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Original Article

Comparison of Renal Side Effects of Tenofovir Disoproxil Fumarate and Entecavir Treatments in Patients with Chronic Hepatitis B Infection; The Results of Five-Year-follow-up

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ABSTRACT

Objective: Tenofovir disoproxil fumarate (TDF) and entecavir (ETV) are the first-line drugs in the treatment of chronic hepatitis B virus (HBV) infection. In our study, the development of renal side effects related to the use of TDF and ETV in chronic HBV patients without renal risk factors was evaluated.

Methods: Patients with chronic HBV infection followed up between 2014 and 2018 were evaluated retrospectively. The patients were divided into ETV-group and TDF-group. Demographic and laboratory findings of the patients were recorded. The change in renal functions was evaluated with the definition of "Decrease in Renal Function (DRF);" a decrease of ≥20% in Estimated Glomerular Filtration Rate (e-GFR) and/or an increase of ≥0.2 mg/dL in serum creatinine compared to the base-level was considered significant. The patients who developed DRF were determined by comparing the creatinine and e-GFR results at the 12th, 24th, 48th, 96th, 144th, 192th, and 240th weeks of treatment with those before treatment.

Results: Of the 126 patients, 77 (61.2%) were in the ETV-group and 49 (38.8%) were in the TDF-group. The groups were homogeneous in terms of demographic characteristics. Pre-treatment mean ALT values were 62.40U/L and 64.88U/L (p=0.273), AST values were 43.77U/L and 44.02 U/L (p=0.720), fibrosis 3.02 and 2.59 (p=0.159) in the TDF and ETV-groups, respectively; and statistically no difference was detected. According to creatinine values, DRF developed in one patient in the TDF-group at week 240, and in two patients in the ETV-group at weeks-48 and 240 (p=0.457). According to e-GFR values, DRF developed in the TDF-group in one patient at week 240. In the ETV group, DRF developed in one patient at week-48, and in two other patients at week-240 (p=0.198) in terms of e-GFR values. There was no statistically significant difference between two-treatment groups in terms of DRF levels.

Conclusion: There is no difference between TDF and ETV treatments in terms of the development of renal toxicity in treatment-naive chronic HBV patients. However, patients who are using these two treatments should be closely monitored in terms of serum creatinine and e-GFR values.

INTRODUCTION

Hepatitis B virus (HBV) is a deoxyribonucleic acid (DNA) virus in the Orthohepadnavirus genus of the hepadnaviridae family.[1] Chronic HBV infection is still a crucial health problem across the world though the vaccine thereof was developed in 1982. In accordance with the data provided by the World Health Organization, Turkey belongs to the middle endemicity region with a positivity rate of 2–7% for chronic HBV infection.[3]

According to current guidelines, immunomodulatory agents and oral nucleos(t)ide analogues (NA) are recommended as the first choice for treating chronic HBV infection.[4] In our country, the primary treatment recommended in the health application communiqué (SUT) is NA. Entecavir (ETV) and tenofovir disoproxil fumarate (TDF) are NAs used in line with this purpose, being potent inhibitors of the HBV polymerase/reverse transcriptase enzyme.[5–10]

NA treatments have been used for many years to maintain a permanent virological response in the treatment

of chronic HBV infection. In fact, some patient groups continue to use these treatments throughout their lives. While long-term drug use reduces the morbidity and mortality rates associated with chronic HBV infection, it often challenges patients and physicians in the management of drug-related side effects.

NAs are excreted by kidneys, and it has been reported in the literature that they contribute to the risk of renal toxicity by causing apoptosis and mitochondrial toxic effects in the renal tubule.[10,11] Since NAs are similar to human nucleosides in the physiopathology of renal toxicity, it is also known to inhibit the human polymerase enzyme, which is responsible for the production of mitochondrial DNA (mtDNA) content. As a result of inhibition, mtDNA encoded proteins are depleted and oxidative phosphorylation is impaired. Reactive oxygen radicals formed can cause damage at the cellular level.[9,12,13]

For patients receiving chronic HBV infection treatment, many factors can impair renal functions in addition to the virus itself and the NA treatments used. These factors can be regarded as advanced age, diabetes mellitus (DM), essential hypertension (HT), HIV and HCV co-infection, nephrotoxic drugs, end-stage liver disease, and solid organ transplantation.[6]

The aim of this study is to compare the long-term renal side effects of both treatments in patients diagnosed with chronic HBV infection and receiving TDF and ETV treatments.

