

Effectiveness and Tolerance of Tenofovir Disoproxil Fumarate in Sub-Saharan Viral B Cirrhotic Patients

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Abstract

Tenofovir reduces viral load during viral cirrhosis B and improves prognosis. The aim of this study was to evaluate the effectiveness and safety of Tenofovir during the treatment of viral B cirrhosis. The study was retrospective and prospective on patients with viral B cirrhosis treated with Tenofovir in the Hepato-Gastroenterology Department of University Hospital Gabriel Touré in Bamako (Mali) and evaluated between three and six months after the start of treatment. We included 89 patients. The mean age was 44.5 ± 16 years with extremes of 18 and 90 years. The sex ratio was 1.2. At inclusion all patients had a detectable viral load with an average of 2651.96 ± 1495.85 IU/ml. Follow-up viral load was undetectable in 84.3% with patients between 3 and 6 months of treatment. The average detectable viral load was only 27.04 ± 21.05 IU/ml. There was also an improvement in hepatocellular function and few side effects. **Conclusion:** This study shows the interest of Tenofovir in the treatment of viral cirrhosis B with very few adverse effects.

Keywords

Cirrhosis, Tenofovir, HBV

1. Introduction

Cirrhosis is serious by its frequent complications [1] [2]. The main causes of this disease are hepatitis B virus (HBV), hepatitis C virus (HCV) and alcohol consumption [3] [4] [5] [6].

In tropical area hepatitis B virus is the most frequent cause of cirrhosis [3] [4]

[5] [6] [7] [8].

Current treatments by nucleic analogue and interferon can stop virus replication and thus stabilization or even improvement of hepatic disease [9]. Tenofovir Disoproxil Fumarate (TDF) effectiveness has been proven with the advantage of having a high genetic barrier against the virus [9] [10]. However, the major risk of this drug is its renal toxicity and bone defect [11].

In Mali, the prevalence of HBs antigen in the general population ranges from 13.9% to 15.5% [12] [13] and this viral marker was found in 55% to 71% of cirrhosis and in 55% to 62.2% of hepatocellular carcinoma [3] [14] [15]. TDF is more and more accessible in the treatment of HBV infection. The risk of this treatment has not been evaluated in our context. We initiated this study with the aim to evaluate the efficiency and safety of TDF in viral B cirrhotic patients.

2. Patients and Methods

The study was retrospective from April 2014 to April 2015 and prospective from May 2015 to October 2016 and took place in the service of Hepato-gastroenterology of CHU Gabriel Touré in Bamako, Mali.

The study included HBV cirrhosis patients treated with TDF. The patients had HBV viral load assay at the start and between 3 and 6 months of the treatment. For the retrospective period the data were collected from the service records. During the prospective period the data were recorded in real time. The study parameters collected were gender, age, causes of consultation, clinical examination data, HBV viral load, adverse effects of TDF, the course of the disease.

All the patients were informed about the course of the study and gave their approval.

Data analysis was done on Epi Info statistical software version 6.04. The chi² statistical test was used to analyze our results with a significance level for $P < 0.05$.

3. Results

At the end of the study, 89 patients were collected. The sex ratio was 1.2 (66 men versus 23 women). The average age of the patients was 44.5 ± 16 years with extremes of 18 and 90 years. The 25 - 34 age group was more represented. Ascites and jaundice were the main causes of consultation (**Table 1**). At inclusion, ascites and hepatomegaly were the most observed clinical signs (**Table 2**). The HBV viral load, detectable in the all patients, was greater than 2000 IU/ml in 49.4% of patients with an average of 2651.96 ± 1495.85 IU/ml. In 65.2% of cases the patients had decompensated cirrhosis. The TDF treatment improved significantly hepatocellular function (**Table 3**). After three months of treatment the viral load became undetectable in 84.3% of patients and the average detectable viral load was only 27.04 ± 21.05 IU/ml. Nephropathy was observed in 8 patients (**Table 4**). The global mortality was 7.9% (7 patients including 3 with nephropathy).

