Full Length Research Paper

Evaluation of hepatotoxicity and nephrotoxicity in HIV patients on highly active anti-retroviral therapy

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A pilot longitudinal study was conducted for 3 months on HIV positive and AIDS patients on antiretroviral therapy, at a day care clinic at the Yaoundé Central Hospital, Cameroon, between April and July 2008. A total of 223 HIV patients were recruited following initiation and each patient benefited from pretherapeutic tests. Social-demographic, clinical and biological data were recorded for each subject and finally analyzed using standard statistical procedures. Out of the 223 subjects on highly active antiretroviral therapy (HAART) in the study, 153 were females (68.6%) and 70 were males (31.6%). The age group that was most represented was 30 - 39 (37.7%). The mean age of patients was 39.34 ± 11.31 years. At initiation the highest administered antiretroviral (ARV) regimen was Zidulam N (34.10%). For hepatotoxicity evaluation, with aspartate aminotransferase (ASAT) study, 5.8% of patients showed degree 1 and 1.3% of patients had degree 2 changes. In alanine amino transferase (ALAT), 3.70% of patients showed degree 1 and 3.95% degree 2 changes. The ARV regimen that was involved in most of these changes was Zidulam N. The assessment of nephrotoxicity in the creatinine study, only 2.24% of patient had degree 1 changes and no particular ARV regimen showed any creatinine changes. The Glomerullar Filtration Rate (GFR) for each ARV regimen showed no significance difference at p = 0.557. The ARV regimen administered to patients during the study did not really affect creatinine levels and hence showed no risk of toxicity to the kidneys.

Key words: Highly active antiretroviral therapy, hepatotoxicity, nephrotoxicity, human immuno virus, acquired immune deficiency syndrome, antiretroviral, regimen.

INTRODUCTION

Severe hepatotoxicity is defined as degree 3 and 4 changes in ASAT or ALAT levels during antiretroviral treatment (Penttila et al., 2007; Macroft et al., 2002; Hendrickson et al., 2009). In cases where ASAT and ALAT degrees were in discordant the higher of the two was used. Abnormal levels of liver enzymes are common among persons infected with human immunodeficiency virus (HIV) and may be caused by multiple factors, including medication toxicity and coinfection with hepatitis C virus (HCV) or hepatitis B virus (HBV) (Egger et al., 2002; Clark, 2008). Co-infection with HCV and HIV is common, occurring in 50 to 80% of individuals who acquired HIV through parenteral exposure. Chronic HBV infection occurs in 10 to 15% of persons infected with HIV in Cameroon (Egger et al., 2002; Jaime et al., 2006; Subbaraman et al., 2007; Myung et al., 2007).

Antiretroviral drugs – related Liver injury (ARLI) is a common cause of morbidity, mortality and treatment discontinuation in HIV-infected patients (Palella et al., 1998; WHO, 2006; Clark, 2008). Virtually every licensed antiretroviral medication has been associated with liver enzyme elevations, although certain drugs may cause

