlighted by the study is that rapid virological response (RVR) rates are low in patients receiving Led + Sof ± R (17). In the study by Backus et al. (18), it was found that RVR rates were low in similar rates. In our study, the rate of RVR was 88.8% in Led + Sof ± R group and 89.8% in PrOD ± R group. Calleja et al. (17) stated that there is a significant relationship between cirrhosis status and RVR rate. They have shown that RVR rates are lower in the cirrhosis group. This was not noted in our study. Although the number of patients with cirrhosis was higher in Led + Sof ± R group, the rate of RVR was similar in both groups. However, it was assumed that cirrhosis might be effective in SVR rates.

Ioannou et al. (19), demonstrated that the SVR rates of Led + Sof and PrOD treatments without ribavirin were slightly higher, but this difference was not statistically significant. Regardless of the treatment regimens, the 12th week SVR rates were 92.8% in all patients with genotype 1. In our study, the 12th week SVR was 98.8% in treatments without ribavirin and 100% in regimens with ribavirin. The 12th week SVR rate in 296 patients with genotype 1 was 99.3%.

In a study with patients over 65, the 12th week SVR rate was 88.3% (20). Of these patients, 95% were with genotype 1 and combinations of different DAAs, Led + Sof ± R and PrOD ± R, were given as the treatment regimen. In our study, there were 117 patients over 65 years of age and the 12th week SVR rate was 100%. It was predicted that the treatment regimens used in our study, especially for patients with genotype 1, did not require different combinations as they provide HCV-RNA negativity in all elderly patients.

In our study, at least one side effect was observed in 128 (42.7%) of 300 patients. The most common side effect was itching followed by weakness, insomnia, headache, anorexia and nausea. Intergroup evaluation revealed that nausea was more common in Led + Sof ± R group and the difference was statistically significant. However, it was thought that this finding did not reflect an important condition because nausea was seen in very few patients. In the study by Welzel et al. (21), 42.7% of patients had at least one side effect. The rate of serious side effects in this study was 9.6%, and the rate of drug cessation due to serious side effects was 6.8%. Fatigue, itching and headache were the most common side effects. While the most common complaint in similar studies is weakness, we found itching as the most common side effect in our study. It should not be forgotten that ribavirin is present in treatment regimens, and any patient suffering from weakness should be evaluated for anemia and drug-related side effects.

In a multicenter study conducted by Calleja et al. (17) on patients with genotype 1, the rates of severe side effects and treatment discontinuation due to serious side effects were 5.5% and 1.5% in Led + Sof group, and 5.4% and 1.7% in PrOD group, respectively. Especially when evaluating the side effect, patients who do not receive ribavirin should be assessed with regard to anemia and TB elevation. In our study, 2 patients in the group receiving PrOD ± R could not complete the treatment because of the grade 3 TB elevation. One patient was receiving ribavirin while the other was not. Regardless of the treatment regimen, it was thought that AST, ALT, PLTs, WBC, albumin, INR and creatinine testing, especially Hb and TB values, were required.

In the study by Rodríguez Osorio et al. (20) on 120 patients aged over 65, the probability of side effects was 65%. The majority of patients with side effects were those who received PIs. The most common side effects included weakness, anemia, itching and high bilirubin levels. This study suggests that the elevation of TB levels in our study group receiving PrOD ± R may be related to the PI paritaprevir.

Since treatment regimens are given for 12 or 24 weeks, easy management of the side effects can be achieved. In addition, some studies show that treatment durations can be shortened to 4, 6 or 8 weeks, depending on patient characteristics. Furthermore, SVR rates were found to be too high for patients who could not complete the treatment. In our study, although 2 patients stopped treatment after 8 weeks of treatment, HCV-RNA levels were negative in the 12th week of SVR.

Study Limitations

The limitation of our study is that the study was a single center experience and only two types of drugs were used in the treatment.

Conclusion

The effectiveness of PrOD and Led + Sof combinations was close to 100% in patients with genotype 1 and it was assumed that HCV infection could be fully eradicated. Today, it should be remembered that antiviral treatment should be given in all patients with CHC infection and positive viral load, unless there are contraindications.

Acknowledgement: We thank the study investigators, coordinators, nurses, patients and their families for their contributions.

Ethics

Ethics Committee Approval: The study was carried out in accordance with principles of the Helsinki Declaration of 1975 as revised in 2008, and with the approval number 08/05/2017/187 of the Gaziantep University Faculty of Medicine Clinical Research Ethics Committee.

Informed Consent: All patients provided written consent and study entry with all clinical investigations conducted according to the principles expressed in the Declaration of Helsinki.

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Authorship Contributions

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