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Treatment of Chronic Hepatitis B With Tenofovir At The University Teaching Hospital Campus of Lome (Togo)

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ABSTRACT

Aims: To describe the clinical, biological and evolutionary features of mono infected patients treated with tenofovir in Togo.

Methods: It is a descriptive, prospective study. Patients were treated with Tenofovir Disoproxil Fumarate (TDF). The inclusion criteria were: active chronic HBV (HBs Ag-positive for more than 6 months, high aminotransferases, the HBV –DNA ≥ 2000 IU / ml for HBeAg negative or ≥ 20 000 IU / ml for HBeAg positive and significant fibrosis) and absence of HCV, HDV, or co-infection HIV.

Results: Among patients with HBV in our department, only 10.68% were treated with TDF. The mean age of patients was 33.01±9.81years. There was male predominance (68%). The circumstances of discovery were mainly during blood donation (65.3%) and a routine checkup (14.7%). Clinical examination was normal in most of cases (86.7%) apart from hepatomegaly (9.3%) and icterus (4%).) The HBeAg was negative in 89.3%; the average DNA was 7.56 ±8.01 log10 IU/ml. Abdominal ultrasonography was performed in all patients and we found hepatomegaly (18.67%), splenomegaly (10.67%), and ascites (5.3%). The assessment of fibrosis and activity had enabled to find a fibrosis higher or equal to 2 in 12 cases (48%) and an activity higher or equal to 2 in 9 cases (36%). The clinical and virologic outcome was marked by an undetectable viral load (HBV-DNA<10 IU/l) in 89.3% of the patients after 1 year of treatment.

Conclusion: TDF had helped to find out an undetectable viral load in in 89.3% of the patients after one year of treatment.

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Introduction

Chronic hepatitis caused by the hepatitis B virus (HBV) affects a high number of people and it was a major cause of mortality and morbidity. It is estimated that approximately 240 million people get chronic infection of hepatitis B virus [1]. Chronic viral hepatitis is a serious but underestimated global public health problem [2]. Diagnosis and management remain complex and many countries lack the human resources and medical infrastructure to provide treatment. New drugs are now available to treat or to stop the spread of the hepatitis B virus infection, but most people with chronic viral hepatitis are unaware of their infection and do not receive appropriate treatment [3]. Up to one third of the chronic viral hepatitis carriers will die of liver cirrhosis or liver cancer if they are not well diagnosed and directed to the appropriate units. Togo is a country located in areas of high endemicity of HBV [4] with high prevalence of chronic HBV-related diseases (43.24%) [5]. Despite this fact the country lacks infrastructures and sufficient resources to combate chronic hepatitis B. The new drugs including tenofovir (TDF) are only actually available in our country for 2 years and the cost of treatment is still at the expense of the patient. We, therefore find this study important, to study the clinical, biological and evolutionary features of mono infected patients with HBV treated with TDF in our department.

Patients and Methods

This is a descriptive prospective study of patients in the department of hepatology and gastroenterology at the teaching hospital campus of Lomé, from february 2012 to july 2015 and treated with TDF for an indefinite period. The only available dose of TDF was administered at a daily dose of 300 mg in the country and is also used for HBV and HIV co-infection. The inclusion criteria were: active chronic HBV (HBsAg positive for more than 6 months, high intermittent or persistent aminotransferases, HBV DNA ≥ 2000 IU / ml for the HBeAg negative or ≥ 20 000 IU / ml for HBeAg positive and necro-inflammation or moderate to severe fibrosis), the absence of HCV, HDV, or HIV co-infection and treatment with tenofovir. We included in this study, patients with a family history of hepatocellular carcinoma and patients with HBV-related cirrhosis. Patients with HDV, HCV or HIV coinfection, inactive chronic carriers of HBV, HBV carriers not treated or treated with another molecule have been excluded. The following parameters were also studied: demographic (age, sex), clinical, biochemical (aminotransferases), serum (HBsAg, total anti-HBc, HBeAg, anti-HBe), virological (DNA of HBV by quantitative PCR). All patients went through abdominal ultrasonography in search of signs of portal hypertension, cirrhosis or hepatocellular carcinoma (HCC). At the level of cirrhosis patients had an upper digestive endoscopy for signs of portal hypertension and determination of alpha fetoprotein in search of hepatocellular carcinoma. The detection of HBsAg was performed according to ELISA sandwich method; as well as the HBeAg, the anti-HBe and the anti-HCV. The DNA of the HBV was measured by the COBAS Ampli Prep technique / HBV COBAS Taq Man Version 2.0 of Roche (Meylan, France) with a positive threshold of 20 IU / ml (linearity from 20 IU / ml to 170.000.000IU / ml). Hepatic fibrosis was assessed by the non-invasive method of the Fibrotest-Actitest. The data were analyzed by SPP 21.0 software.

