Am J Transl Res 2024;16(12):7591-7599
www.ajtr.org /ISSN:1943-8141/AJTR0160482

Original Article

Clinical effectiveness of entecavir versus tenofovir disoproxil fumarate tablets in chronic hepatitis B treatment

You Zhou[1], Yanyan Shen[1], Jian He[2,3], Xuefeng Yang[2,3]

[1]Department of Ultrasound Diagnosis, The Affiliated Nanhua Hospital, Hengyang Medical College, University of South China, Hengyang 421002, Hunan, China; [2]Hunan Provincial Clinical Research Center for Metabolic Associated Fatty Liver Disease, Hengyang 421002, Hunan, China; [3]The Affiliated Nanhua Hospital, Hengyang Medical College, University of South China, Hengyang 421002, Hunan, China

Received September 12, 2024; Accepted November 5, 2024; Epub December 15, 2024; Published December 30, 2024

Abstract: Objective: To analyze the clinical effectiveness of Entecavir (ETV) and Tenofovir Disoproxil Fumarate (TDF) Tablets for the treatment of chronic hepatitis B (CHB). Methods: Clinical data from 100 CHB patients admitted to our hospital from April 2022 to April 2024 were retrospectively reviewed. Of these, 45 cases in the control group received ETV, and 55 cases in the research group received TDF tablets. Data on clinical effectiveness, safety (creatine kinase elevation, fatty liver, and lactic acidosis), hepatic function (total bilirubin [TBIL], alanine aminotransferase [ALT], and aspartate aminotransferase [AST]), viral markers (hepatitis B virus-deoxyribonucleic acid [HBV-DNA] and hepatitis B surface antigen [HBsAg]), and quality of life (the MOS 36-Item Short-Form Health Survey [SF-36], assessing cognitive, physical, emotional, role, social functions) were comparatively analyzed. Results: The research group showed an evidently higher overall effective rate and a markedly lower incidence of total adverse reactions than the control group (all P<0.05). Additionally, statistically lower post-treatment TBIL, ALT, AST, HBV-DNA, and HBsAg levels and higher SF-36 scores across all five dimensions were observed in the research group (all P<0.05). Moreover, the research group showed markedly higher negative conversion rates of HBsAg after treatment compared to the control group (P<0.05). Conclusion: TDF provides better clinical effects in the treatment of CHB than ETV and thus it is worthy of clinical promotion.

Keywords: Entecavir, tenofovir disoproxil fumarate tablets, chronic hepatitis B, clinical effectiveness

Introduction

Hepatitis B virus (HBV) is a non-cytopathic virus that infects liver cells and triggers liver inflammation [1]. The immune system may clear the virus within 180 days after infection, allowing full recovery. However, in some cases, the infection progresses to chronic hepatitis B (CHB) [2, 3]. HBV is a significant cause of liver cirrhosis and a major contributor to the incidence and mortality of primary liver cancer, with approximately 300 million people worldwide currently affected by CHB [4]. Despite the high efficacy of the HBV vaccine (up to 100%), nearly 820,000 people still died from HBV in 2019 [5]. There is no specific radical cure for CHB, which seriously impairs patients' physical and mental health and quality of life [6]. Current treatments aim to alleviate immune dysfunction, improve hepatic function, and inhibit ongoing viral replication [7]. This study seeks to provide further insights into effective CHB treatments.

Entecavir (ETV), a guanosine nucleoside analogue, is a first-line antiviral drug for CHB treatment, noted for its anti-HBV polymerase activity [8]. It also exerts an anti-tumor effect by inhibiting tumor cell proliferation and inducing apoptosis through down-regulating lysine-specific demethylase 5B (KDM5B), helping prevent HBV reactivation in tumor patients [9]. In the study by Kao WY et al. [10], ETV has certain health benefits for the recurrence and clinical outcomes of HBV-related hepatocellular carcinoma (HCC) after hepatectomy. Tenofovir Disoproxil

https://doi.org/10.62347/RKNH8649

Fumarate (TDF), a potent nucleoside analogue with a high drug resistance barrier, is another antiviral drug commonly used in CHB treatment [11]. It has shown efficacy and safety in treating HBV-infected patients, without causing abnormal significant weight gain or increase in cholesterol levels after treatment [12]. In the study of Liang X et al. [13], TDF tablets demonstrated long-term, persistent viral suppression in CHB patients, with no drug resistance up to 4.5 years (240 weeks). This study attempts to comparatively analyze the clinical effectiveness of ETV and TDF Tablets in the treatment of CHB, aiming at providing more clinical references for CHB treatment.

