Viral Hepatitis and Incidence of Hepatotoxicity Cases among Patients Infected with HIV under HAART at the Bertoua Day Hospital, Cameroon

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Abstract

The present study was aimed at optimizing the biomedical handling of the hepatotoxicity caused by the HAART accentuated in case of coinfection with the hepatitis viruses among the patients infected with the human immunodeficiency virus (HIV). We performed a prospective transversal survey from 18th March 2014 to 30th October 2014, on patients infected with HIV followed at the Bertoua day hospital with the general objective to evaluate the impact of the viral coinfection (HIV-Hepatitis Virus) on the incidence of hepatotoxicity cases caused by the HAART. We included in our survey, all HIV positive patients, eligible to the antiretroviral treatment, registered in our survey place for the follow-up of this treatment and having accepted to participate in the survey. We excluded in our survey, all patients who were not registered at the Bertoua day hospital for the follow-up of the antiretroviral treatment, all patients presenting a hepatic affection other that the infection with hepatitis virus, all patients having a bad observance of the antiretroviral treatment. We made the screening of the hepatitis B and C infections with the help of two tests: a fast screening test with the small strips to hepatitis B and C (DIASPOT type) and a confirmation test with the fast diagnosis cassettes (BIOLINE type). We analyzed the socio-demographic parameters (Age and Sex), Biological parameters (HIV, HCV, HBV, Transaminases) and the therapeutic parameters (therapeutic protocol). Two hundred and sixty one (261) HIV positive patients have been included in our survey, among which we counted 197 women and 64 men with a sex ratio of 0.32 in favor of women. We noted the presence of 53 coinfection cases with HIV-HBV (20.3%) and 30 coinfection cases with HIV-HCV (11.5%), that is a total of 83 coinfection cases (31.8%). The prevalence’s of hepatotoxicity cases among the coinfected and monoinfected patients were 85.54% and 5.05% respectively and their incidence rates were also of 22.6% and 6.1% respectively. The time limit of the hepatotoxicity appearance among our patients, varied from 4 to 6 months.

Keywords: Hepatotoxicity; HIV; Hepatitis C; Hepatitis B; HAART.
1. Introduction

The infections to viral hepatitises B and C represent a major problem of public health all over the world [1] and are considered since May 2010, like the fourth priority of public health to the world scale by the World Health Organization (WHO), after the HIV infection, the malaria and the tuberculosis [2]. They are the most often asymptomatic to the acute stage as to the chronic stage until an advanced stage of the hepatic illness [3]. The chronic infection to viral hepatitis B (HBV) is estimated to 350 million people in the world and 500,000 people die every year following to this infection. The contamination with the HBV represents a major risk for the appearance of the cirrhotic disease of the liver and the hepato cellular carcinoma which is the biggest reason of morbidity and cancerous mortality in the world [4]. Viral hepatitis C (HVC) is responsible to chronic infection among more of 80% of contaminated people and represent also as the HBV, a major reason of the stern fibroses of the liver, the cirrhosises and the hepato cellular carcinomas. It comes out approximately that 170 million of people are infected with HVC in the world with more of three millions of new infection cases occurring every year [4, 5]. The Sub-Saharan Africa is a zone of strong prevalence of the HBV (15%) and HCV (7%) and remains one of the regions seriously touched by the HIV with close to an adult out of 20 living people with HIV [4-6]. These hepatic viruses share a same transmission channel that the HIV [2]. Therefore it finds itself a big risk of coinfections with HIV and HBV or HVC [7]. The studies show that 9.8% of living people with HIV in Cameroon arecoinfected with the HBV [8] and 2.5% of adults living with HIV are coinfected with the HCV [1]. This coinfection increases the hepatotoxicity risk of the HAART [9] and the hepatic lesions which result from it are a major reason of mortality and morbidity among the patients infected with HIV [10, 11]. In front of these deleterious effects caused by this hepatotoxicity on the handling of the HIV infection, we have judge necessary and appropriate to make this survey with the aim to optimize the biomedical handling of the hepatotoxicity caused by the HAART accentuated in case of coinfection with the hepatitis viruses among the patients infected HIV followed at the Betoua day hospital. To reach at this aim, we have focused our general objective to evaluate the impact of the viral coinfection on the incidence of hepatotoxicity cases among patients infected with HIV under HAART. Our specific objectives were to make an assessment of knowledge of our patients on the infections to hepatitis virus B and C and to determine the prevalence of these infections among these patients in order to minimize the number of linked death to the hepatotoxicity of the HAART accentuated by these viral coinfections.