MATERIALS AND METHODS

Study population

This study was designed as a retrospective, comparative case series for patients treated with the diagnosis of chronic HBV infection between January 1, 2014, and December 31, 2018, at University of Health Sciences, Sultan 2. Abdulhamid Khan Training and Research Hospital, Infectious Diseases and Clinical Microbiology Clinic. Patient data obtained from the hospital software system were scanned retrospectively. Among these patients, those who received interferon or other NA treatment, as well the ones with TDF and ETV switch treatment were excluded from the study. In addition, patients over 60 years of age, receiving hemodialysis, co-infected with HDV, HCV, HIV, using ETV 1 mg tablet (tb) treatment, having DM or essential HT, using concurrent immunosuppressive therapy, receiving chronic nonsteroidal anti-inflammatory drug (NSAID) treatment, and using diuretics were excluded from the study.

Thus, the study group consisted of patients aged 18–60 years, who used TDF or ETV as initial treatment, used oral antiviral treatment for at least 3 months, followed up regularly, used oral antiviral treatment continuously without switching between oral antiviral treatment regimens. The patients were divided into two groups as TDF group and ETV group according to the oral antiviral treatment used.

Demographic information (age and sex) of patients in both antiviral treatment groups, pre-treatment alanine aminotransferase (ALT) and aspartate aminotransferase (AST) values, pre-treatment HBeAg positive/negative status, and histological activity index (HAI) and fibrosis rates as a result of pre-treatment liver biopsy were analyzed retrospectively.

The biochemical test results of these patients at weeks 12, 24, 48, 96, 144, 192, and 240 after oral antiviral treatment were recorded in the SPSS 15.0 statistics program of Microsoft Office Excell Professional®.

Definitions and reference ranges

Biochemical analyses as serum urea, serum creatinine, AST, ALT of the patients in this study were measured using in-house Gulhane Military Medicine Faculty kits applied to Abbott Architect C-16000 model autoanalyzer devices (Chicago, Illinois, USA).

Serological tests were measured using the Abbott Architect plus i2000SR device and the Architect Reagent Kit (Chicago, Illinois, USA).

Histopathological examination of liver biopsy specimens was evaluated using the ISHAK 1995 scoring system. HAI was scored between 0 and 18 and fibrosis score was scored between 0 and 6.[14] The normal reference range for ALT level was 5–40 U/L, while the normal reference range for AST level was 5–40 IU/L. Reference range for serum urea level was stated as 15–44 mg/dL, and the reference range for serum creatinine level was stated as 0.6–1.4 mg/dL. Estimated Glomerular Filtration Rate (e-GFR) was calculated according to the CKD-EPI system.

For the definition of Decrease in Renal Function (DRF), ≥20% decline in e-GFR and/or ≥0.2 mg/dL increase in serum creatinine compared to pre-treatment values were considered significant.[15]

Statistical reviews

Statistical analysis of the data was performed with SPSS 15.0. Arithmetic mean and standard deviation were used for parametric data, and median and range were used for non-parametric data as central tendency and prevalence criteria. Chi-square and Fisher's exact tests were used to compare categorical data (HbeAg, sex) among the groups, and Mann–Whitney U statistical analyses were used to compare continuous data (ALT, AST, HAI, fibrosis, and age) among the groups. Statistical significance was tested at a confidence level of 0.95.

Comparison of the proportion of patients with DRF between the TDF and ETV groups was evaluated by Kaplan-Meier analysis (log-rank test). The reduction in cases pre- and post-treatment was examined with the Friedman test.

Ethics committee

This study was approved by the Hamidiye Non-Interven-

tional Research Ethics Committee, University of Health Sciences University, in accordance with the Declaration of Helsinki, with the decision number 19/06 dated 25.01.2019.