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Abbreviations: HAART, Highly active antiretroviral therapy; ARV, antiretroviral; ASAT, aspartate aminotransferase; ALAT, alanine amino transferase; GFR, glomerullar filtration rate; CHU, centre hospitalier universitaire; SGOT, serum glutamyl oxaloacetate transferase.
liver injury more frequently than others (Allston, 1993; Clark et al., 2002). Several major mechanisms of ARLI have been described. These include metabolic host-mediated injury, hypersensitivity reactions, mitochondrial toxicity and immune reconstitution phenomena (Ofotukun et al., 2007). The management of ARLI should be based on its clinical severity and underlying pathogenic mechanism (Nunez and Martin-Carbonero, 2006, Rodriguez et al., 2006). Liver function test abnormalities require careful interpretation on one hand, some drugs (e.g. nevirapine and less frequently efavirenz increase gamma-glutamyl transpeptidase serum levels). This laboratory result is often misinterpreted as a maker of liver damage, when isolated elevation of this enzyme actually reflects enzyme induction (Hogg et al., 2001; Aberg et al., 2004; Pitt et al., 2009). Hyperbilirubinaemia alone should not be equated with liver injury, as indirect hyperbilirubinaemia may be related to medications, such as indinavir or atazanavir, (Lesly et al., 2006; Wilkin and Gulick, 2008). This risk is increased in patients with underlying Gilbert’s syndrome, a genetic disorder (Gallant et al., 2005; Lesly et al., 2006; Jones and Nelson, 2007). On the other hand drug-induced liver injury that is associated with an elevated direct bilirubin and clinical jaundice has a poor clinical outcome. A cholestatic profile should only be considered when there is an associated increase in serum alkaline phosphatase as well as bilirubin (Manzardo et al., 2007). Elevated aminotransferases also need to be interpreted within their clinical context. For example, increased liver enzymes in a patient with chronic HBV infections do not necessarily imply drug injury but may reflect HBV-related hepatic flares, which often occur during the natural course of the disease (Mocroft et al., 2002; French et al., 2004; Corona and Rainmondi, 2007). With the widespread use of HAART and the availability of new antiretroviral medications, ARLI has gained prominent attention owing to its negative impact on clinical outcomes. Drug-associated hepatotoxicity also creates an economic burden on already strained medical budgets, since additional visits and hospital admissions are often required for appropriate patient care and management (Grinspoon and Carr, 2005; Huffman et al., 2007; Borgoyne and Tan, 2008). Furthermore antiretroviral drug discontinuation hampers maintenance of HIV suppression. Fortunately, the vast majority of episodes of ARLI are asymptomatic and most ALAT elevations resolve spontaneously as described for many other medications, probably through a process called adaptation (Cote et al., 2002; Yeni et al., 2004; Dixon and Cunningham, 2007), HAART is on the increase in Cameroon due to the State intervention in subsidizing the ARV, with the capital Yaoundé being the most important and strategic in the country, it receives a variety of facilities. It should be noted that because this center is among the most important and strategic in the country, it receives a variety of patients from all over the country. The subjects can hence be considered as being nationally represented.

HAART is implicated.

MATERIALS AND METHODS

Study location-Type

This was an analytic longitudinal study, with a laboratory based focus, where well documented HIV positive patients were recruited following initiation to antiretroviral at the day care hospital at the Yaoundé central Hospital, between April 2008 and July 2008. 223 HIV patients were recruited following initiation and each patient benefited from pretherapeutic tests, subsidized by the Cameroon Government. Social-demographic, clinical and biological data were recorded for each subject and finally analyzed using standard statistical procedures. This was a longitudinal study, analytic in nature where patients were followed up following the rhythm of clinical follow up of HIV patients eligible for treatment for a period of 1 month.

This study was carried out in Yaoundé, the capital city of the Republic of Cameroon. The HIV outpatient clinic of the Yaoundé central Hospital was used. This center was chosen because of its high patient attendance as well as logistic and administrative facilities. It should be noted that because this center is among the most important and strategic in the country, it receives a variety of patients from all over the country. The subjects can hence be considered as being nationally represented.

Sampling procedure

Consecutive sampling was used. A total of 240 HIV patients were recruited in the clinic during the study period (April 2008 to July 2008). 223 finally fulfilled the study criteria. The minimum acceptable sample size N was calculated using the Lorenz formula for two-tailed dichotomous variables:

\[ N = \frac{Z^2 \cdot \alpha \cdot PQ}{i^2} \]

Where, \( Z \) = \( Z \) the normal distribution value for which; \( \alpha = 0.05 \) (the standard normal deviation = 1.96); \( \alpha = 1 \) First order error or operational error; \( P \) = Relative prevalence or the proportion of subjects to attend to; \( Q = Complement of P \); \( i = \) precession (sampling error), level of error we want to accept (i = 0.05 for a 95% confidence interval).