Information and methodology

Patient information

Inclusion criteria: Patients who met the diagnostic criteria for CHB [14]; Patients who received antiviral treatment for the first time; Patients with alanine aminotransferase (ALT) levels exceedingly twice the upper limit of the normal range, HBV≥2×10^4 U/mL; Patients with complete medical records; and Patients with normal communication and cognitive abilities. Exclusion criteria: Those who have allergic reactions to ETV or other drugs used; Breast-feeding or pregnant women; Other types of hepatitis virus infection; Metabolic dysfunction complicated with liver tumor; or Psychological disorders or mental illnesses.

Following rigorous screening based on these criteria, 100 CHB patients admitted to The Affiliated Nanhua Hospital, Hengyang Medical College, University of South China from April 2022 to April 2024 were selected. Among these, 45 cases in the control group were treated with ETV, and 55 cases in the research group were treated with TDF tablets. This retrospective research was approved by the Ethics Committee of the Affiliated Nanhua Hospital, Hengyang Medical College, University of South China.

Medication regimens

The dosing for the two treatment regimens follows established protocols from prior studies [13, 15, 16]. The control group was treated with ETV (Amyjet Scientific Inc., E558910), administrated once daily with a dosage of 0.5 mg. The research group was treated with TDF (Amyjet Scientific Inc., MBS6048503-C) tablets, 300 mg, once a day. Both groups of patients continued their medication for 24 weeks.

Patients with chronic hepatitis B choose ETV and TDF tablets for several reasons: (1) Efficacy: Both ETV and TDF are effective antiviral drugs with a high resistance barrier and robust therapeutic outcomes; (2) Patient-Specific Considerations: The selection between ETV and TDF depends on various patient-specific factors, including age, gender, stage of liver disease, family history of cirrhosis or hepatocellular carcinoma, as well as comorbidities like diabetes and hypertension. For instance, ETV may be preferred for patients at risk for renal impairment; (3) Cost and Availability: Treatment selection can also be influenced by local healthcare resources and the patient's financial situation, allowing for a regimen tailored to each patient's needs; (4) Clinical Guidelines: Based on the latest clinical guidelines, ETV is particularly recommended for patients predisposed to osteoporosis or renal impairment.

Endpoints

(1) Clinical effectiveness. Markedly effective: significant improvement in all hepatic function indicators; Effective: improvement in various hepatic function indicators compared to before treatment; Ineffective: no improvement or worsening of hepatic function indicators. The total effective rate is the sum of markedly effective and effective rates. (2) Safety. Adverse reactions, such as creatine kinase elevation, fatty liver, and lactic acidosis, were recorded, and the incidence rate of each adverse event was calculated. (3) Hepatic function. Levels of total bilirubin (TBIL), ALT, and aspartate aminotransferase (AST) were evaluated with an automatic biochemical analyzer to assess liver function. (4) Viral markers. An automatic immunoluminescence analyzer was utilized to measure serum hepatitis B surface antigen (HBsAg) levels. HBsAg quantitation >250 U/mL were reassessed after a 1:500 dilution. Serum hepatitis B virus-deoxyribonucleic acid (HBV-DNA) levels were quantified using fluorescence PCR detection kit, with a sensitivity limit of 50 U/mL. The negative conversion rate of HBV-DNA is proportion of patients achieving HBV-DNA negativity. The negative conversion rate of HBsAg

Table 1. Comparison of baseline characteristics between the two groups

Indicators	Control group (n=45)	Research group (n=55)	χ^2/t	P
Sex (male/female)	23/22	32/23	0.500	0.480
Age (years old)	50.84±7.58	49.29±7.88	0.995	0.322
Disease course (years)	7.73±2.93	7.89±3.14	0.261	0.795
Smoking history (with/without)	25/20	21/34	3.008	0.083
Alcoholism history (with/without)	17/28	25/30	0.599	0.439

Table 2. Comparison of clinical effectiveness between the two groups

Indicators	Control group (n=45)	Research group (n=55)	χ^2	P
Markedly effective	15 (33.33)	24 (43.64)		
Effective	20 (44.44)	29 (52.73)		
Ineffective	10 (22.22)	2 (3.64)		
Overall effective rate	35 (77.78)	53 (96.36)	8.096	0.004

Table 3. Comparison of safety between the two groups

Indicators	Control group (n=45)	Research group (n=55)	χ^2	P
Creatine kinase elevation	5 (11.11)	1 (1.82)		
Fatty liver	3 (6.67)	1 (1.82)		
Lactic acidosis	2 (4.44)	1 (1.82)		
Total	10 (22.22)	3 (5.45)	6.153	0.013

is the percentage of HBsAg negative cases to the total number of cases. (5) Quality of life. Quality of life assessment was made using the MOS 36-Item Short-From Health Survey (SF-36) [17] from five domains (cognitive, physical, emotional, role, and social functions). Each domain range from 0 to 100, with higher scores indicating better quality of life.