RESULTS

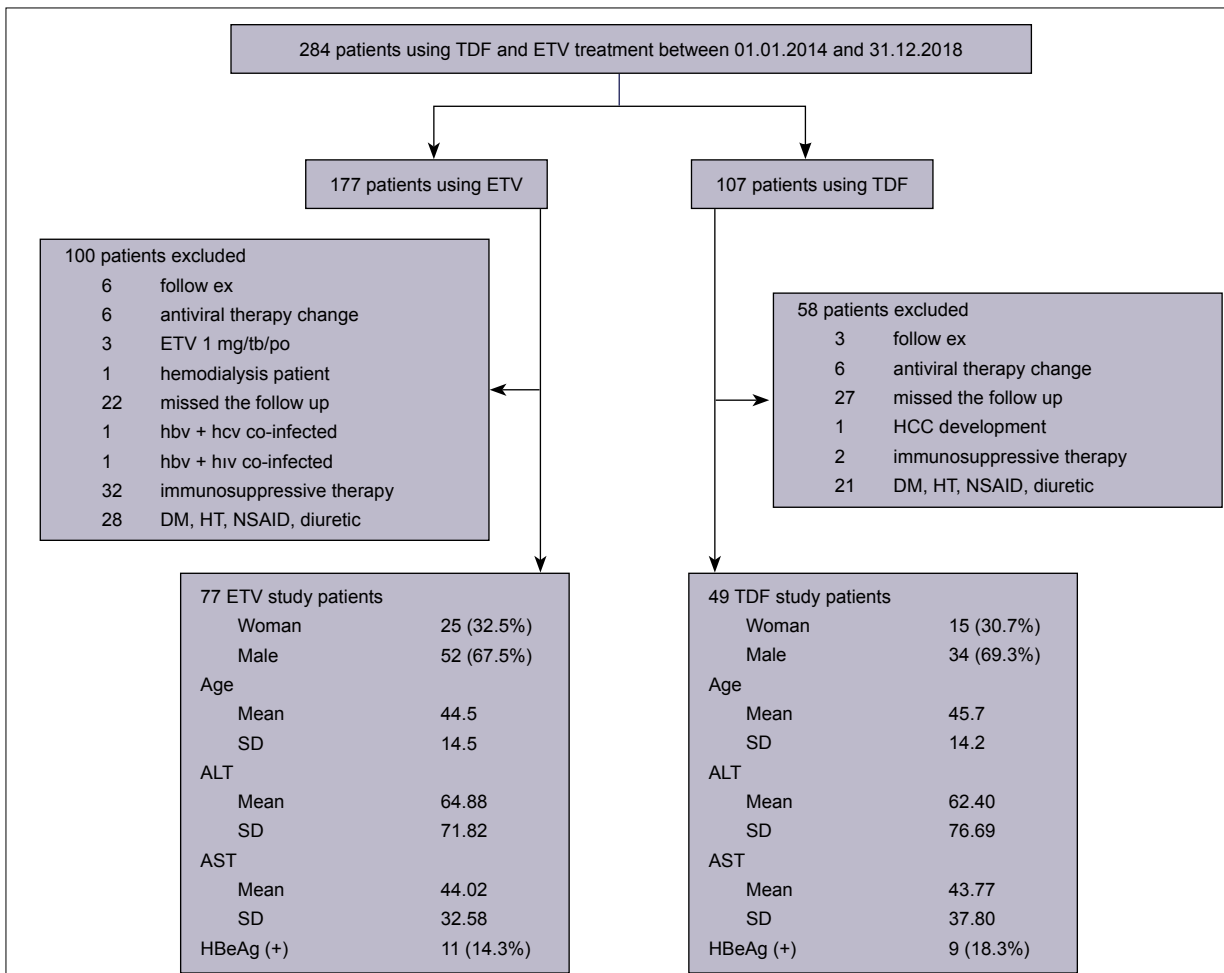
A total of 284 cases were reached in the pre-study file screening. 177 cases were using ETV treatment and 107 cases were using TDF treatment.

In the group using ETV treatment (ETV group), six of the patients who died during their follow-up, six of the patients having a history of using a different NA agent in the past, three of the patients receiving ETV 1 mg tb 1×1 po/day treatment, one of the patients being a hemodialysis patient, one of the patients co-infected with HBV and HCV, one of the patients co-infected with HBV and HIV, 32 of the patients undergoing concurrent immunosuppressive treatment, 28 of the patients having concomitant comorbid diseases such as DM, HT, or a history of NSAID, diuretic drug use, and 22 of the patients not attending their follow-ups regularly were excluded from the study. Therefore, 77 cases in the ETV group were included in the study (Fig. 1).