Using \( Z_{1-\alpha/2} = 1.96 \), \( P = 17\% \) (prevalence for hepatotoxicity) = 0.05

\[ N = \frac{(196)^2 \times (0.17) \times (0.83)}{0.05^2} \equiv 217 \text{ subjects.} \]

Selection of patients

The inclusion criteria was to accept a well-documented HIV positive patients on ARV to participate in the study; the exclusion criteria was to avoid patients with hepatitis B and C infections, patients taking alcohol and tobacco, to reject HIV positive patients who were hypertensive and also HIV positive patients who were diabetic. Finally, the refusal of patients to participate in the study.

A subject was considered. HIV positive when they presented hypertension and also HIV positive patients who were diabetic. Finally, the refusal of patients to participate in the study.

Reagents used liver enzymes were provided by Hospitex.
diagnostics s.r.l and the mono-reagent procedure was used. For Alanine aspartate transaminase (ALAT) or serum glutamyl pyruvate transaminase (SGPT) measurements, the kinetics enzymatic method (Thomas et al., 1998) was used. The reference values for women were ≤ 31 IU/l and for men ≤ 35 IU/l. The JAFFE creatinine method was used (Thomas et al., 1998) and the reference values were; women 6 – 12 mg/l and Men 8 - 13mg/l.

Increments in the creatinine and transaminase values were classified following the scale of toxicity in Table 3, the WHO classification of secondary biological effects (degree 1, 2, 3 and 4 toxicities) (WHO, 2006).

The creatinine clearances were calculated using the Cock-Croft-Gault formula for glomerula filtration rate(Cock-Croft and Gault, 1978), which are classified below according to renal insufficiencies. Creatinine clearances were classified as follows: Severe Renal insufficiency 15 - 30 ml/min/ 1.7 m²; moderate Renal insufficiency 30 - 59 ml/min/ 1.7 m²; Mild Renal Insufficiency 60 - 89 ml/min/ 1.7 m²; normal > 90 ml/min/ 1.7m²

Collection of specimens

Blood samples were collected on vacutainer dry tubes using needles adapted for the vacutainer system. The tubes were well labeled as well as the Ependorf tubes that were used for transportation of serum to the CHU Biochemistry laboratory.

Venous Blood was collected and the blood spun in a centrifuge to obtain the sera, in which some were used for transaminase measurement in the laboratory at the day care hospital and some of the sera put in the ependorf tube for transportation to the Centre hospitalier universitaire (CHU) biochemistry laboratory for creatinine measurements.

The blood samples were again collected 1 month after the initiation of antiretroviral therapy from the patients, following the national rhythm for following up of HIV patients on ARV (WHO, 2006).

Measurement of transaminases.

Transaminases values were obtained using the enzymatic kinetic methods of Thomas et al. (1998), with the reagents provided by Hospitex diagnostics s.r.l. The DU 500 uv-spectrophotometer Hospitex diagnostics EOS (Brovo, 2004) and mono-reagent procedure was used for the transaminase measurements. The Hospitex monoreagents are liquid and ready to use. With the monoreagent (“sample-starter” procedure) the entire contents of one bottle of AST R2 is added in the AST R1 bottle, or for minor use too, for every 4 ml of R1 reagent, 1 ml of R2 reagent was added.

Measure of ASAT or SGOT

The reference values were for women ≤ 31 IU/l and men ≤ 35 IU/l. The Clinical significance of transaminase activity is to catalyze interconversion of amino acids and oxoacids by transfer of amino groups. Aspartate alanine transferase (ASAT) or serum glutamyl oxaloacetate transferase (SGOT) catalyses the reversible reaction of transamination between L-aspartate and 2-Oxoglutarate, by exploiting the pyridoxal- 5-phosphate as a cofactor. ASAT is widely distributed but higher concentrations are found in heart, liver, skeletal muscles, Kidneys and erythrocytes. This procedure uses the enzymatic kinetics method adapted from (Thomas et al., 1888), where ones the serum (100 µl) was introduced into working reagent in the cuvettes (1000 µl), it was mixed and incubated on the spectrophotometer for 1 min at 37°C and then it recorded the changes in absorbance. After obtaining the absorbance the test value was read directly from the spectrophotometer screen.

