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Chronic Hepatitis B Virus Infection: Biological Parameters in Patients Treated with Tenofovir Disoproxil Fumarate

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Abstract

Chronic hepatitis B causes a liver disease characterized by inflammation of the liver parenchyma. The aim of this study was to investigate the evolution of biological parameters in patients treated with Tenofovir for chronic B infection at the Commune V referral health center in Bamako. We obtained a prevalence of 14.15%. The most represented age group was 31 - 40 years, with 36.8%. The sex ratio was 1.44 in favour of men. Viral load was undetectable after 18 months of treatment in 25 patients (42.37%). Tenofovir, the 1st-line drug in Mali, is effective on the biological parameters monitored in patients.

Keywords

Viral Hepatitis B, Tenofovir, Biological Parameters

1. Introduction

Viral hepatitis B is a liver disease characterized by inflammation of the liver parenchyma secondary to infection with the hepatitis B virus [1]. An estimated 296 million people have chronic hepatitis B, of whom 221 million live in low- and middle-income countries. Without intervention, deaths from HBV are expected to peak at 1.14 million by 2035 [2]. In 2019, approximately 1.5 million people newly acquired chronic HBV infection; of these, 990,000 (66%) were in the AFR [3]. Infection with the hepatitis B virus (HBV) is a major public health problem worldwide particularly in areas of high prevalence such as sub-Saharan Africa.

It's due to its progressive complications (cirrhosis and hepatocellular carcinoma), the frequency of comorbidities (notably HIV infection), and management difficulties in the particular context of our country's limited financial resources [4]. In Mali, a study carried out in the district of Bamako and the commune of Kati in the general population and among blood donors reported a prevalence of HBsAg carriage of 13.97% in 2019 [5]. The treatment of chronic viral hepatitis B is based on two classes of drugs: interferon alpha and nucleos(t)id analogues. The aim of treating chronic hepatitis B is to improve patient survival and quality of life by preventing the disease from progressing to cirrhosis or hepatocellular carcinoma, or even death [6]. Of these, Tenofovir, the most widely used molecule in Mali, can have adverse effects. In addition to regular clinical monitoring, follow-up of patients treated with this molecule requires biological monitoring. The aim of this study was to investigate the evolution of biological parameters in patients treated with Tenofovir for chronic B infection at the reference health center in Commune V, Bamako.

2. Material and Methods

This was a prospective descriptive and analytical study, running from March 2022 to June 2023. It took place in the hepato-gastroenterology unit of the Centre de Santé de Référence de la commune V de Bamako. All chronic hepatitis B patients on Tenofovir, with a complete follow-up medical record, were included. Criteria for initiation on Tenofovir were based on EASL 2017 recommendations:

- In patients with HBV DNA > 2000 IU/ml and significant histological lesions (>A1 or >F1) regardless of ALT level.
- In patients with HBV DNA > 20,000 IU/ml and ALT>2N without the need for biopsy.
- In cirrhotic patients with detectable HBV DNA, whatever its value, and whatever the transaminase value.

Data collection was based on patients' medical records. A survey form was drawn up and included the following parameters: sociodemographic characteristics, date of treatment initiation, results of biological parameters at initiation and follow-up: transaminases (AST and ALT), creatinine levels and clearance, phosphoremia, 24-hour proteinuria, viral load, HBs antigenemia, alfa fetoprotein, PT, fibro test, HBsAb, HBeAg, hemoglobin (Hb), white blood cells (WBC) and platelets. The Chi^2 test was used to compare data. Differences of less than 0.05 were considered statistically significant. Data entry and analysis were performed using SPSS version 25 software.

Each file was identified by an anonymous number. Data collected on participants was kept confidential.

3. Results

Out of 749 consultations, 106 patients were chronic carriers of the hepatitis B virus, representing a prevalence of 14.15%. The average age of patients was 38.02

± 1.21 years, with extremes of 12 and 75 years. The most represented age group was 31 - 40 with 36.8% as shown in Figure 1.

In our study, we recorded 63 men (59.4%) for 43 women (40.6%), *i.e.* a sex ratio of 1.44 as shown in Figure 2. At initiation, creatinine and ALT levels were normal. Viral load was above 2000 IU/ml in 73.68% of cases at initiation.