In the group using TDF treatment (TDF group), among 107 patients, three of the patients who died during their follow-up, six of the patients having a history of using a different NA in the past, two of the patients undergoing concurrent immunosuppressive treatment, one of the patients developing hepatocellular carcinoma in the follow-ups, 21 of the patients having concomitant comorbid diseases such as DM, HT, or a history of NSAID, diuretic drug use, and 27 of the patients not attending their follow-ups regularly were excluded from the study. Therefore, 49 cases in the TDF group were included in the study (Fig. 1).

As a result, a total of 126 patients were included in this study, of which 68% (86) were male and 32% (40) were female.

There was homogeneity in both treatment groups in terms of pre-treatment demographic characteristics and baseline test results. When the mean age, sex distribution,



DM: Diabetes mellitus; HT: Essential hypertension; NSAID: Non-steroidal anti-inflammatory drug; ETV: Entecavir; TDF: Tenofovir disoproxil fumarate; SD: Standard deviation; ALT: Alanine aminotransferase; AST: Aspartate aminotransferase.

Figure 1. Flow chart and study groups according to inclusion criteria in the study.

ALT and AST values, HBeAg positive/negative status, HAI and fibrosis mean values were examined at the beginning of the treatment in both groups, no statistically significant difference was found (p>0.05) (Table 1).

The pre-treatment mean serum creatinine value was detected as 1.02 mg/dL in the TDF group, while it was detected as 0.96 mg/dL in the ETV group. The difference between the two groups was not statistically significant (p=0.567). The mean serum creatinine values of the patients in both groups were monitored during the 240-week treatment follow-up. There was no statistically significant difference between the TDF and ETV groups in terms of mean serum creatinine levels at weeks 12, 24, 48, 96, 144, 192, and 240 (p>0.05) (Table 2).

An increase of ≥0.2 mg/dL was found in serum creatinine levels in 2.04% (1 patient) of 49 patients in the TDF group and 2.59% (2 patients) of 77 patients in the ETV group (Table 3). There was no statistically significant difference between the TDF and ETV groups in terms of the number of patients with DRF due to the increase in serum creatinine (p=0.457) (Table 3). When the follow-ups of three patients who developed DRF were examined, it was observed that serum creatinine values decreased and DRF status improved. It was evaluated that such an increase may be due to instantaneous abnormal results in laboratory measurement systems secondary to dehydration.

Pre-treatment mean value of e-GFR was calculated as 84.20 mL/min in the TDF group, and 91.02 mL/min in the ETV group. The difference between the two groups was not statistically significant (p=0.133). When the mean e-GFR of the patients in the TDF and ETV groups at weeks 12, 24, 48, 96, 144, 192, and 240 was analyzed, no statistically significant difference was observed between the two groups (p>0.05) (Table 4).

When compared to 20% or more reduction in e-GFR values in the follow-ups, one of 49 patients in the TDF group was observed to develop DRF at week 240, and a total of three patients among 77 patients in the ETV group were observed to develop DRF: One at week 48 and other two at week 240. The number of patients who developed DRF in the ETV group was observed to be higher than the TDF group. However, no statistically significant difference was found between the TDF and ETV groups in terms of the number of patients with DRF according to e-GFR values (p=0.198) (Table 3).

No significant renal toxicity occurs due to the use of TDF

Table 1. Demographic characteristics of patients and baseline test results before treatment

	TDF (n=49) (Mean±SD)	ETV (n=77) (Mean±SD)	p-value
Age	45.65±14.16	44.53±14.48	0.670
Gender (M/W)	34/15	52/25	0.827
ALT (U/L)	62.40±76.69	64.88±71.82	0.273
AST (U/L)	43.77±37.80	44.02±32.58	0.720
HAI	6.72±2.58	6.25±2.25	0.358
Fibrosis	3.02±1.32	2.59±1.01	0.159
HBeAg (+/-)	9/40	11/66	0.541

SD: Standard deviation; n: Number of patients; M: Male; W: Woman; HAI: Histological activity index; TDF: Tenofovir disoproxil fumarate; ETV: Entecavir; ALT: Alanine amino transferase; AST: Aspartate amino transferase.