Measurements of ALAT or SGPT

The reference values were for women < 35 IU/l and men < 40 IU/l. The clinical significance of transaminase activity is to catalyze interconversion of amino acids and oxoacids by transfer of pyruvate amino groups. ALAT or SGPT catalyzes the reversible reaction of transamination between alanine and pyruvates by exploiting the pyridoxal – 5 – phosphate as a cofactor. ALAT is present in high concentrations in the liver and to a lesser extent in kidney, heart and skeletal muscle, pancreas, spleen and lung. Increase levels of ALAT are generally a result of liver disease associated with some degree of hepatic necrosis such as cirrhosis, carcinoma, viral or toxic hepatitis and obstructive jaundice. Typically, ALAT is generally lower than ASAT values. Elevated ALAT levels have also been found in extensive trauma and muscle disease, circulatory failure with shock, hypoxia, myocardial infarction and hemolytic disease (Penttila et al., 1975; Allston, 1993).

The working solutions were provided by Hospitex diagnostics and the procedure is exactly like that above for ASAT. Quality control was done by using control serum DIRCAL which is a quality control serum for clinical chemistry used to control the precision and accuracy of manual and automated methods. Most parameters are in the normal or in the borderline between normal and pathological. Quality Controls was necessary, each time the kit is used to make the quality controls and to check that values obtained are within the acceptance range provided in the insert. Each laboratory should establish its own mean and standard deviation and adopt a quality control program to monitor laboratory testing.

Measurement of serum creatinine

All serum creatinine measurements were done in the Biochemistry laboratory of the Centre Hospitalier Universitaire (CHU). The colorimetric Jaffe kinetic method was used and the spectrophotometer used was the SECOMAM spectrophotometer at 492 nm wave length.

The Clinical signification of creatinine is a product of degradation of creatinine present in the muscular tissues. It constitutes a good marker for renal function (Berns and Kasbekar, 2006). The level of serum creatinine has the tendency to remain constant. An elevated level of serum creatinine (associated with an elevated level of serum urea) translates a diminution in the renal glomerular filtration (RGF). The principle of method is to measure the formation of a colorimetric complex between creatinine and alkaline picrate. The rate of formation of this complex is proportional to the creatinine present in the serum. By the kinetics method, the effects of substance interference are reduced (Butler, 1975). The reagent composition was as follows; Reagent 1 – Picric Acid; Reagent 2 – Sodium hydroxide; Standard – Creatinine at 20 mg/l; Control serum DIRTROL at 1.7 mg/l (reference rage 13 – 20 mg/l). The procedure is shown in Table 1.

The standard, control serum and test serum were pipetted in the mixture of Reagent 1 and 2, mixed and the absorbance (A) read from the spectrophotometer 2 min later as adopted from (Lesly et al., 2006). The concentration of serum creatinine was calculated as follows:

\[
\text{Serum Creatinine} = \frac{A \text{sample} \times \text{standard concentration}}{A \text{standard}}
\]

The creatinine values were obtained in mg/l.
Table 1. Procedure for creatinine measurements (Lesly et al., 2006).

<table>
<thead>
<tr>
<th>Pipette into cuvettes</th>
<th>Standard creatinine 20 mg/l (µl)</th>
<th>Control serum (µl)</th>
<th>Serum (µl)</th>
<th>Reagent 1; Picric acid (µl)</th>
<th>Reagent 2; sodium hydroxide (µl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard</td>
<td>100</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Serum</td>
<td>-</td>
<td>-</td>
<td>100</td>
<td>-</td>
<td>-</td>
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<tr>
<td>Control serum</td>
<td>-</td>
<td>100</td>
<td>-</td>
<td>-</td>
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</tr>
<tr>
<td>Reagent 1</td>
<td>500</td>
<td>500 µl</td>
<td>500</td>
<td>500</td>
<td>500</td>
</tr>
<tr>
<td>Reagent 2</td>
<td>500</td>
<td>500 µl</td>
<td>500</td>
<td>500</td>
<td>500</td>
</tr>
</tbody>
</table>

Table 2. WHO scale of toxicities for creatinine and transaminases (WHO, 2007).