2. Materials and Methods

We performed a prospective transversal survey from 18th March 2014 to 30th October 2014, on patients infected with HIV followed at the Bertoua day hospital with the general objective to evaluate the impact of the viral coinfection (HIV-Hepatitis Virus) on the incidence of hepatotoxicity cases caused by the HAART. We included in our survey, all HIV positive patients, eligible to the antiretroviral treatment, registered in our survey place for the follow-up of this treatment and having accepted to participate in the survey. We excluded in our survey, all patients who were not registered at the Bertoua day hospital for the follow-up of the antiretroviral treatment, all patients presenting a hepatic affection other that the infection to hepatitis virus, all patients having a bad observance of the antiretroviral treatment. We made the screening of the hepatitis B and C infections with the help of two tests: a fast screening test with the small strips to hepatitis B and C (DLIAPOT type) and a confirmation test with the fast diagnosis cassettes (BIOLINE type). We analyzed the socio-demographic parameters (Age and Sex), Biological parameters (HIV, HCV, HBV, Transaminases) and the therapeutic parameters (therapeutic protocol). The prescribed therapies in our study were: 2 INTI + Efavirenz (52.8%); 2 INTI + Nevirapine (47.19%); 2 INTI+ LPV/r (46.62%). Hepatotoxicity, defined by the increase level of transaminases was classified according to the criteria’s set by the AIDS Clinical Trials Group (ACTG) relative to the upper limit of the normal (ULN) [15-16] as follows: grade 1 (1.25–2.5 × ULN); grade 2 (2.51–5.0 × ULN); grade 3 (5.1–10 × ULN); and grade 4 (>10 × ULN). The patients have been informed verbally about the aim of the survey and they signed an informed consent. The gotten results have been analyzed with the help of the Excel software 2010 and R software version-2.13.0. We used the chi-square test to compare the percentages and the Accepted significance was fixed to 5%.

3. Results

Two hundred and sixty one (261) HIV Patients have been included in our survey, among which we counted 197 women and 64 men with a sex ratio of 0.32 in favor of women. We noted the presence of 53 coinfection cases with HIV-HBV (20.3%) and 30 coinfection cases with HIV-HCV (11.5%), that is a total of 83 coinfection cases (31.8%).

3.1 Prevalence of Hepatitis B and C Infections According to the Age Groups of HIV Patients

The average age of coinfected patients was 38.93 years ± 8.10 with ages ranging between 15 to 65 years. The prevalences of hepatitis B and C were more raised in the age group of 20 to 29 years with 96.2% and 98.1% respectively. The percentage differences were not statistically meaningful with P values of 0.29 for the hepatitis B and 0.21 for the hepatitis C (Figure 1).
Figure 1: Graphical representation showing the prevalence of hepatitis B and C infections according to the age groups of HIV patients.

3.2 Distribution of Coinfected Patients According to the Different Sexes

The sex ratio of coinfected patients was 0.45 in favor of women. The women represented the biggest part of coinfected patients with 57 (68.97%) cases out of the 83 cases known. The coinfection cases with HIV-HVB were also the most represented among the women with a rate of 59.64% compared to coinfection cases with HIV-HCV which presented a rate of 40.36% (Figure 2). The general prevalence of coinfection cases among the female sex was 21.9% with 13% for the coinfection cases with HIV-HVB and 8.9% for the coinfection cases with HIV-HCV. The percentage differences were not statistically meaningful with P-values of 0.16 and 0.59 for the coinfection cases with HIV-HVB and HIV-HCV respectively.

Figure 2: Graphical representation showing the coinfection patients’ distribution according to different sexes.

3.3 Transaminase Levels before the HAART According to the Type of HIV Patients

Before the HAART, only the coinfected HIV patients presented an increase level of transaminases (Table 1).

<table>
<thead>
<tr>
<th>HIV Patients</th>
<th>Numbers</th>
<th>Transaminases</th>
<th>ALT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>AST N 1.5XN 2XN &gt;2XN</td>
<td>N 1.5XN 2XN &gt;2XN</td>
</tr>
<tr>
<td>Coinfected</td>
<td>83(31.80%)</td>
<td>0 83(31.80%) 0 0 0</td>
<td>83(31.80%) 0 0</td>
</tr>
<tr>
<td>Monoinfected</td>
<td>178(68.19%)</td>
<td>178(68.19%) 0 0 0 0</td>
<td>178(68.19%) 0 0</td>
</tr>
</tbody>
</table>

Table 1: Showing the type’s distribution of HIV patients according to the transaminase levels before the HAART.