Table 3. Number of patients who developed renal function decline (RFA) at weekly follow-ups

	n/N[5]	Mean time (week)[6]	95% CI	p
Creatinine				
TDF	1/49[1]	240	240.00–240.00	0.457
ETV	2/77[2]	237.26	229.71–244.81	
e-GFR				
TDF	1/49[3]	240	240.00–240.00	0.198
ETV	3/77[4]	237.26	230.72–243.79	

[1]1 patient at week 240, [2]1 patient 48 weeks, 1 patient at week 240, [3]1 patient at week 240, [4]1 patient 48 weeks, 2 patients 240 weeks, [5]n/N: Number of patients followed by RFA/total number of patients, [6]Mean time to emergence of RFA, CI: Confidence interval.

Table 2. Mean serum creatinine values according to the follow-up weeks of the patients

	TDF		ETV		p-value
	n	Mean±SD	n	Mean±SD	
Pre-treatment creatinine	49	1.02±0.15	77	0.96±0.16	0.567
12 weeks creatinine	49	1.01±0.14	77	0.97±0.17	0.258
24 weeks creatinine	49	1.00±0.14	72	0.98±0.16	0.350
48 weeks creatinine	49	1.00±0.17	70	0.97±0.14	0.194
96 weeks creatinine	47	1.00±0.15	53	0.98±0.15	0.648
144 weeks creatinine	33	1.00±0.14	40	0.96±0.15	0.690
192 weeks creatinine	25	0.99±0.13	24	0.97±0.18	0.158
240 weeks creatinine	20	1.02±0.15	13	1.07±0.25	0.181

SD: Standard deviation; n: Number of patients; TDF: Tenofovir disoproxil fumarate; ETV: Entecavir.

Table 4. Mean e-GFR values according to the follow-up weeks of the patients

	TDF		ETV		p-value
	n	Mean±SD	n	Mean±SD	
Pre-Treatment e-GFR	49	84.20±14.64	77	91.02±17.61	0.133
12. week e-GFR	49	85.40± 15.26	77	89.93±17.09	0.570
24. week e-GFR	49	85.72±15.35	72	89.62±17.07	0.419
48. week e-GFR	49	86.46±17.03	70	89.78±17.07	0.810
96. week e-GFR	47	85.10±14.40	53	90.70±16.93	0.650
144. week e-GFR	33	83.65±15.46	40	90.54±19.58	0.166
192. week e-GFR	25	83.90±15.00	24	87.67±20.59	0.219
240. week e-GFR	20	82.28±16.10	13	91.02±17.61	0.177

SD: Standard deviation; n: Number of patients; TDF: Tenofovir disoproxil fumarate; ETV: Entecavir.

or ETV in the treatment of patients with chronic HBV infection without risk factors for renal toxicity. Both drugs can be used safely in these patients.

DISCUSSION

Outcome criteria in the treatment of chronic HBV infection have not yet been fully determined. Patients have to use oral antiviral drugs for a long time. The first question that comes to mind in diseases with such long treatment periods is whether the drugs have long-term side effects.

One of the parameters to be considered in the treatment of patients with chronic HBV infection is the presence of comorbidities. In the presence of comorbidity, the frequency and severity of side effects increase significantly. Deterioration in renal functions and development of osteoporosis/osteopenia is among the side effects recommended to be followed up in nucleos(t)ide treatment.[4]

Patients with chronic HBV infection, decompensated cirrhosis, HT, proteinuria, diabetes, glomerulonephritis, using nephrotoxic drugs and having solid organ transplantation are among the patient groups at high risk for renal toxicity. Patients at risk for renal disease should be monitored closely for their renal function, regardless of the NA treatment they receive. Patients with decompensated cirrhosis, HT, proteinuria, diabetes, glomerulonephritis, using nephrotoxic drugs and having solid organ transplantation together with chronic HBV infection are among the high-risk patient groups in terms of renal toxicity.[6]