Statistical methods

Statistical software SPSS 19.0 was used for data analysis. Measurement data were statistically described as Mean ± SEM, and independent samples t-tests were used for comparisons between groups, while paired t-tests were applied for within-group comparisons before and after treatment. Count data were expressed by rates (%), and comparisons between the two groups were made by the χ^2 test. A significance level of 5% ($P<0.05$) was adopted.

The sample size for the control and research group was estimated using the sample size calculation method for binomial proportions. The sample size for both groups met the minimum sample size requirement of 32 cases.

Results

Comparison of baseline characteristics between the two groups

No significant differences were observed between the research and control groups in baseline characteristics, including sex, age, disease course, and smoking or alcohol use history (all $P>0.05$) (**Table 1**).

Comparison of clinical effectiveness between the two groups

The two groups were statistically different in clinical effectiveness, with an overall effective rate of 77.78% in the control group and 96.36% in the research group ($P<0.05$) (**Table 2**).

Comparison of safety between the two groups

Complication rates, including creatine kinase elevation, fatty liver, and lactic acidosis, were compared between the two groups. The results showed that the total incidence of complications in the control group was 22.22%, which was significantly higher than 5.45% in the research group ($P<0.05$) (**Table 3**).

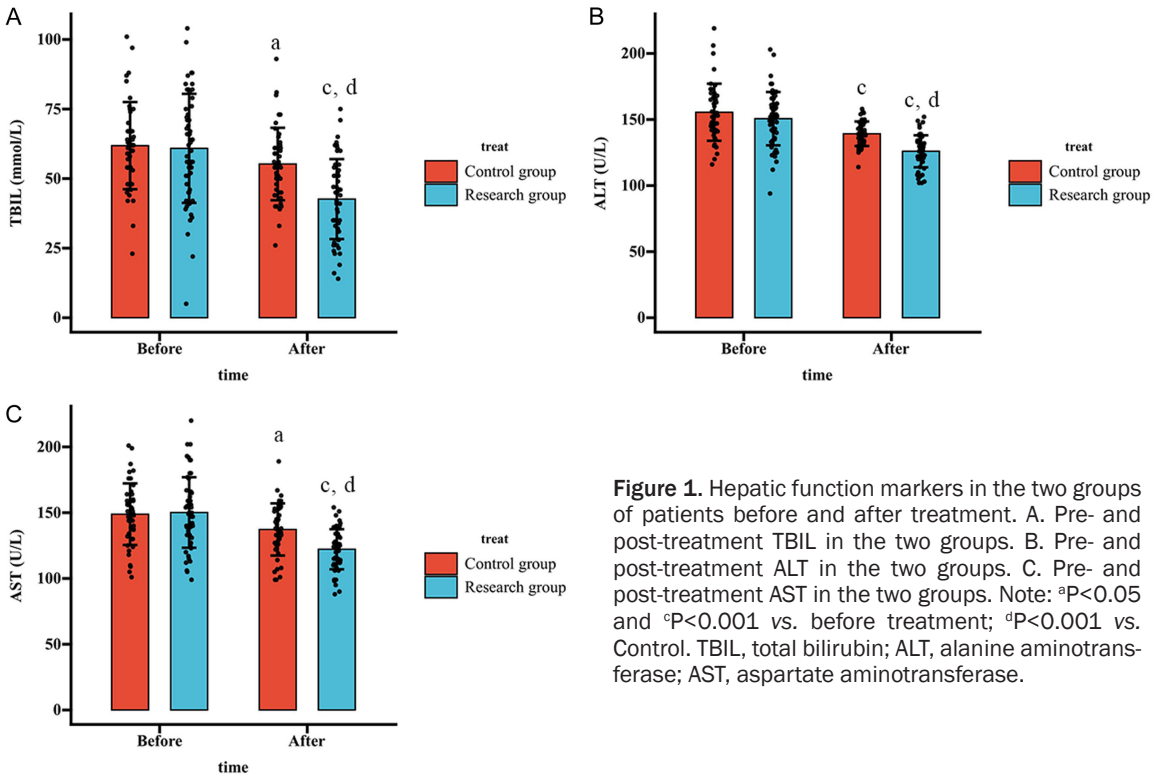

Figure 1. Hepatic function markers in the two groups of patients before and after treatment. A. Pre- and post-treatment TBIL in the two groups. B. Pre- and post-treatment ALT in the two groups. C. Pre- and post-treatment AST in the two groups. Note: [a]P<0.05 and [c]P<0.001 *vs.* before treatment; [d]P<0.001 *vs.* Control. TBIL, total bilirubin; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Table 4. Comparison of hepatic function between the two groups