<table>
<thead>
<tr>
<th>Biological entity</th>
<th>Toxicity of degree 0; normal</th>
<th>Toxicity of degree 1; weak</th>
<th>Toxicity of degree 2; modern</th>
<th>Toxicity of degree 3; severe</th>
<th>Toxicity of degree 4; vital</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transaminase</td>
<td>&gt;1.25 × N</td>
<td>1.26 - 2.5 × N</td>
<td>2.6 - 5.0N</td>
<td>5.1-10 × N</td>
<td>&gt;10 × N</td>
</tr>
<tr>
<td>Creatinine</td>
<td>≤1.25 × N</td>
<td>1.26 - 2.0 × N</td>
<td>2.1-3.0 × N</td>
<td>3.1-6.0 × N</td>
<td>&gt;6 × N or dialysis</td>
</tr>
</tbody>
</table>

Table 3. The scale of gravity of clinical toxicity and recommendations (WHO, 2007).

| Degree 1 | Minor reactions | No change of treatment. |
| Degree 2 | Moderate reactions | Follow up the treatment as much as possible. |
| Degree 3 | Severe reactions | Substitute the ARV in cause without stopping the ARV treatment. |
| Degree 4 | Severe and fatal reactions | Stop the ARV treatment immediately; follow up the patient for sometime and reintroduce the ARV treatment when the patient state is stable by changing the ARV |

Estimation of the glomerular filtration rate

The glomerular filtration rate (GFR) was calculated from the serum creatinine concentrations (CrS). In our scope of work, the Schwartz formula was not used, the Cockcroft-Gault formula was used (Lesley et al., 2006).

\[
GFR (\text{ml/min}) = \frac{140 \cdot \text{age (years)} \times \text{weight (kg)} \times (1 \text{ if male or 0.85 female})}{7.2 \times \text{CrS (mg/l)}}
\]

This formula can also be written for CrS (umol/l) as:

\[
GFR \text{ ml/min) = } \frac{140- \text{ age (years)} \times \text{weight (kg)} \times (1 \text{ if male or 0.85 female})}{0.84 \times \text{CrS (umol/l)}}
\]

Evaluation of toxicities

Hepatotoxicity and nephrotoxicity were evaluated using the toxicity scale classified by the (WHO, 2007); as shown in Table 2. Where N is the normal value of enzyme or substrate in serum. The scale of gravity of clinical toxicity and recommendations are shown in Table 3. This explains the reaction types and what to do if it occurs.

Data analyses

The predisposing variables were age, sex, ARV therapy regimens, Hepatitis B and C infections, measurements of ALAT, ASAT, creatinine and GFR (ml/min). The data analysis were done using SPSS, Epi Info windows version 3.4 and Excel 2003 to determine means and standard errors between variables. These values were used to plot graphs for the presentations.

RESULTS

Sociodemographic characteristics of the study sex distribution of the study population

Among the 223 subjects for the study 153 were females (69%) and 70 were males (31%) as shown in Figure 1.

Distribution of the study population by age group

The most represented age group in this study population was 30 - 39 age groups with a percentage distribution of 37.70% of our study population (Figure 2). The age group 40 - 49 was also more frequent with a 24.20% presentation. The least represented age group was the 70 - 79 age groups with a percentage of 1.80%.

Distribution of the ARV regimen in the study population

The most administered ARV regimen in the study population was Zidolam N taken in 76 subjects representing 34.10% of the study population. ALUVIA/Duovir and Tenofovir/Duovir were the least administered
regimens taken in one subject each, representing 0.40% as shown in Figure 3.

