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Clinico-Biological Evaluation of Patients with Chronic Viral Hepatitis B on Tenofovir

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Abstract: Introduction: Viral hepatitis B is a major public health problem worldwide. The aim of this study was to evaluate the clinico-biological parameters in patients with chronic hepatitis B on Tenofovir. Patients and method: This was a cross-sectional study with retrospective data collection from April 1, 2019 to March 31, 2021, i.e. two years. Patients aged at least 15 years, regardless of sex, with a complete follow-up file were included. Results: A total of 920 files were evaluated, of which 145 met the inclusion criteria, i.e. a frequency of 15.76%. A male predominance was found (sex ratio 2.62). The average age was 33.24 years with extremes of 17 and 63 years. Students were more represented (36.6%). Incidental discovery was the most frequent mode (29.7%). Asthenia was the most frequent clinical manifestation (28.27%). Cytolysis was found in 82.76% of cases at the start of treatment. Creatinine levels were normal in most cases. HBV DNA was > 2000 IU/ml in 92.41% of cases. Abdominal ultrasound was normal in 51.25% of cases. Biological fibrosis scores (APRI and FIB-4) were used in almost one third of patients. The evolution was marked by a virological response of 82.35% at the 12th month and a normalization of transaminases in 91.6% of cases. Conclusion: Viral hepatitis B, a public health problem, is frequent among young people in our context. Tenofovir, effective, allows to obtain a significant virological response and a normalization of transaminases.

Keywords: Chronic Hepatitis B, Tenofovir, HBV-DNA, Transaminases, Patients, Chad

1. Introduction

Viral hepatitis B occupies a major place in terms of public health worldwide. Indeed, the number of people with chronic hepatitis B virus infection according to the WHO was estimated at 257 million or 3.5% of the population in 2015. This chronic form is responsible for 887,000 deaths from cirrhosis or primary liver cancer. Most people infected with hepatitis viruses do not know their status. However, they are at high risk of developing severe chronic liver disease [1].

The prevalence of hepatitis is variable around the world. It is low in the West. France is classified as a low endemic country for HBV, denoted by a prevalence of HBsAg of less than 2% [2].

In 2018, 3,843 cases of chronic hepatitis B were reported in Canada, corresponding to a national rate of 10.6 per 100,000 people [3].

In the Maghreb, prevalences of (1 to 2.35%) were reported in Morocco and (4 to 7%) in Tunisia [4].

Sub-Saharan Africa is located in a zone of high endemicity where the prevalence is > 8% with 65 million chronic carriers and 56,000 deaths per year [5]. In West Africa prevalences of 11% and 11.1% were reported in 2018 in Senegal and Mali [6, 7].

In Chad, the prevalence of HBV is estimated at 16.1% classifying Chad as a high endemic area [8].

Tenofovir is recognized today as an effective molecule at the global level because it allows to considerably reduce the

viral load and even eliminate the virus. Despite the high prevalence of HBV in Chad, few studies have been carried out in our knowledge on the clinical-biological parameters; hence the interest of this work which aimed to evaluate the clinical and biological parameters of HBV-infected patients on tenofovir.

2. Patients and Method

The Gastroenterology/Internal Medicine Department of the CHU-RN served as a setting. This was a cross-sectional study with retrospective data collection from April 1, 2019 to March 31, 2021, i.e. two years.

Our study population consisted of patients with chronic viral hepatitis B followed in the Gastroenterology Department. Patients aged at least 15 years without distinction of sex, treated with Tenofovir and having a complete follow-up file as well as decompensated or not cirrhotics were included. Patients in the FPC stage were not included in the study. Fibrosis was assessed by the APRI score and FIB-4 in the absence of Fibrotest. It was considered minimal for a score F0-F1 and moderate for a score ≥ F2. A score of F4 was considered severe fibrosis or even cirrhosis.

Analysis of Data

Data were entered and analyzed on the following software: SPSS 18.0, Excel, Word. The Chi-square test was used with significance level $p<0.05$.

3. Results

One hundred and forty-five files were included out of 920 exploited, i.e. 15.76%.

Socio-demographic characteristics of patients.

In this series, men were in the majority (72.4%). The sex ratio (M/F) was 2.62. The most represented age group was 20-29 years (37.9%) with a mean age of 33.24 years. Students/pupils were the most represented in this study (36.6%) followed by civil servants (31.1%).

Clinically, incidental discovery of HBV accounted for 29.7% of cases. Asthenia was the most common clinical manifestation (28.27%).