Indicators		Control group (n=45)	Research group (n=55)	t	P
TBIL (mmol/L)	Before	61.84±15.67	60.87±19.60	0.269	0.789
	After	55.24±13.02[a]	42.64±14.36[c]	4.551	<0.001
ALT (U/L)	Before	155.51±21.59	150.65±20.19	1.161	0.249
	After	139.22±9.30[c]	125.96±12.12[c]	6.028	<0.001
AST (U/L)	Before	148.87±23.42	150.15±26.82	0.251	0.802
	After	137.24±19.83[a]	122.22±15.25[c]	4.281	<0.001

Note: [a]P<0.05 and [c]P<0.001 *vs.* before treatment. TBIL, total bilirubin; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Comparison of hepatic function between the two groups

Baseline TBIL levels were comparable between the control and research groups, with values of (61.84±15.67) mmol/L and (60.87±19.60) mmol/L, respectively. After treatment, TBIL levels decreased to (55.24±13.02) mmol/L in the control group and (42.64±14.36) mmol/L in the research group. For ALT levels, the control group and the research group showed pre-treatment levels of (155.51±21.59) U/L and (150.65±20.19) U/L, respectively; after treatment, the ALT level reduced to (139.22±9.30) U/L in the control group and to (125.96±12.12) U/L in the research group. Regarding AST levels, pre-treatment values were (148.87±23.42) U/L in the control group and (150.15±26.82) U/L in the research group prior to treatment. After treatment, these values decreased to (137.24±19.83) U/L in the control group and (122.22±15.25) U/L in the research group. No significant differences were noted between the two groups in baseline hepatic function indexes (TBIL, ALT, and AST) (all P>0.05). All these indexes showed an evident decline in both groups after treatment (all P<0.05), with even lower levels in the research group (all P<0.05), as shown in **Figure 1** and **Table 4**.

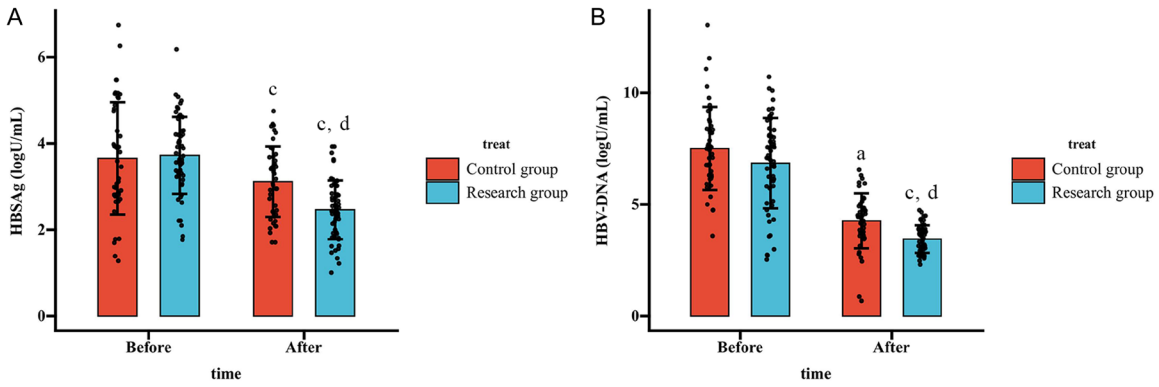

Figure 2. Viral markers in the two groups of patients before and after treatment. A. Pre- and post-treatment HBV-DNA in the two groups. B. Pre- and post-treatment HBsAg in the two groups. Note: [a]P<0.05 and [c]P<0.001 *vs.* before treatment; [d]P<0.001 *vs.* Control. HBV-DNA, hepatitis B virus-deoxyribonucleic acid; HBsAg, hepatitis B surface antigen.

Table 5. Comparison of viral markers between the two groups

Indicators		Control group (n=45)	Research group (n=55)	χ^2/t	P
HBV-DNA (logU/mL)	Before	7.50±1.86	6.84±2.02	1.684	0.095
	After	4.26±1.23[c]	3.45±0.62[c]	4.269	<0.001
HBsAg (logU/mL)	Before	3.65±1.30	3.72±0.89	0.318	0.751
	After	3.12±0.82[a]	2.46±0.68[c]	4.401	<0.001
HBV-DNA negative conversion rate		1 (2.22)	5 (9.09)	2.070	0.150
HBsAg negative conversion rate		0 (0.00)	6 (10.91)	5.222	0.022

Note: [a]P<0.05 and [c]P<0.001 *vs.* before treatment. HBV-DNA, hepatitis B virus-deoxyribonucleic acid; HBsAg, hepatitis B surface antigen.

