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Two-year Single-Center Real-Life Data of Tenofovir Disoproxil Fumarate Treatment for Chronic Hepatitis B Patients in Togo

Aklesso Bagny[1,2*], Lidawu Roland-Moïse Kogoe[1], Laconi Yeba Kaaga[1], Debehoma Redah[1], Late Mawuli Lawson-ananissoh[1,2], Henoc Mawunyo Gbolou[1], Yendoukoa Yves Kanake[1], Koulinga Mikotakatola[1]

[1]Departement of Gastroenterology, Teaching hospital campus of Lome, Togo.
[2]Departement of Gastroenterology, University of Lome, Togo.

ABSTRACT

Objective: to evaluate the treatment efficacy of Tenofovir disoproxil fumarate (TDF) in patients with chronic hepatitis B (CHB) in the Teaching hospital campus of Lome.

Patients and method: retrospective cross-sectional study, conducted in the outpatient department of the Hepato-Gastro-Enterology department of the Teaching hospital campus of Lome from January 2018 and December 2020. Patients with HBsAg were included. Outpatient patients having achieved at least HBeAg, anti-HBe antibody, anti-HCV antibody, anti-HBc IgG; viral load hepatic assessment; retroviral serology. Some patients had achieved actitest-fibrotest. Patients with abdominal pain, clinical signs of portal hypertension or hepatocellular insufficiency had achieved alphafetoprotein, protidogram, and abdominal ultrasound. These explorations made it possible to classify patients into different virological profiles.

Results: More than sixty-four percent of the patients were male. The patients were asymptomatic at 97.37%. HBeAg was positive in 15.19% of patients. The viral load was detectable in 80.43% of cases with a value of 52000000 IU / ml +/- 280000000UI / ml. Ninety-five point twenty-four patients had an inflammatory activity less than 2 and 52.38% a fibrosis greater than 2 on the Metavir grid. The APRI and Fib-4 scores found a strong predictive value for fibrosis in 16.22% and 11.01% of cases, respectively. HBeAg negative chronic hepatitis was the most common virologic profile (58%). Cirrhosis was the most common complication (9.97%). Tenofovir was the therapeutic molecule used. At 12 months of

***Correspondence to Author:**
Dr Aklesso Bagny
Gastroenterologist and Hepatologist, Departement of Gastroenetrology, Teaching hospital Campus of Lome, Togo.
Tel : +22890125159

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treatment, HBe seroconversion was noted in 100% of cases, an undetectable viral load in 50% of cases and normalization of the hepatic balance in 84% of cases. No side effects of the treatment were reported

Conclusion: TDF treatment shows high rate of complete virologic response in CHB patients. TDF is tolerable and safe during the 96 weeks of treatment period. Monitoring of HBV DNA level and drug adherence is important for achieving complete suppression of HBV DNA, particularly in patients with high viral load.

Key words: Hepatitis B, biology, treatment, tenofovir, Togo

INTRODUCTION

Hepatitis B infection is globally a well-recognized public health problem. Nearly two billion people worldwide have serologic evidence of past or present HBV infection, while 350 million people are chronically infected [1]. Its prevalence varies throughout the world, but is highest in tropical regions [2,3]. It is estimated that 5–15% of adults in sub-Saharan Africa are chronically infected with HBV [4]. There is a 15–25% risk of dying prematurely in adulthood from HBV-related cirrhosis and hepatocellular carcinoma, while a small proportion of those with acute infections may also succumb to fulminant liver failure [5]. In sub-Saharan Africa, HBV is most commonly spread from mother to child at birth or from person to person in the early childhood. More than half of the population becomes infected during their lifetime and more than 8% of the inhabitants remain chronic carriers [6]. In Togo, Agbenu et al [7] reported a prevalence of 10% in 2008. Although much work has been done on the prevalence of HBV infection in sub-Saharan Africa, there is few findings on the virological profile and therapeutic response of chronic HBsAg carriers in Togo. The aim of this work is to evaluate the treatment efficacy of Tenofovir disoproxil fumarate (TDF) in patients with chronic hepatitis B (CHB) in the Teaching hospital campus of Lome.