As shown in Table 1, creatinine levels were elevated in 5 patients (6.02%) at 6 months and in 3 patients (4.35%) at 12 months. It was normal in all patients at 18 months. ALT levels were normal at the start of treatment in 64 patients (60.38%). This proportion was 76 (91.57%) patients at M6; 64 (92.75%) patients at M12 and 60/60 (100%) patients at M18.Viral load was above 2000 IU/ml in 64.86%, 26.09% and 10.17% of cases at M6, M12 and M18 respectively. Viral load was undetectable after six (6) months of treatment in 5 patients (6.76%).

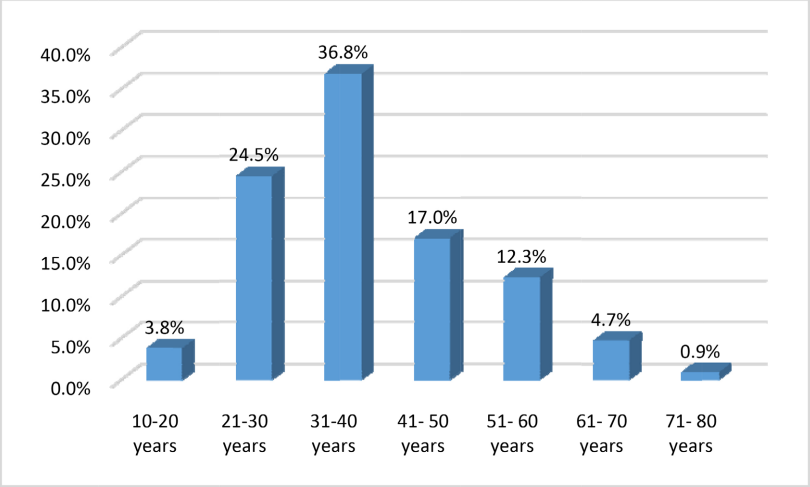

Figure 1. Age range.

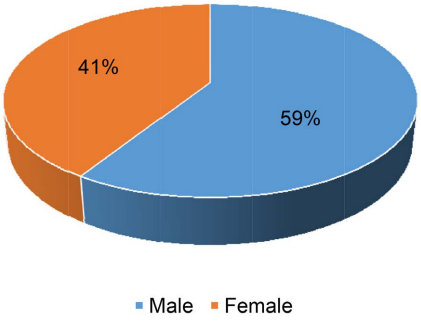

Figure 2. Gender of patients.

Table 1. Biological parameters.

Biological parameters	M6	M12	M18
High creatinine levels	5 (6.02%)	3 (4.35%)	0
ALT ≥ 40 UI/L	7 (8.43%)	5 (7.25%)	0
Viral load ≥ 2000 UI	48 (64.86%)	18 (26.09%)	6 (10.17%)

After 12 months on Tenofovir, 13 patients (18.84%) had an undetectable viral load, and after 18 months, 25 patients (42.37%) had an undetectable viral load.

4. Comments and Discussion

Our study consisted in evaluating the evolution of biological parameters in 106 patients treated with Tenofovir at the reference health center in Commune V, Bamako, for chronic hepatitis B virus infection on Tenofovir. We considered a follow-up period of 18 months for patients on treatment.

The mean age of patients was 38.02 ± 1.21 years, with extremes of 12 and 75 years. The most represented age group was 31 - 40, with 36.8%. Our mean age is close to that of Katilé *et al*., who were 36.9 ± 10.8 years in Mali [7], and Dembélé with 35.11 ± 11.12 years in Mali [8]. However, Elaboudi in Morocco in 2015 [9], in his study of chronic B virus carriers on entecavir, and Anzouan-Kacou *et al*. in 2016 in Côte d'Ivoire [10], whose chronic hepatopathy patients were on tenofovir, found mean ages higher than ours.