Comparison of viral markers between the two groups

HBV-DNA and HBsAg levels were measured for both groups. Before treatment, the HBV-DNA level was (7.50±1.86) logU/mL in the control group and (6.84±2.02) logU/mL in the research group, which decreased to (4.26±1.23) logU/mL and (3.45±0.62) logU/mL after treatment, respectively. For HBsAg, pre-treatment level was (3.65±1.30) logU/mL in the control group and (3.72±0.89) logU/mL in the research group, with post-treatment levels reducing to (3.12±0.82) logU/mL in the control group and (2.46±0.68) logU/mL in the research group. The two groups had similar HBV-DNA and HBsAg levels before treatment (all P>0.05). Both markers showed significant reductions after treatment (all P<0.05), with lower levels in the research group versus the control group (all P<0.05). Additionally, we calculated the negative conversion rates of HBV-DNA and HBsAg in both groups. The research group showed markedly higher negative conversion rates of HBsAg after treatment compared to the control group (all P<0.05), as shown in **Figure 2** and **Table 5**.

Comparison of quality of life between the two groups

Prior to treatment, cognitive function scores were (71.24±6.03) points in the control group and (70.96±6.99) points in the research group, increasing after treatment to (79.58±6.6) points and (85.49±8.32) points, respectively. In terms of physical function, scores were (71.93±4.91) points in the control group and (70.58±6.11) points in the research group before treatment, which increased to (82.51±4.07) points and (84.78±6.41) points after treatment, respectively. Regarding emotional function, the control group scored (71.0±6.34) points and the research group scored (73.18±6.25) points before treatment, which increased to (80.22±5.40) points and (84.49±5.67) points after treatment, respectively. As for role function, the scores of the control and research groups before treatment were (67.42±6.53) points and (69.27±7.98) points, respectively;