On the paraclinical level, all patients put on treatment had had transaminases, creatininemia and viral load (HBV DNA). Cytolysis was found in more than 80% of cases before the start of treatment. Creatinine levels were normal in 120 patients (82.8%). There were 91 patients with a viral load >20,000 IU/mL, i.e. 62.76%. The mean viral load was 99254481.6 IU/mL with extremes ranging from 105 to 4881997971 IU/Ml.

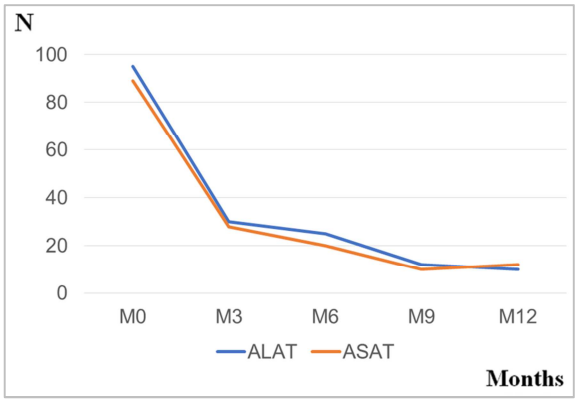

Figure 1. *Changes in transaminases during treatment.*

Table 1. *Summary of virological and biological assessments.*

	Transaminases (N=145)		Créatininémie (N=145)		ADN-VHB (N=145)	
	n	%	n	%	n	%
M0	145	100	145	100	145	100
M3	49	33,79	75	51,72	0	0
M6	111	76,55	96	66,2	90	62,06
M9	79	54,48	0	0	0	0
M12	108	63,44	80	55,17	85	58,62

Abdominal ultrasound performed in 80 patients was normal in 41 (51.25%). The evaluation of fibrosis was done by the APRI score and the FIB-4 in the absence of fibrotest. According to the APRI score 18 patients in this series had fibrosis ≥ F2 including 9 (moderate fibrosis) and 9 (severe fibrosis).

Using the FIB-4 score in this study population, 14 patients were classified as having fibrosis ≥ F2. The AUROC value of the FIB-4 score (0.728) was slightly higher than that of the APRI score (0.627).

Evolution of biological parameters under Tenofovir treatment At initiation, 62.76% of patients had a viral load >20,000 IU/mL. During the course of treatment, a considerable reduction was observed (HBV-DNA < 10 IU/mL) in more than 50% of cases.

Biochemical efficacy was assessed by the evolution of transaminases. Before the start of treatment, they were normal in 17.24% of cases. After 3 months of treatment, this rate increased to 85.71% and 91.6% at one year.

4. Discussion

Out of a total of 920 exploited patient records, 145 were included, i.e. a frequency of 15.76%. This result is higher than those of Salamata et al. in 2018 in Senegal (9.12%) who had put 55 patients out of 603 on treatment [6]. This difference could be explained by the criteria for putting patients on treatment on the one hand and on the other by the criteria for recruiting patients. It should also be remembered that in the management of chronic viral hepatitis B, not all positive cases are necessarily eligible for treatment.

Sociodemographic aspects

In this series, men are in the majority (72.4%). The M/F sex ratio was 2.62. This result is similar to those of Moussa et al. in 2022 in Chad and Touré et al. in 2021 in Senegal [9, 10]. The same finding was also made by Katilé et al. in Mali in 2018 who found a sex ratio (M/F) of 1.67 [7].

This male predominance is consistent with the literature and would be explained by the theory of low HBsAg clearance in men [11].

The most represented age group is 20-29 years with an average age of 33.24 years, thus relatively young. This relatively young age was also reported by Salamata et al [6] in 2018 in Senegal who found an average age of 33 years. In China, Guangqin et al [12], had found an average age of 39.7 years. This average age although higher than our series is still young. The youth of the study population in this series is in line with the reality of the country, because at the national level the Chadian population is young for the most part [13]. In fact, in Africa and Asia, it has been shown that infection occurs most often in early childhood [11]. The young average age found in this study and that of Guangqin confirms this hypothesis [12].

On the socio-professional level, students are the most represented (36.6%). This high representation of students could be explained on the one hand by the fact that this population is the most sexually active and on the other hand by the fact that the high level of education facilitates access to information. The second category of population represented is that of civil servants in more than 30% of the cases, thus reinforcing the theory that the high level of education facilitates access to information.

Clinically, the circumstances of discovery of chronic Hepatitis B carriage were incidental in (29.7%).

This result is similar to those of Salamata et al (26.2%) [6].

This incidental finding reflects the silent nature of chronic hepatitis. Asthenia was the most common clinical manifestation (28.27%).