The percentages difference was statistically meaningful with a P-value=15.74x10^{-5}.
3.4 Transaminase Levels on the Third Month of the HAART According to the Type of HIV Patients

On the 3rd month of the HAART 74 (89.15%) of coinfected HIV patients presented an increase level of transaminases equivalent to twice the normal, while only 19 (10.67%) of monoinfected HIV patients, presented a transaminase level equivalent to 1.5 times the normal (Table 2).

Table 2: Showing the type’s distribution of HIV patients according to the transaminase levels on the third month of the HAART.

<table>
<thead>
<tr>
<th>HIV Patients</th>
<th>Numbers</th>
<th>Transaminases</th>
<th></th>
<th></th>
<th></th>
<th>ALT</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>AST</td>
<td>1.5XN</td>
<td>2XN</td>
<td>&gt;2XN</td>
<td>N</td>
<td>1.5XN</td>
<td>2XN</td>
</tr>
<tr>
<td>Coinfected</td>
<td>83(31.80%)</td>
<td>0</td>
<td>1(1.2%)</td>
<td>74(89.15%)</td>
<td>8(9.63%)</td>
<td>0</td>
<td>1(1.2%)</td>
<td>74(89.15%)</td>
</tr>
<tr>
<td>Monoinfected</td>
<td>178(68.19%)</td>
<td>159(89.32%)</td>
<td>19(10.67%)</td>
<td>0</td>
<td>0</td>
<td>159(89.32%)</td>
<td>19(10.67%)</td>
<td>0</td>
</tr>
</tbody>
</table>

The percentages difference was statistically meaningful with a P.value=15.74x10^{-5}.

3.5 Transaminase Levels after the Sixth Month of the HAART According to the Type of HIV Patients (After Modification of the Initial Therapeutic Protocol)

On the sixth month of treatment, 38.55% of coinfected HIV patients knew an increase level of transaminases superior to twice the normal in spite the modification of the initial therapeutic protocol, while 26.4% of monoinfected HIV patients recovered the normal transaminases (Table3).

Table 3: Showing the type’s distribution of HIV patients according to the Transaminase levels on the sixth month of the HAART (After modification of the initial therapeutic protocol).

<table>
<thead>
<tr>
<th>HIV Patients</th>
<th>Numbers</th>
<th>Transaminases</th>
<th></th>
<th></th>
<th></th>
<th>ALT</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>AST</td>
<td>1.5XN</td>
<td>2XN</td>
<td>&gt;2XN</td>
<td>N</td>
<td>1.5XN</td>
<td>2XN</td>
</tr>
<tr>
<td>Coinfected</td>
<td>83(31.80%)</td>
<td>0</td>
<td>0</td>
<td>51(61.44%)</td>
<td>32(38.55%)</td>
<td>0</td>
<td>0</td>
<td>51(61.44%)</td>
</tr>
<tr>
<td>Monoinfected</td>
<td>178(68.19%)</td>
<td>47(26.4%)</td>
<td>131(73.59%)</td>
<td>0</td>
<td>0</td>
<td>47(26.4%)</td>
<td>131(73.59%)</td>
<td>0</td>
</tr>
</tbody>
</table>

The percentages difference was statistically meaningful with a P.value= 1.95 e^{-11}.

3.6 Type’s Distribution of HIV Patients According to the Grade of Hepatotoxicity after the Sixth Month of the HAART

We counted 71 (85.54%) of hepatotoxicity cases among the 83 coinfected HIV patients, with a incidence rate of 22.6%. the grade 1 and 2 represented 55.42% and 30.12% respectively, the grade 3 and 4 were absent(Table 4). The incidence rate of hepatotoxicity cases among the monoinfected HIV patients was 6.1%, with a prevalence of 5.05%.