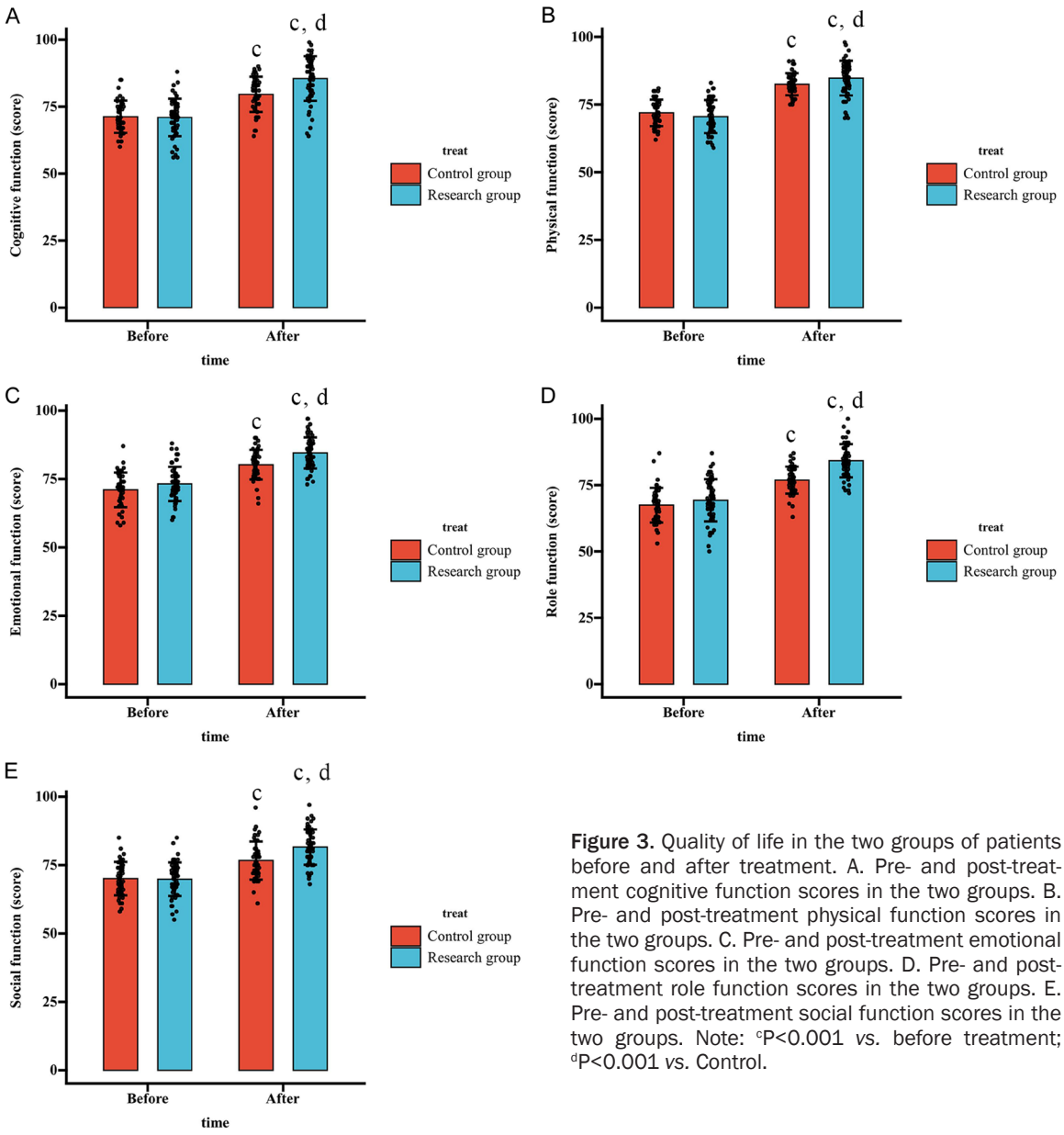

Figure 3. Quality of life in the two groups of patients before and after treatment. A. Pre- and post-treatment cognitive function scores in the two groups. B. Pre- and post-treatment physical function scores in the two groups. C. Pre- and post-treatment emotional function scores in the two groups. D. Pre- and post-treatment role function scores in the two groups. E. Pre- and post-treatment social function scores in the two groups. Note: [c]P<0.001 *vs.* before treatment; [d]P<0.001 *vs.* Control.

after treatment, the role function score increased to (76.89±5.08) points in the control group and (84.18±6.26) points in the research group. For social function, the pre-treatment scores were (70.04±6.09) points in the control group and (69.84±6.12) points in the research group, which increased to (76.64±6.97) points and (81.56±6.45) points after treatment, respectively. The SF-36 assessment revealed no significant differences in cognitive, physical, emotional, role, and social function scores between the groups before treatment (all P>0.05). However, a significant increase in all SF-36 domain scores was observed in both groups after treatment (all P<0.05), with particularly higher scores in the research group compared to those in the control group (all P<0.05), as shown in **Figure 3**.

Discussion

Chronic hepatitis B (CHB) is a prevalent and highly contagious disease, with an increased incidence among older individuals and those with low socio-economic status [18]. The treatment for CHB remains challenging due to the absence of a radical cure, and current clinical guidelines may not apply universally [19].

Hence, ongoing research is essential to optimize CHB management.

In this study, we observed significantly higher clinical effectiveness in the research group, with an overall effective rate of 96.36%, compared to 77.78% in the control group. This suggests that for CHB patients, TDF tablets provide a higher efficacy compared to ETV. The therapeutic mechanism of TDF involves its conversion into tenofovir diphosphate, which combines with deoxynucleoside substrates to inhibit viral polymerase activity, effectively downregulating HBV-DNA levels and blocking HBV replication [20-22]. In the study by Liu R et al. [23], TDF also demonstrated a comparable cure rate and cost-benefit ratio to tenofovir alafenamide.

In terms of safety, the incidence of complications such as creatine kinase elevation, fatty liver, and lactic acidosis in the research group (5.45%) was notably reduced compared to the control group (22.22%), indicating that TDF tablets can better reduce the risk of complications in CHB patients. While increasing the dosage of ETV or TDF may enhance efficacy to some extent, it could also increase the risk of side effects. Consistent with our findings, Murray KF et al. [24] reported that TDF is well tolerated in adolescent CHB patients, with a lower incidence of grade 3/4 adverse events compared to placebo.

Hepatic function indicators (TBIL, ALT, and AST) showed significant improvement in the research group post-treatment, with levels reduced both compared to pre-treatment values and to those in the control group. This indicates that TDF tablets can significantly enhance hepatic function and reduce liver damage in CHB patients. Supporting our findings, Wang XH et al. [25] demonstrated that TDF offered superior protection of hepatic function and improved overall survival rates in HBV-related HCC patients following radical resection compared to ETV. Analysis of HBV-DNA and HBsAg levels before and after treatment further confirmed the advantages of TDF, with significantly lower levels and a higher post-treatment HBsAg conversion rate in the research group compared to the control group. This highlights the role of TDF in viral suppression and elimination. Feng Y et al. [26] also reported the clinical effectiveness and safety of TDF for pregnant women with HBV infection, reducing ALT abnormalities and achieving a rapid decline in HBeAg and HBsAg levels, corroborating the results of this study. Similarly, Ma X et al. [27] reported that the inhibitory effect of TDF on virological response in CHB patients was significantly better than that of ETV, which is in line with our research findings. Finally, the SF-36 scores in cognitive, physical, emotional, role, and social functions improved significantly in the research group, suggesting that TDF treatment greatly enhanced the quality of life for CHB patients. This study has demonstrated that, TDF offers greater clinical advantages over ETV in the management of CHB patients. These advantages are evident across various dimensions, including efficacy, safety, enhancement of hepatic function, suppression of viral markers, and improvement in quality of life. Our findings provide a more informed choice and robust clinical evidence for the treatment of CHB patients.