Table 1. Causes of consultation.

Causes for consultation	Number	%
Ascites	17	19.1
Jaundice	16	18
Ascites + IMO	12	13.5
Hematemesis	11	12.3
Abdominal pain	09	10.1
Emaciation	07	7.9
Hepatomegaly	06	6.7
Consciousness disorder	04	4.5
bloating	04	4.5
Hematemesis + hematochesis	03	3.4
Total	89	100

Table 2. Clinic signs.

Clinical signs	Number	%
ascites	64	71.9
Hepatomegaly	49	55.1
Jaundice	45	50.6
Splenomegaly	27	30.3
CVC	25	28.31
Neurological disorders	15	16.9

Table 3. Cirrhotic biological course during the treatment.

Biology	At inclusion n (%)	3 - 6 months later n (%)	P
Protrombine rate (n = 89) <50	31 (34.8)	19 (21.3)	0.045
Bilirubin (n = 89) >35	42 (47.2)	36 (40.4)	0.364
Albumin (n = 89) <35	37 (41.6)	18 (20.2)	0.002
Platelet (n = 89) <150.10 ³	57 (64)	36 (40.4)	0.001

Table 4. Adverse effects of treatment.

Biological assessment	Period	Month 1 n (%)	Month 2 n (%)	Month 3 - Month 6 n (%)
	Creatininemia > 120 (n = 89) <120		4 (4.5) 85 (95.5)	6 (6.7) 83 (93.3)
Glycosuria (n = 89)		No	No	No
Phosphoremia (n = 89)		No	No	1 (1.1)
Urate protein (n = 89)		No	No	2 (2.2)

4. Discussion

At the end of this study, 89 HBV cirrhotic patients were included. This sample was limited by the difficulties to perform in some patients biological tests including viral load for financial reasons. The sex ratio in our study was 1.2 in favor of men. This frequency was lower than that found by Doumbia *et al.* which was 2.28 [16]. On the other hand, Diarra reported 1.09 in favor of women [17]. This male predominance could be explained by the frequency of the chronic carriage of HBV in men, causing the most cirrhosis in our context [16].

The average age of the patients was 44.5 ± 16 years. This frequency is similar to those reported by Maïga *et al.* [18], Diarra *et al.* [2], Diarra [17] and Doumbia *et al.* [16] which were respectively 43.25 years, 41.5 years, 42 years and 43.8 years. Ascites and hepatomegaly were the most common clinical signs with 71.55 and 55.1% respectively; Doumbia *et al.* [18] found jaundice (58.1%), hepatomegaly (36.2%) as the main signs. For Pariente [19] ascites is a telltale sign of cirrhosis.

A viral load greater than 2000 IU/ml in almost the half patients attests the frequency of virus replication and therefore also cirrhosis activity. Hepatocellular function was also advanced in 65.2% of patients. In the same context Diarra *et al.* [17] reported that 90.2% of patients were at B or C stage of the Child-Pugh score.

The treatment by TDF improved significantly hepatocellular function ($P = 0.045$ to 0.002). This result is certainly attributed to the control of viral replication because the viral load became undetectable in 84.3% of patients. This non detectability occurred between 3 - 6 months of treatment with an average of detectable viral loads of only 27.04 ± 21.05 IU/ml. Guindo [20], in a VHB hepatitis treated by the same drug, reported a non-detectable viral load in 32.14% of patients within.

During treatment, renal injury was observed in seven patients. Guindo [20] found no adverse effect in the same time limit. In one study [11], it was reported a hypercreatininemia, hyperphosphatemia after 48 first weeks of treatment.

The mortality was 7.9%. On the seven deaths, three had renal involvement during treatment. But the benefit of this treatment greater than the adverse effects and justifies its use during HBV infection at any stage.

5. Conclusion

The interest of Tenofovir in the treatment of viral cirrhosis B is well established. A national policy must work for the availability of this drug. Emphasis should also be placed on birth vaccination against HBV.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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