METHODS

This was a retrospective cohort study conducted in adult chronic hepatitis B patients. They were enrolled between January 2018 and December 2020 at Campus University Hospital in Lome, Togo.

The Patients included were patients who had a diagnosis of CHB (defined as a positive serum hepatitis B surface antigen (HBsAg) test for at least 6 months), high serum HBV DNA (> 20000 IU/ml in HBe-positive cases and > 20000 IU/ml in HBe-negative ones), high serum alanine aminotransferase (ALT) at screening (> 2-fold upper normal limit. The definition of upper normal limit of ALT was 50 U/L in men and 35 U/L in women), and had persistently taken TDF for at least one year. The exclusion criteria included hepatitis C virus (HCV) or HIV coinfection. These cases were further classified according to the presentation of hepatitis B e antigen (HBeAg) (HBe-positive and -negative), and prior treatment history (treatment-naïve and -experienced). The therapeutic efficacy, including serum ALT, HBV DNA levels, and the portion of patients with HBeAg or HBsAg loss, were recorded at screening and every 24 weeks (6 months) thereafter. The biochemical, virological, and serological responses were defined as serum ALT < 40 U/L, HBV DNA < 20 IU/ml and HbeAg loss, respectively. The renal function and serum creatinine level were also recorded at the next follow-up visit of each subject.

The method of HBV DNA quantification in our study is using real-time PCR (Cobas AmpliPrep/Cobas TaqMan HBV Test). Data including gender, positive ratio of HBe-positive or negative, treatment naïve status, and concurrent cirrhosis or HCC at screening are expressed as percentages of the total patient number. Statistical comparisons were made using Pearson's chi-square test to compare the positive ratio of therapeutic responses of each group. Independent *t* test was used to analyze

the changes in serum creatinine level. A *P*-value below 0.05 was considered statistically significant.

RESULTS

A total of 578 patients were included in this study. Mean age was 29,15 ans +/- 11,16 and 64.5% were a male. In 53.6% of the cases, they were students from the University of Lome. In 37.40% of the cases, the detection of HBsAg was made during a screening or health check-up. In 96.4% of cases, patients were asymptomatic. Among these patients, 13.9% were Hbe-positive, and 98% were treatement-naive. The treatment-experienced subjects having previous traitements with lamivudine and entecavir. The median HBV DNA level was 8.2±7.4log_{10} IU/mL. The mean HBV DNA level was higher in the HBe-positive patients (7.5 log_{10} IU/mL) than in the HBeAg-negative patients (mean HBV DNA 3.3 log_{10} IU/mL). There were 10% cases with cirrhotic liver and 5.9% with HCC at screening, which diagnosed with typical ultrasound or computed tomography (CT) images (Table 1).

The biochemical responses between HBe-positive and HBe-negative cases is displayed in Figure 1. The ratio of biochemical response at 48 weeks was 80% in HBe-positive patietns, 90 % in HBe-negative patients. At 96 weeks the biochemical reponse was 10 % in HBe-positive and 5% in HBe-negative.

Table 1 : Baseline characteristics of enrolled patients

	Mean	Effective (n)	Percentage(%)
Age (years)	29,1+/-11,2		
ALT (IU/mL)	47,4+/-44,9		
HBV DNA (log10 IU/mL)	7,7+/-8,4		
Sex (Male/Female)		373/205	
HBe Ag positive		81	13,9
Liver cirrhosis		57	10
HCC		47	8,1