Nevertheless, this study has some limitations. Conducting a prospective analysis could help mitigate information collection bias. Additionally, a multicenter study design could further enhance the accuracy and generalizability of our results. Finally, further research into the underlying mechanisms associated with ETV and TDF use in CHB treatment would deepen our understanding of their therapeutic mechanisms. Addressing these limitations will be the focus of future research efforts.

Conclusively, TDF tablets demonstrate superior clinical advantages over ETV for CHB treatment, including improved clinical effectiveness, reduce complications, enhanced hepatic function, effective viral suppression, and significantly improved quality of life, making them worthy of clinical promotion.

Acknowledgements

This work was supported by the construction of Innovative Provinces in Hunan (2021SK4031).

Disclosure of conflict of interest

None.

Address correspondence to: Jian He and Xuefeng Yang, Hunan Provincial Clinical Research Center for Metabolic Associated Fatty Liver Disease, Hengyang 421002, Hunan, China. Tel: +86-18670472669;

E-mail: 18670472669@163.com (JH); Tel: +86-0734-8358185; E-mail: yangxuefeng63@outlook.com (XFY)

References

[1] Khan T, Rihan FA and Ahmad H. Modelling the dynamics of acute and chronic hepatitis B with optimal control. Sci Rep 2023; 13: 14980.

[2] de Almeida Ponde RA. Detection of the serological markers hepatitis B virus surface antigen (HBsAg) and hepatitis B core IgM antibody (anti-HBcIgM) in the diagnosis of acute hepatitis B virus infection after recent exposure. Microbiol Immunol 2022; 66: 1-9.

[3] Cheng HY, Lin HC, Lin HL, Uang YS, Keller JJ and Wang LH. Association between nonselective beta-blocker use and hepatocellular carcinoma in patients with chronic hepatitis B without cirrhosis and decompensation. Front Pharmacol 2022; 12: 805318.

[4] Campbell C, Wang T, Burrow R, Mandal S, Hippisley-Cox J, Barnes E and Matthews PC. Estimating the epidemiology of chronic Hepatitis B Virus (HBV) infection in the UK: what do we know and what are we missing? Wellcome Open Res 2023; 7: 203.

[5] Robinson A, Wong R and Gish RG. Chronic hepatitis B virus and hepatitis D virus: new developments. Clin Liver Dis 2023; 27: 17-25.

[6] Freeland C, Racho R, Kamischke M, Moraras K, Wang E, Cohen C and Kendrick S. Health-related quality of life for adults living with hepatitis B in the United States: a qualitative assessment. J Patient Rep Outcomes 2021; 5: 121.

[7] Tsai E. Review of current and potential treatments for chronic hepatitis B virus infection. Gastroenterol Hepatol (N Y) 2021; 17: 367-376.

[8] Ramesh D, Vijayakumar BG and Kannan T. Advances in nucleoside and nucleotide analogues in tackling human immunodeficiency virus and hepatitis virus infections. ChemMedChem 2021; 16: 1403-1419.

[9] Lourenco T and Vale N. Entecavir: a review and considerations for its application in oncology. Pharmaceuticals (Basel) 2023; 16: 1603.

[10] Kao WY, Tan EC, Lee HL, Huang YH, Huo TI, Chang CC, Chiou JF, Hou MC, Wu JC and Su CW. Entecavir versus tenofovir on prognosis of hepatitis B virus-related hepatocellular carcinoma after curative hepatectomy. Aliment Pharmacol Ther 2023; 57: 1299-1312.

[11] Jeong S, Shin HP and Kim HI. Real-world single-center comparison of the safety and efficacy of entecavir, tenofovir disoproxil fumarate, and tenofovir alafenamide in patients with chronic hepatitis B. Intervirology 2022; 65: 94-103.

[12] Byun KS, Choi J, Kim JH, Lee YS, Lee HC, Kim YJ, Yoo BC, Kwon SY, Gwak GY and Lim YS. Tenofovir alafenamide for drug-resistant hepatitis B: a randomized trial for switching from tenofovir disoproxil fumarate. Clin Gastroenterol Hepatol 2022; 20: 427-437, e425.

[13] Korean Liver Cancer Association (KLCA) and National Cancer Center (NCC) Korea. 2022 KLCA-NCC Korea practice guidelines for the management of hepatocellular carcinoma. Korean J Radiol 2022; 23: 1126-1240.