Results

During the period of this study 4410 patients have consulted in our department, including 819 cases of viral hepatitis (18.6%). There were 702 cases of hepatitis B (15.9%) and 117 cases of hepatitis C (2.65%). Among patients with HBV, 75 were put under treatment with TDF (10.68%). The mean age of patients was 33.01±9.81 years old with extremes of 15 and 57 years old. There was male predominance (68%) with a sex ratio of 1.9. The mean age of women was 29 years old against 32.1years old in men (p = 0.058). There was predominance (53.3%) of the age group of [30-45]; very few of our patients were insured (8%) (Table1).

Clinically, the circumstances of discovery were essentially during blood donation (65.3%), etiologic assessment of cirrhosis (18.7%) and a routine checkup (14.7%). Clinical examination was normal in most of the cases (86.7%), apart from hepatomegaly (9.3%) and jaundice (4%). Livercheckup had enabled to notice: ALT 72.87±19.4 IU/l, AST 58.88±83.1 IU/l, ALP 190.51±116.5 IU/l, GGT 66.53±68.4 IU/l, albumin 43.54±5.1 g/l, prothrombin 54.76±10.7%, the level of alpha fetoprotein 1.11± 1 ng/ml. The HBeAg was negative in 89.3% of cases; the average DNA was 7.56 ±8.01 log10 IU/ml. Abdominal CT scan was performed in all patients and we found hepatomegaly (18.67%), splenomegaly (10.67%), a dilation of the portal vein (4%), and an ascites (5.3%). The assessment of fibrosis and activity was based on the fibrotest-actitest and had helped to find a fibrosis higher or equal to 2 in 12 cases (16%) and an activity higher or equal to 2 in 9 cases

Table 1: Demographic data

	Number (n)	Percentage (%)
Averageage 33.1±9.8years old		
[15-30[	25	33.3
[30-45[	40	53.3
[45-60[	10	13.4
Sex		
male	51	68
female	24	32
Marital status		
married	23	30.67
unmarried	52	69.33
Socio-economic level		
low	57	76
average	11	14.7
high	7	9.3
Health insurance		
yes	6	8
no	69	92
Home/ Residence		
Urban	35	46.67
suburban	13	17.33
rural	22	36

Table 2: Circumstances of HBV discovery

	Number (n)	Percentage (%)
Blood donation	49	65.3
Etiological research of cirrhosis	14	18.7
Health checkup	11	14.7
Anomaly of the liver tests	08	10.7
Pre-natal consultation	07	9.3

(12%). We got a fibrosis F4 in 4 cases (5.33%). The gastroscopy performed in 9 patients had revealed 3 cases (4%) of esophageal varices of which 3 of grade 2 and a case (1.33%) of grade 3.

Creatinine was stable in all patients, and no cases of kidney failure were reported as tenofovir side effect.

The clinical and virologic outcome was marked by an undetectable viral load (DNA-HBV<10 IU/l) in 89.3% of the patients after 1 year of treatment.