**Distribution of ARV regimen by degrees of toxicity to changes in SGOT**

Zidulam N had the highest degree 2 toxicity (3.95%) and other protocols had (0.00%) degree 2 toxicity. As for degree 1 toxicity Stocrin Lamivir had the highest with 12.50% followed by NVP/Duovir with 7.14%, then Zidulam N with 6.58%, as shown in Figure 4. There was variation in degrees of toxicity to changes in SGOT indicating that for this criterion, the protocols could have induced degree changes in transaminases.

**Distribution of ARV regimen by degree of toxicity changes in SGPT**

Stocrin/Duovir presented with high value of degree 2 toxicities (2.00%) and may represent a potentially toxic
Figure 3. Distribution of ARV regimen among the study population.

Figure 4. Distribution of ARV regimen by degrees of toxicity to changes in SGOT.
protocol. However; Zidulam N and Stocrin L appeared with considerable degree 1 toxicity 8.0 and 13.0% respectively, no degrees 3 and 4 changes were encountered as shown in Figure 5.

Distribution of ARV regimen by degrees of toxicity in creatinine

It was noticed that Stocrin D and Triomune showed the highest degree 1 toxicity values, indicating that these could potentially bring degree changes. However, Zidulam N also appeared with considerable degree 1 toxicity, coupled with its highest SGOT degree 2 toxicity and SGPT degree 1 toxicity as shown in Figure 6.

Distribution of ARV regimens by the difference state of renal insufficiencies

There was no significant correlation between the GFR and ARV. This means that the obtained values were either due to sample size or other related factors. Mild renal insufficiencies (MIRIs) were the most represented renal insufficiencies encountered among the patients, with the highest cases with Zidulam N (25.60%) followed by Triomune (21.9%) and the least being ALUVIA and Tenofovir with 0.87%. During the study 27.8% of patients had MRI and 21.0% had normal renal function as shown in Figure 7.

DISCUSSION

Out of the 223 subjects involved in the study, 153 were females (68.6%) and 70 were males (31.6%). The age group 30 - 39 was the more active age group and could afford the minimum package that was required for pre therapeutic tests. The age group that was more represented was 30 - 39 (37.70%) and the least represented 70 - 79 (1.80%).

During the study, the subjects were put on seven types of ARV regimen with their percentages represented beside each ARV. It was difficult to get patients on protease inhibitors (PIs) because mostly first lines ARV were prescribed. Some studies have been done to show toxicity predisposition of the liver due to prolong HAART, at the John Hopkins university school of medicine, at Baltimore (Stephen et al., 2005), involving 298 patients aimed to determine which ARV was associated with hepatotoxicity in HIV positive patients and the another by Sabbaramann et al. (2007), on 91 patients with the same aim. Another study done by Gallant et al. (2005) showed changes in renal function associated with tenofovir.
treatment. Hepatic and Renal complications were considered as increase in ASAT/ALAT levels with mostly degree 3 and 4 been severe and fatal.

Some studies have evaluated hepatotoxicity and nephrotoxicity and incidence during ARV treatment were 2 to 14% and 1 to 5% respectively (Izzedine et al., 2005; Wilkin and Gulick, 2008).

During the study period, SGOT values were measured
after one month of initiation with mean value of 23.91 IU/L, 92.8% had degree 0.5.8% had degree 1, 1.3% had degree 2 and 0.00% had degree 3 and 4 changes. With these changes 38.50% was associated to Zidulam N at p < 0.05 indicating that for this criterion, this may be the regimen that may induce high degree changes in SGOT.

For SGPT with mean value 21.631 U/l, 93.7% had degree 0, 3.70% had degree 1, 3.95% had degree 2, all the degree 2 changes were induced by Stocrin/Duovir protocol; with degree 1 changes associated with Zidolam N and Triomune. Therefore zidolam N and stocrin /Duovir can induce mild changes in Transaminases.