Table 4: Showing the type’s distribution of HIV patients according to the hepatotoxicity grade after the sixth month of the HAART.

| HIV Patients | Numbers | Grade of Hepatotoxicity |          |          |          |          |          |
|--------------|---------|-------------------------|----------|----------|----------|----------|
|              |         | Grade 1                 | Grade 2  | Grade 3  | Grade 4  |          |          |
| Coinfected   | 83(31.80%) | 46(55.42%)             | 25(30.12%) | 0        | 0        |          |          |
| Monoinfected | 178(68.19%) | 9(5.05%)         | 0        | 0        | 0        |          |          |

The percentages difference was statistically meaningful with a P.value=1.95 e^{-11}.
3.7 Distribution of Hepatotoxicity Cases According to the Viral Coinfection Type (HIV-HBV and HIV-HCV)

We counted 58 (69.87%) of HIV-HBV coinfection cases against 13 (15.67%) of HIV-HCV coinfection cases among the 71 (85.54%) of hepatotoxicity cases (Table 5). The incidence rate of hepatotoxicity cases among these patients were 15.8% and 3.6% respectively for the coinfection cases with HIV-HBV and HIV-HCV.

Table 5: Showing the distribution of hepatotoxicity cases according to the viral coinfection type (HIV-HBV and HIV-HCV).

<table>
<thead>
<tr>
<th>Coinfection type</th>
<th>Numbers</th>
<th>Grade of Hepatotoxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Grade 1</td>
</tr>
<tr>
<td>HIV/HBV</td>
<td>58 (69.87%)</td>
<td>29 (34.93%)</td>
</tr>
<tr>
<td>HIV/HCV</td>
<td>13 (15.67%)</td>
<td>17 (20.49%)</td>
</tr>
<tr>
<td>Total</td>
<td>71 (85.54%)</td>
<td>46 (55.42%)</td>
</tr>
</tbody>
</table>

The percentages difference was statistically meaningful with a P.value=1.46 e^{-13}.

3.8 Knowledge Assessment of HIV Patients about the Viral Hepatitises B and C

The biggest part of our patients didn't have any knowledge about the transmission and prevention modes of hepatitises B and C (Table 6).

Table 6: Showing the distribution of patients according to their knowledge about the Viral Hepatitises B and C

<table>
<thead>
<tr>
<th>Patients Knowledge</th>
<th>Yes</th>
<th>No</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Numbers</td>
<td>%</td>
<td>Numbers</td>
</tr>
<tr>
<td>Hepatitis B and C</td>
<td>134</td>
<td>51.34</td>
<td>127</td>
</tr>
<tr>
<td>Transmission modes</td>
<td>78</td>
<td>29.89</td>
<td>183</td>
</tr>
<tr>
<td>Prevention modes</td>
<td>67</td>
<td>25.68</td>
<td>194</td>
</tr>
</tbody>
</table>

The percentages difference was not statistically meaningful with a P.value=0.2.

4. Discussion

The HIV infection aggravates the prognosis of the hepatic diseases caused by the HCV and HBV [12, 13]. Since the use of powerful antiretroviral associations in the HIV infection, the life of HIV patients stretched itself. The morbidity and mortality caused by HVB and HCV become from then essential factors to take in account in their handling [14]. Our survey returns 83 cases of viral coinfection, in a population of 261 people infected with HIV, under HAART, that is a prevalence of 31.8%. On the 83 coinfection cases, we noted the presence of 53 (20.3%) cases of HIV/HBV coinfection and 30 (11.5%) cases of HIV/HCV coinfection. The estimated prevalence of chronic hepatitis B in our survey population was raised, very superior to the one observed in the cohort European EuroSida which was of 8.7% [15] and also comparable to the one made on the population been born in sub-Saharan Africa which was of 10.8%, as well as of the one observed in these countries (9%) [16]. The estimated prevalence of the HCV infection was on the other hand very weak compared to those estimated in the ANRS-Vespa investigation (22%) [17] and National investigation (28%) in 2001 [18]. It is also weak compared to the results of the Germivic (24.5%) [19]. Nevertheless, these numbers corroborated with the general tendency of the infection caused by the hepatitis viruses which varies according to the studies between 20% and 90% [20 - 22]. This result can be justified by the fact that our survey takes place in a high endemic zone of the hepatitis B[21].The Academic College of Infectious and Tropical Illnesses advanced the numbers which confirm this high endemicity: 95% of people have some anti-HBSantibodies and 8% to 15% are carriers of chronic HBS antigens. This confirms the prevalence found in our survey population [23].