Discussion

This prospective study is the first to show the results of chronic hepatitis B treatment in Togo. Our methodology is similar to the one of Kissi and al in west Africa[6] and that of Nwokediuko and al[7] in Asia. Our sample was made of 75 patients with chronic hepatitis B and cirrhosis. This remark is frequent in our practice where most of patients did not know they are hepatitis B virus carriers or they consulted late at the stage of cirrhosis.

The mean age of patients was 33.01±9.8 years

old which clearly shows that the population is young even younger than other studies from West Africa [6, 8]. The mean age is higher in Europe than 45 years old [9, 10]. This result can be explained by the fact that the contamination of HBV in Africa is most often occurred through mother to child transmission and during childhood. There was male predominance (68%) as in majority of studies in Africa [6, 8], Europe and in Asia [10-12]. The circumstances of HBV discovery varied and were mainly dominated by blood donation and cirrhosis. These results show that, the research of HBV in routine in our context is not systematic, which explains the fact that the diagnosis is made at the stage of complication (cirrhosis) or during a free checkup like blood donation. The systematic research of HBV in routine could help to reduce cases of dangerous complications like cirrhosis or hepatocellular carcinoma. The majority (89.3%) of our patients was HBeAg negative as in most of European studies [13, 14]. This high prevalence of the negative HBeAg is the current world wide trend [15] apart from Asia where there is still high prevalences of HBeAg positive [12]. The indication of the HBV treatment according to World Health Organization is based on the ALT rate higher than the normal, the DNA of HBV and the severity of the liver disease based on the METAVIR score, APRI score or FIB4, the fibroscan or fribotest-actitest [16]. In our study we focused on ALT dosages, the HBV DNA and the fibrotest-actitest. The ALT of our patients was 72.87±19.4 IU/l. This result is comparable to the African data[6], but much less than the European and Asian data [12] where we had respectively found 110 IU/l and 155.4IU / l. The average DNA in our study was 7.56 ±8.01 log10 IU/ml. This rate is comparable to that of Kissi and al[6] who found 7.4±7.7log10 IU/ml, however it is much higher than the one of Sang Kyung Jun and al [12] who found 4.9±2.3 log10 IU/ml in Kore.

The assessment of the severity of the disease in our context was based on the clinic in the search of signs of cirrhosis decompensation as jaundice and ascites in 4% respectively. These data were confirmed by abdominal CT scan. The fibrosis was evaluated by a non -invasive test (fibrotest - actitest) as suggested by the majority of the recommendations [18]. This test had enabled to find a significant fibrosis in approximately 21.33% of cases and/or a significant activity in 12% of cases. Actually, it has been revealed that most of chronic HBV carriers with HBeAg negative were often discovered late at a stage of liver disease [10]. Based on clinical arguments, ultrasonography, endoscopic and non-invasive fibrosis test, we found in our study 5.3% of patients at the stage of cirrhosis before treatment. In Turkey [9] a study had found 3.7% of cirrhotic patients whereas another study in Korean [11] found 51% before the TDF treatment.

All our patients were naïve to anti-viral treatment. It is said that the anti-viral long-term treatment enables a regression of histological lesions [10]. Treatment with TDF is efficient in monotherapy in naïve patients [19] as the results of our study indicated with 89.3% of patient who had an undetectable viral load after one year treatment.

Table 3: Physical examination data

	Number (n)	Percentage (%)
Normal examination	65	86.7
Hepatomegaly	7	9.3
Jaundice	3	4
Ascite	3	4

Conclusion

The TDF is the first treatment of HBV in our country but the cost of this treatment is still entirely at the expense of the patient.TDF had enabled to find out an undetectable viral load in 58.6% of negative HBeAg patients after a year of treatment. Improving patient care could also include reducing the cost of treatment and implementing treatment in all regions of the country.

Conflicts of Interest: The authors have no conflicts to disclose

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