With regards to creatinine measurements, of the 223 subjects 218 (97.75%) had degree 0 and 5 subjects (2.24%) had degree 1 changes in creatinine and the others were not observed. The GFR with respect to ARV showed no observed changes. Some 62 subjects (27.8%) had MRI, 114 subjects (51.12%) had MIRI and 47 subjects (21.07%) had Normal Renal function. MRI occurred with a high frequency (51.12%). Following degree changes in creatinine and GFR classification, we found that there was no significant renal toxicity within the ARV regimen. The associated changes in SGOT, SGPT and creatinine were not significant, indicating that the regimen that causes degree changes in transaminases may not necessary cause degree changes in creatinine. The test of serum creatinine is more reliable than the urea test. In effect the level of serum urea is affected by other factors as nutrition, the degree of dehydration and protein metabolism, (the serum creatinine levels are not affected by these factors.) Clearance test can also be used to measure the RGF (Allston, 1993).

The minority of drug-induced liver injury can be overt and have serious consequences and therefore it is critically important for the clinician to understand risk factors associated with poor outcomes and the pathogenic mechanisms of disease (Jones and Nelson, 2007; Katende-Kyenda et al., 2008). Damage or diseases to the tissues such as myocardial infarction, viral hepatitis, liver necrosis, cirrhosis and muscular dystrophy usually result in the release of ASAT on blood with consequent increase in ASAT level as adopted (Penttila et al., 1975; Thomas et al., 1888).

Nephrotoxicity can be defined as degree 3 or 4 increases in serum creatinine values or glomerular filtration rate (GFR), values less than 30 ml/min in patients on ARV (Fine and Atta, 2007; Burgoyne and Tan, 2008). Antiretroviral therapy (ART has made a significant impact on the morbidity of patients with HIV infection). However, many of these agents have nephrotoxic potential and are implicated in causing both acute and chronic Kidneys disease. Safely employing these medications requires a thorough understanding of risks factors that predispose to kidney injury, which include both patient-related characteristics as well as drug-related factors. Acute tubular toxicity, crystal nephropathy and acute interstitial nephritis are among the common renal manifestations of these drugs in Cameroon. Adefovir and tenofovir are associated with tubular toxicity (Palella et al., 1998; Egger et al., 2002; Bae et al., 2008).

Crystalluria, crystal nephropathy and nephrolithiasis have been established with indinavir and atazanvir in immunocompromised patients. Rarely enfuvirtide may promote a glomerulopathy. Frequent exposure to other nephrotoxic non-antiretroviral drugs also contributes to kidney disease (Rossi et al., 2007; Minzi et al., 2009). Identification and reversal of potentially modifiable risk factors prior to drug administration is important to limiting kidney injury. Recognition of drug related nephrotoxicity will promote earlier resolution of acute Kidney injury and reduce the development of chronic kidney disease (Falutz, 2007; Huffman et al., 2007; Pitt et al., 2009).

The kidney glomeruli are target organs for every hematogenous infection. Viral infection can cause primary glomerulonephritis (Subbaraman et al., 2007). HIV infection, hepatitis B and C as wells as bacterial infections are all typical causes of renal disease. Nephrotoxic agents precipitate renal disease that affects the intestitium and the tubular apparatus in particular and these have to be differentiated from glomerulonephritis (Van Schalkwyk et al., 2008). Both forms can cause renal impairments and can lead to end-stage renal disease. While HIV associated nepahropy (HIV-AN) is predominantly found in Afro Americans (80 - 85%). In the HAART era the greater task will be to examine the renal safety of antiretroviral agents (Wilkin and Gulick, 2008; Ha et al., 2003).

Conclusion

Hepatic and renal complications due to the use of antiretroviral have not yet received enough attention in our African milieu. It is therefore important to have adequate evaluation of complications associated with liver and kidney toxicities.

Our study showed degree1 and 2 changes in transaminases; degree changes in creatinine and moderate and mild renal insufficiencies.

It is shown in this study that ARV regimens in application are well tolerated by HAART patients at the Day Care Hospital in Yaoundé Central Hospital, Cameroon. Therefore, ARV induced hepatotoxicity and nephrotoxicity was not of frequent occurrence during the course of this study.

In order to establish a long term exposure of HAART to toxicity complication, an ongoing study is in progress.

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