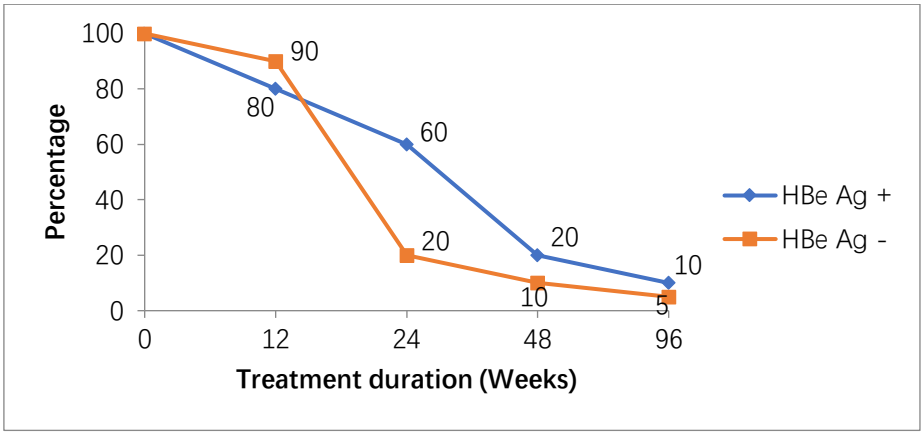

Figure 1 : The biochemical reponse of patients according to HBe status

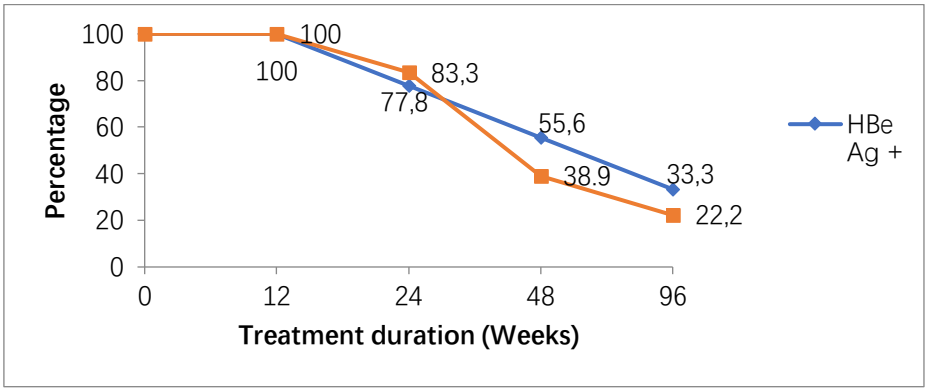

Figure 2 : virological responses of patients according to HBe status

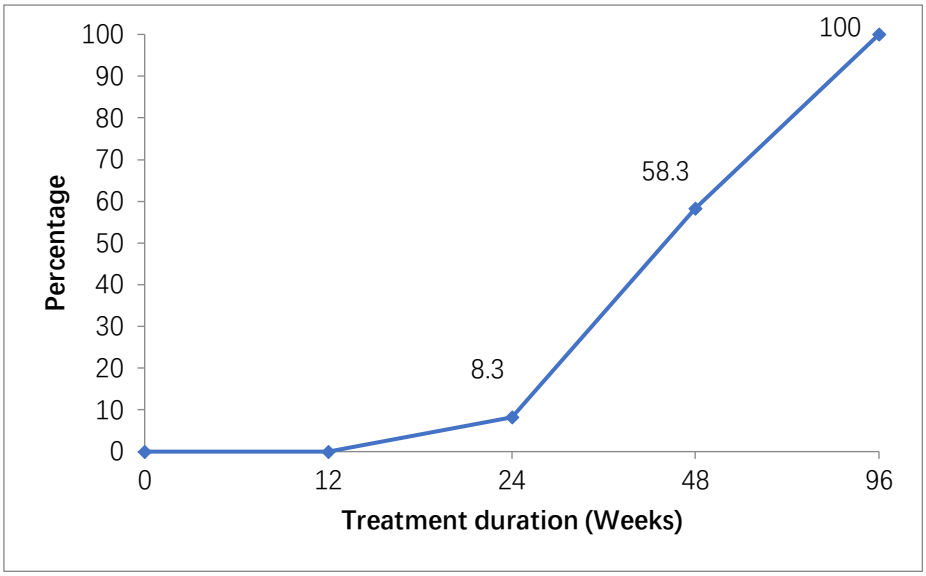

Figure 3: Serological response among the HBe-positive subjects

The virological responses are shown in figure 2. The rate of virological response at 48 weeks was 44,4% in HBe-positive patients and 61,1% in HBe-negative patients. The overall virological response after 48 weeks of TDF treatment was 57%.

The serological response among the HBe-positive subjects if dispayed in Figure 3. There were 8,3% patients who achieved HBeAg loss at 24 weeks, and 58,3% cases at 48 weeks.

DISCUSSION

Togo is an endemic country for hepatitis B, with a huge burden of CHB patients. CHB is a major global health problem, and the goal of CHB treatment is to reduce viral replication, subsequent liver inflammation and fibrosis, and risk of developing cirrhosis and HCC [8]. In this study the mean age was 29.1 years, our CHB patients were younger than those reported from European and african populations [9, 10]. It may be due to early exposure of the subjects to HBV during perinatal period like in other african countries [11]. In this study 64.5% CHB subjects were males, this sexual diffrence is similar in those studies [12-14]. In this series, the prevalence of HBeAg-negative CHB was 86.1%. In CHB, HBeAg-negative is prevalent in 80-90% in Italy, [15] Greece [16] and Asia. In our study ALT and HBV DNA levels were significantly lower in HBeAg-negative subjects. These results are in accordance with recent studies [17,18], where HBV DNA levels were lower in a majority of HBeAg negative CHB patients. The HBeAg loss or seroconversion rate was very high (100%) during the observational period compared with previous studies [19,20]. This study showed that 22.2% and 33.3% of virologic response (< 20 IU/mL) at 96 week of the treatment in each group of HBeAg-negative and HBeAg-positive, respectively. Real-life data also showed that TDF monotherapy has an excellent antiviral efficacy [21]. TDF is effective to achieve the complete virologic response in CHB patients. Monitoring of HBV DNA level and drug adherence is important for achieving complete suppression of HBV DNA, particularly in patients with high viral load [19].