Many studies have shown that TDF is a potential nephrotoxic drug in HIV-HBV co-infected patients.[16,17] However, according to the studies conducted by Pol et al.,[18] examining patients with chronic HBV who received TDF monotherapy, an increase of 0.5 mg/dL in serum creatinine level was detected in only 1% of patients with HBV infection who received TDF monotherapy, but no increase was found in the 4-year follow-up. In the study, it was recommended to monitor the renal function and serum phosphate levels of patients receiving TDF at regular intervals during the treatment. In a series of 440 cases using TDF conducted by the Vireal study group in which 58 centers participated, a decrease of ≥20% in basal e-GFR was found in 12% of the cases after TDF among 182 naive patients, and a decrease of ≥30% in basal e-GFR was found in 4%. In this study, the treatment of seven patients was terminated due to TDF-induced kidney involvement. In these cases, renal failure was found in three patients, renal dysfunction in two patients, and renal tubular disease in two patients, respectively. Risk factors for renal toxicity in patients with renal involvement were defined as ≥65 years of age, having borderline e-GFR before treatment, co-infected with HIV, having history of ADV use, or use of nephrotoxic or renally excreted drugs.[19] According to a prospective open-label study by Heathcote et al.,[20] the creatinine and e-GFR levels of patients using TDF did not change for 3 years. Follow-up patients showed an increase in mean serum creatinine of only 0.02 mg/dL over 3 years. None of these patients terminated TDF treatment during the treatment period. It was found that the increase in serum creatinine was 0.5 mg/dL in only two patients and the serum phosphorus level decreased below 2 mg/dL in four patients. Buti et al.[21] published the 7th-year follow-up results of patients with chronic HBV infection receiving TDF therapy. Renal dysfunction developed in 21 (3.6%) of 585 patients who were followed up and treated. Pre-treatment renal risk factor was not detected in 12 patients who developed renal dysfunction under TDF treatment. When the other nine patients with renal dysfunction were examined, it was stated in the study that one or more of the clinical pictures such as HT, DM, renal parenchyma disease (HBV-related glomerulonephritis and IgA nephropathy), and nephrolithiasis were present in the cases. Although the authors found no substantial evidence that TDF is a nephrotoxic agent, they recommend considering the possible TDF-associated proximal tubular damage in these patients. In addition, they recommend that patients receiving TDF treatment without a renal risk factor should be monitored every 6 months, while serum creatinine and phosphorus values should be monitored at shorter intervals in patients with comorbidities.

In our study, patients using TDF and ETV in a 5-year period were evaluated in terms of renal functions (serum creatinine, e-GFR). In our study, patients with risk factors for

renal toxicity were excluded, wherein none of the cases had renal impairment at a level that required drug changes or discontinuation due to TDF or ETV treatments during the 5-year treatment follow-up. Increase in serum creatinine (≥0.2 mg/dL) and decrease in e-GFR (≥20%) were detected in only one (2%) of 49 patients who received TDF treatment. Renal failure was not detected in any of our patients, and TDF treatment was not discontinued for any reason. In the above-mentioned studies, it was thought that the reason for higher incidence of renal side effects related to the use of TDF may be due to the fact that patients in the renal risk group were not excluded from the study. However, patients with risk factors for renal toxicity were not included in our study.

In a retrospective cohort study by Gish et al.,[15] a total of 160 patients, 80 using TDF and 80 using ETV, were compared in terms of renal side effects. In this study, no significant difference was found between patients receiving TDF therapy and patients receiving ETV therapy in terms of affecting kidney function. However, the use of TDF is stated to be a risk factor for renal failure in patients with liver or kidney transplantation, with underlying comorbidities, or with decreased renal function before treatment. It is also stated that these patients can receive TDF treatment as long as they are followed closely. In our study, similar to the study by Gish et al.,[15] no statistical difference was found in terms of renal side effects in the TDF and ETV groups.

The serum creatinine and phosphorus levels of patients with chronic HBV infection treated with TDF are recommended to be monitored at regular intervals, and drug dose adjustment or drug change should be considered when the serum phosphorus level falls below 2 mg/dL.[10] The limitation of our study is not checking the serum phosphorus levels of the patients included in our study on a regular basis.

At present, a high success rate is achieved in the treatment of patients with chronic HBV infection, and our patients can live longer without HBV-induced complications. When following these patients for renal side effects and DRF, it should be kept in mind that patients grow old such that e-GFR values decrease every year. In our study, the e-GFR levels of the patients were examined by taking into account that a decrease of 1 mL/min per year due to aging is normal.

In the study, 126 patients with chronic HBV infection with moderate fibrosis (3/6) treated with TDF and ETV for 5 years were evaluated in terms of renal functions. None of the patients in the TDF and ETV groups developed any side effects that required discontinuation of the drug or switched to another treatment agent. Acute or chronic renal failure did not develop in any of the patients in the TDF and ETV groups.