This result is in accordance with the literature, according to which asthenia is generally the main symptom in chronic hepatitis [2, 14].

Complementary examinations are essential for the decision to start treatment and the follow-up of chronic hepatitis B carriers. The cost of these examinations, which must be paid for by the patient, is often beyond the reach of the population in our developing country context. However, at the initiation of treatment, all patients had transaminase tests. In 82.76% of cases, cytolysis was found. The level of ALT activity is one of the criteria for therapeutic decisions according to the WHO. Indeed, the development of fibrosis is slow in patients with persistently normal ALT activity, compared to patients with increased ALT activity [15]. Renal function was also assessed in 100% of our patients before starting Tenofovir therapy. Thus, it was normal in 82.8% of cases. Renal function plays a crucial role in the decision to start treatment.

The HBV-DNA is a key test for the decision to start treatment and was also performed in all patients before the start of antiviral treatment. It is > 2000 IU/ml in 92.41% of cases.

However, as far as imaging is concerned, abdominal ultrasound performed in 80 patients was normal in 41 patients (51.25%). In Senegal, imaging was normalized in 42.71% of cases [6].

The Fibrotest, which is the reference test to evaluate fibrosis, allowed us to classify patients into three stages: minimal, advanced and severe.

Of 44 patients (35.2%) in our study population who had the opportunity to perform this test, 38 had significant fibrosis, while many did not know their fibrosis status due to financial difficulties. As an alternative to Fibrotest, the APRI score allowed us to find eighteen (18) patients with significant F2, F3 fibrosis. Among these 18 patients, 9 had severe fibrosis or even. Among these 18 patients, 9 had severe fibrosis or even cirrhosis. Twenty-six (26) or 59.1% had no fibrosis.

The analysis between APRI scores and the reference test which is the Fibrotest had shown a good diagnostic performance; indeed the AUROC was 0.627 (CI=95%: 0.405-0.849). This result is comparable to those of Touré et al [10] in Senegal in 2017 who had found an AUROC 0.650 (CI95%: 0.594-0.706). The cross-tabulation between the FIB-4 score, another means of assessing fibrosis, and the Fibrotest also allowed us to find a good diagnostic performance but slightly higher than that of APRI because the AUROC is 0.728 (CI=95%: 0.569-0.887). This result is superior to those of Touré et al [10] in Senegal in 2017 who had obtained an AUROC of 0.650.

Indeed, several studies have shown the usefulness of APRI and FIB-4 scores in the assessment of HBV-related liver fibrosis [14]. These less expensive and accessible scores should be popularized in resource-limited countries like ours.

The AUROC value of the FIB-4 score, closer to 1, is better indicated for the evaluation of liver fibrosis.

Therapeutically, the molecule used in this study is Tenofovir. Indeed, Tenofovir is currently the molecule recommended by the WHO and other learned societies for the treatment of hepatitis B. Studies have shown its efficacy compared to Entecavir [6, 16]. The efficacy of Tenofovir treatment in this series was evaluated by two criteria, namely virological response and biochemical response. The virological response is materialized by an undetectable viral load (< 10 IU/ml).

At six months of treatment, 52.22% of our patients had an undetectable viral load and at M12 a virological response of 82.35% was found.

Our result is comparable to the Senegalese study which found a virological response of 85% after 120 weeks of treatment [6].

The authors are unanimous as to the efficacy of Tenofovir in the management of chronic hepatitis B, due to its strong genetic barrier, its dual activity on HBV and HIV and its affordability compared to other molecules [16, 17].

The biochemical response, which is the second criterion for evaluating therapeutic efficacy with Tenofovir, was assessed through the evolution of transaminase values in our patients. At initiation, transaminases were normal in 17.24%.

This rate increased to 85.71% after 3 months of treatment (M3), and 91.6% after 12 months (M12). The biochemical response was 100% after 120 weeks of treatment in Senegal [6]. However, in the series by Sombié et al. in Burkina Faso, ALT normalized to 71.8% during treatment [17]. In another study, it was 87% [18]. The evolution of tenofovir was marked by clinical improvement in all cases.

5. Conclusion

Chronic hepatitis B virus infection remains a major public health problem worldwide. In Africa, the situation is dramatic due to the fact that the disease affects much more young people. Tenofovir is certainly recognized today as an effective molecule for the treatment of HBV by considerably reducing the viral load. However, the decision to initiate it requires additional tests, the cost of which is often not accessible to a large part of our population with limited resources. In patients currently with a viral load of 10 IU/mL and having eliminated HBsAg, the search for anti-HBsAb is necessary.

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