In terms of biochemical response, decrease in ALT level was significant after TDF treatment. There was no ALT flare during the TDF treatment.

Regarding safety profile, TDF was well tolerated without renal impairment during the follow up period. It has been suggested that long-term use of TDF results in renal impairment and proximal tubular dysfunction [22,23]. The risk of renal dysfunction is higher in patients with decompensated liver disease, hypertension, diabetes mellitus, and organ transplantation [22,23]. Our results showed that TDF was safe.

CONCLUSION

Patients with chronic hepatitis B virus infection

are predominantly young adult males. Chronic HBeAg negative infection is the most common virologic profile.TDF treatment shows high rate of complete virologic response in CHB patients. TDF is tolerable and safe during the 96 weeks of treatment period. Monitoring of HBV DNA level and drug adherence is important for achieving complete suppression of HBV DNA, particularly in patients with high viral load.

DECLARATIONS

Ethics approval and consent to participate

Ethical approval was obtained from the Institutional Review Board of the Faculty health sciences of the University of Lome (Togo). We also obtained administrative approval from the General Managers of the Teaching hospital Campus of Lome

For the purpose of confidentiality, participant's data were processed using specific unique identifiers

Consent for publication

Not applicable

Availability of data and material

The datasets generated during the current study are available from the corresponding author on request.

Competing Interests

The authors declare that they have no competing interests.

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None

Authors Contributions

AB designed the study, write the protocol and corrected the manuscript, LRMK, LMLA managed analysis and discussion, YLK managed the literature searches, DVR, YYK, MHG**,** and KM managed data collection

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