Although DRF was observed at serum creatinine level in one case in the TDF group and in two cases in the ETV group, the development of DRF was not statistically significant among the two groups (p=0.457). Despite the fact that DRF was observed in one patient in the TDF group and in three patients in the ETV group according to e-GFR levels, the numerical DRF in both treatment groups was not statistically significant (p=0.198).

Ethics Committee Approval

This study approved by the University of Health Sciences Hamidiye Non-Interventional Research Ethics Committee (Date: 25.01.2019, Decision No: 19/06).

Informed Consent

Retrospective study.

Peer-review

Internally peer-reviewed.

Authorship Contributions

Concept: B.S., R.A.Ç., E.Y., L.G.; Design: B.S., R.A.Ç., E.Y., E.T.; Supervision: B.S., L.G., R.A.Ç., S.Ç.E.; Fundings: B.S., L.G., S.A.I., S.Ç.E.; Materials: B.S., E.T., R.A.Ç.; Data: B.S., E.Y., L.G.; Analysis: B.S., E.T.; Literature search: B.S., E.T., L.G.; Writing: B.S., S.A.I., S.Ç.E.; Critical revision: B.S., S.A.I.

Conflict of Interest

None declared.

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Kronik Hepatit B Hastalarında Tenofovir Disoproksil Fumarat ve Entekavir Tedavilerinin Renal Yan etkilerinin Karşılaştırılması: Beş Yıllık Analiz Sonuçları

Amaç: Tenofovir disoproksil fumarat (TDF) ve entekavir (ETV) molekülleri kronik hepatit B virüs (HBV) enfeksiyonu tedavisinde ilk seçenek ilaçlardır. Çalışmamızda, renal toksisite için risk faktörü taşımayan kronik HBV hastalarında TDF ve ETV kullanımına bağlı renal yan etki gelişimi araştırıldı.

Gereç ve Yöntem: Çalışmada 2014–2018 yılları arasında kronik HBV tanısıyla tedaviye alınan naif hastalar retrospektif değerlendirildi. Tedavilerine göre hastalar ETV grubu ve TDF grubu olarak ikiye ayrıldı. Hastalara ait demografik bilgiler ve laboratuvar bulguları kaydedildi. Renal fonksiyonlardaki etkilenme "Renal Fonksiyonda Azalma" (RFA) tanımlaması ile değerlendirildi. RFA tanımlaması; tedavi öncesine göre; e-GFR'de ≥%20 azalma ve/veya serum kreatininde ≥0.2 mg/dL artış anlamlı kabul edildi. Tedavinin 12., 24., 48., 96., 144., 192. ve 240. haftalarındaki kreatinin ve e-GFR sonuçları, tedavi öncesiyle karşılaştırılarak RFA gelişen hastalar belirlendi.

Bulgular: Çalışmaya alınma kriterlerine göre ETV grubunda 77 (%61.2), TDF grubunda 49 (%38.8) olmak üzere toplam 126 hasta dahil edildi. Gruplar demografik özellikler açısından homojendi. Tedavi öncesi TDF ve ETV kollarında sırasıyla; ortalama ALT değerleri 62.40 U/L ve 64.88 U/L (p=0.273), AST değerleri 43.77 U/L ve 44.02 U/L (p=0.720), fibrozis 3.02 ve 2.59 (p=0.159) olup istatistiksel olarak iki kol arasında fark saptanmadı. Serum kreatinin değerlerinde ki değişim incelendiğinde TDF grubunda 240. haftada bir hastada, ETV grubunda ise 48. ve 240. haftalarda farklı iki hastada RFA gelişti (p=0.457). e-GFR değerlerinde ki değişim incelendiğinde TDF grubunda 240. haftada bir hastada, ETV grubunda ise 48. haftada bir hastada, 240. haftada ise iki farklı hastada olmak üzere toplamda üç hastada RFA gelişti (p=0.198). İki grup arasında RFA gelişimi açısından anlamlı fark saptanmadı.

Sonuç: Tedavi naif kronik HBV hastalarında renal toksisite gelişimi açısından TDF ve ETV tedavileri arasında fark yoktur. Ancak bu iki tedaviyi kullanan hastaların serum kreatinin ve e-GFR değerleri yakın takip edilmelidir.

Anahtar Sözcükler: e-GFR; ETV; kronik hepatit B, serum kreatinin; TDF.