The average age was 38.93 years ± 8.10 with ages ranging between 15 to 65 years. The prevalences of hepatitises B and C were more raised in the age group of 20 to 29 years with 96.2% and 98.1% respectively. This relates to the general average age of living people with HIV under ARV treatment in Cameroon which varies between 25 years to 45 years. The coinfection with HIV-HBV or HIV-HCV touches this same age group. This situation is not different in several countries from Africa (South Africa, Zambia, Burundi, and Rwanda) where the average age also varies between 25 years to 45 years according to the report UNO/AIDS 2010 on the HIV in the world while in Europe, the average age is found around 40 years [24].

The sex ratio of HIV coinfected patients was 0.45 in favor of women, with a general prevalence of viral coinfection among the woman of 21.9% that is 13% for the HIV-HBV coinfection and 8.9% for the HIV-HCV coinfection. This result is similar to the one gotten by Jibrinet al. in his survey in Nigeria where the sex ratio was also of 1.06 in favor of women [25].
These results gotten in our survey, could justify itself by the fact that in Africa in general, more precisely in Cameroon the women represent the biggest fraction of the living people with HIV [21]. The follow-up of the antiretroviral therapy is more regular in women than in men, because of their natural physiology (pregnancy/hormonal contraception)[26], it is the reason they also represented the biggest part of our survey population. This result could also explain itself by the fact of their biological, social and economic vulnerability, which more predisposes them to these viral affections.

Before the intake of the HAART, only the HIV coinfected patients (31.80%) presented an increase level of transaminases equivalent to 1.5 times the normal compared to the group of HIV monoinfected patients (68.19%) which presented normal transaminases (P-value=1.574x10^{-5}) (Table 1). After the intake of the HAART, more precisely on the third month of this treatment, 74 (89.15%) of the HIV coinfected patients presented an increase level of transaminases equivalent to twice the normal, while 19 (10.67%) of HIV monoinfected patients, presented an increase level of transaminases equivalent to 1.5 times the normal (P-value=1.46 e^{-13}) (Table 2). This result has also been made by Antonello and al, in his survey entitled HAART and liver [27], After the sixth month of treatment, 38.55% of HIV coinfected patients knew an increase level of transaminases superior to twice the normal in spite of the initial therapeutic protocol modification, while 26.4% of HIV monoinfected patients recovered a normal level of transaminases (P-value=1.46 e^{-13}) (Table 5). The prevalence’s of hepatitises B and C, the biggest fraction of our survey population did not have any knowledge about the hepatitis viruses’ existence, as well as about the transmission and prevention modes of diseases caused by these viruses.

5. Conclusion

Our survey in spite of its limits to know: difficulties of the regular follow-up of patients (loss of view, transfer, abandonment of ARV drugs, death); doubt on the intake of a drug and impossibility to identify the hepatotoxic drug among the other drugs taken by the patient under HAART, returns a prevalence of 31.8% of viral coinfection (HIV-Hepatitis Virus), with 20.3% for the HIV-HBV coinfection and 11.5% for the HIV-HCV coinfection. The prevalence’s of hepatitoses cases among the HIV coinfected and monoinfected patients were 85.54% and 5.05% respectively and their respective incidence rates were 22.6% and 6.1%. The time limit of the appearance of this hepatotoxicity among our HIV patients under HAART, varied from 4 to 6 months. With the increasing use of the antiviral drugs currently more and more available and the advent of new more efficient antiretroviral treatment, an another stage of our survey towards the world community of health would be to test the impact of the antiretroviral treatment on the future evolution of its undesirable effects (hepatic-toxicity, kidney-toxicity, Blood cells-toxicity and others...).
To prevent the important needs which are going to appear in the next decades, with the viral coinfection (VIH-Hepatitis Virus) which is a predisposing factor to the hepatotoxicity of the HAART, the Cameroonian authorities could undertake a better organization of the therapeutic handling of this coinfection with: Making financially affordable the screening and the treatment of the hepatitis Camong the living People with HIV; while also making vaccination campaigns against the hepatitis B; While educating, informing and communicating with the living people with HIV on the hepatitis B and C and while insisting on the transmission and prevention modes of these diseases; while Creating laboratories of molecular biology which are going to predict the linked hepatotoxicity risks of drugs by the pharmacogenomic/toxicogenomic techniques, which will detect the predisposing genes to the potentially hepatic lesions of drugs before the initiation of hepatotoxic treatments.

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References