In their studies, they reported ages of 43 and 40.4 respectively. These differences could be explained by the fact that, in their studies, some patients were already at the cirrhosis stage, which is a late complication occurring several years later in the course of the disease. This explanation was supported by the 2015 study by Kim *et al*. who found that patients without cirrhosis were younger than cirrhotic patients, with a mean age of 38.4 and 45.2 years [11].

Males accounted for 59.4% of those surveyed, with a ratio of 1.44 in favor of males. This result is similar to the study by Dembélé R. [8] in Mali and Ankouane *et al*. [12] in Cameroon, who respectively obtained a male predominance of 72.8% (n = 195) and 74.6% (n = 290). This male predominance could be explained by men's greater accessibility to the healthcare system and the national socio-economic context.

Hepatic cytolysis represented by elevated transaminaseswas present in over a quarter of our patients (36%). The same observation was made by Elaboudi in 2015 in Morocco. Indeed, 27.5% of his patients had cytolysis as part of the pre-therapeutic workup [9]. Katilé *et al*., in 2019 in Mali, in their study found rather 48.6% of men and 83.7% of women who presented cytolysis during screening and before starting treatment [7].

With regard to pre-treatment assessment of renal function, creatinine levels were measured in 106 patients (100%). It came back elevated in one (1) of our patients, *i.e*. 0.94%.This was a case of functional renal failure whose renal function returned to normal after rehydration. Normal renal function was a prerequisite for starting patients on Tenofovir, as the molecule is already nephrotoxic.

Before starting treatment, B viral DNA quantification was carried out in 89.62% of our patients (n = 95). Of the patients who underwent the test, 73.68% had a viral load of over 2000 IU/ml. In Elaboudi's study [9], the percentage of patients with a viral load of over 2000 IU/ml was higher than ours (80%). In the Katilé study, only 30% of patients had this level of B virus viral load [7]. In the Anzouan-kacou study, patients took longer to achieve viral clearance and an

undetectable viral load, given the very high pre-treatment levels [10]. After six (6) months of treatment, 5 patients out of 74 (6.76%) had an undetectable viral load. After 12 months on Tenofovir, 13 out of 69 patients had an undetectable viral load (18.84%). Sombié *et al*. in 2015, [13] in Burkina Faso, in their study on the treatment of chronic hepatitis B with tenofovir, found an undetectability of HBV-DNA of 89.6% at 5 years, which was higher than ours.

This difference may be explained by the earlier time to viral load control in our study (6 months and one year). After 18 months on tenofovir, 25 out of 59 patients (42.37%) had an undetectable viral load.

Biochemical response, the second criterion for assessing therapeutic efficacy with tenofovir, was assessed through changes in transaminase levels in our patients. Thus, 64 out of 106 patients (60.38%) had a normal ALAT level at the start of treatment. This proportion was 76/83 (91.57%) patients at M6; 64/69 (92.75%) patients at M12 and 60/60 (100%) patients at M18. In Sombié *et al*., 2010, [14] ALT normalized to 71.8% during treatment. In another study, it was 87% [13]. The literature reports an ALT normalization rate of around 66 to 76% on tenofovir or lamivudine [13].

Tolerance to tenofovir treatment was assessed by monitoring creatinine levels. It returned to normal in 93.98%, 95.65% and 100% of cases at M6, M12 and M18 respectively. Patients who developed changes in renal function during treatment underwent further renal function tests.Overall, tolerance to tenofovir was good in our study. The same observation has been made in other studies using this same molecule in the treatment of chronic viral hepatitis B [14]. These include Diallo *et al*. in Senegal in 2018 [15], Anzouan-kacou *et al*. in Côte d'Ivoire in 2016 [10] and Sombié *et al*. in Burkina Faso [13].

The main limitation of our study was that the tests were carried out in different laboratories, using different techniques and methods. We also noted a lack of follow-up tests, in particular fibrotest to assess liver fibrosis, 24-hour proteinuria and phosphorus levels, which were not included in our study, given the small number of patients who were able to undergo these tests.

5. Conclusion

Chronic hepatitis B infection remains a major public health problem in Africa. Most of the patients treated in our department were young and predominantly male. Tenofovir, the 1st-line drug in Mali, is effective on the biological parameters monitored in patients.

Conflicts of Interest

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

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