[14] Liang X, Gao Z, Xie Q, Zhang J, Sheng J, Cheng J, Chen C, Mao Q, Zhao W, Ren H, Tan D, Niu J, Chen S, Pan C, Tang H, Wang H, Mao Y, Jia J, Ning Q, Xu M, Wu S, Li J, Zhang X, Zhang W, Xiong C and Hou J. Long-term efficacy and safety of tenofovir disoproxil fumarate in Chinese patients with chronic hepatitis B: 5-year results. Hepatol Int 2019; 13: 260-269.

[15] Li J, Hu C, Chen Y, Zhang R, Fu S, Zhou M, Gao Z, Fu M, Yan T, Yang Y, Li J, Liu J, Chen T, Zhao Y and He Y. Short-term and long-term safety and efficacy of tenofovir alafenamide, tenofovir disoproxil fumarate and entecavir treatment of acute-on-chronic liver failure associated with hepatitis B. BMC Infect Dis 2021; 21: 567.

[16] You H, Wang F, Li T, Xu X, Sun Y, Nan Y, Wang G, Hou J, Duan Z, Wei L, Jia J and Zhuang H; Chinese Society of Hepatology, Chinese Medical Association; Chinese Society of Infectious Diseases, Chinese Medical Association. Guidelines for the prevention and treatment of chronic hepatitis B (version 2022). J Clin Transl Hepatol 2023; 11: 1425-1442.

[17] Zhang M, Li Y, Fan Z, Shen D, Huang X, Yu Q, Liu M, Ren F, Wang X, Dai L, Wang P, Ye H, Shi J, Yang X, Zhang S and Zhang J. Assessing health-related quality of life and health utilities in patients with chronic hepatitis B-related diseases in China: a cross-sectional study. BMJ Open 2021; 11: e047475.

[18] Gnyawali B, Pusateri A, Nickerson A, Jalil S and Mumtaz K. Epidemiologic and socioeconomic factors impacting hepatitis B virus and related hepatocellular carcinoma. World J Gastroenterol 2022; 28: 3793-3802.

[19] Zhu M, Wang H, Lou T, Xiong P, Zhang J, Li L, Sun Y and Wu Y. Current treatment of chronic hepatitis B: clinical aspects and future directions. Front Microbiol 2022; 13: 975584.

[20] Kawuma AN, Wasmann RE, Sinxadi P, Sokhela SM, Chandiwana N, Venter WDF, Wiesner L, Maartens G and Denti P. Population pharmacokinetics of tenofovir given as either tenofovir disoproxil fumarate or tenofovir alafenamide in an African population. CPT Pharmacometrics Syst Pharmacol 2023; 12: 821-830.

[21] Iannuzzi S and von Kleist M. Mathematical modelling of the molecular mechanisms of in-

teraction of tenofovir with emtricitabine against HIV. Viruses 2021; 13: 1354.
[22] Darmadi D, Lindarto D, Siregar J, Widyawati T, Rusda M, Amin MM, Yusuf F, Eyanoer PC, Lubis M and Rey I. Factors affecting HBV DNA suppression in chronic hepatitis B patients treated with tenofovir disoproxil fumarate. F1000Res 2023; 11: 1521.
[23] Liu R, Qiao J, Zhang L and Dou Z. Therapeutic effectiveness analysis of tenofovir alafenamide and tenofovir disoproxil fumarate on the treatment for chronic hepatitis B. Medicine (Baltimore) 2024; 103: e37953.
[24] Murray KF, Szenborn L, Wysocki J, Rossi S, Corsa AC, Dinh P, McHutchison J, Pang PS, Luminos LM, Pawlowska M and Mizerski J. Randomized, placebo-controlled trial of tenofovir disoproxil fumarate in adolescents with chronic hepatitis B. Hepatology 2012; 56: 2018-2026.
[25] Wang XH, Hu ZL, Fu YZ, Hou JY, Li WX, Zhang YJ, Xu L, Zhou QF, Chen MS and Zhou ZG. Tenofovir vs. entecavir on prognosis of hepatitis B virus-related hepatocellular carcinoma after curative resection. J Gastroenterol 2022; 57: 185-198.
[26] Feng Y, Yao N, Shi L, Zhu Y, Liu J, He Y, Zhao Y and Chen T. Efficacy and safety of long-term postpartum antiviral therapy in hepatitis B virus-infected mothers receiving prophylactic tenofovir disoproxil fumarate treatment. Eur J Gastroenterol Hepatol 2023; 35: 212-218.
[27] Ma X, Liu S, Wang M, Wang Y, Du S, Xin Y and Xuan S. Tenofovir alafenamide fumarate, tenofovir disoproxil fumarate and entecavir: which is the most effective drug for chronic hepatitis B? A systematic review and meta-analysis. J Clin Transl Hepatol 2021; 9: 335-344.