EUROPEAN ACADEMIC RESEARCH
Vol. V, Issue 1/ April 2017

Impact Factor: 3.4546 (UIF)
DRJI Value: 5.9 (B+)

ISSN 2286-4822
www.euacademic.org

Effect of Tenofovir, an antiretroviral Drug in Renal Functional among Patients with Human Immunodeficiency Virus

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Abstract:

This study was conducted during the period from April 2015 to July 2015 to assess the Effect of Tenofovir, an antiretroviral drug in renal functional among Patients with human immunodeficiency virus. Fifty patients with HIV were selected as a test group from the Voluntary Counseling and Testing Center, Blue Nile state, Sudan. The test group was compared with a control group which included 50 healthy volunteers. Blood specimens were collected from both groups and urea and creatinine were estimated. Age and gender of the test group were matched with the control group. Spectrophotometeric methods were used for measurement of urea and creatinine. Statistical package for social science (SPSS version 16) computer software was used for data analysis. The results indicated a significant increase in the mean of the plasma levels of urea of the test group when compared with the control group (38 ± 6 mg/dL) versus (25± 7 mg/dL) (p=0.000),

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and a significant elevation in the mean of plasma levels creatinine in HIV patients with Tenofovir, an antiretroviral drug when compared with healthy volunteers (2.2± 0.5 mg/dL) versus (0.7± 0.1 mg/dL) (p=0.000). In conclusion the urea and creatinine levels was invariably higher in HIV patients with Tenofovir, an antiretroviral drug than in those Health volunteers.

Key words: Tenofovir, an antiretroviral drug, urea, creatinine.

INTRODUCTION:

The human immunodeficiency virus (HIV) is a lentivirus (a subgroup of retrovirus) that causes HIV infection and acquired immunodeficiency syndrome (AIDS).[1][2] AIDS is a condition in humans in which progressive failure of the immune system allows life-threatening opportunistic infections and cancers to thrive. Without treatment, average survival time after infection with HIV is estimated to be 9 to 11 years, depending on the HIV subtype.[3] Infection with HIV occurs by the transfer of blood, semen, vaginal fluid, pre-ejaculate, or breast milk. Within these bodily fluids, HIV is present as both free virus particles and virus within infected immune cells. HIV infects vital cells in the human immune system such as helper T cells (specifically CD4+ T cells), macrophages, and dendritic cells.[4] HIV infection leads to low levels of CD4+ T cells through a number of mechanisms, including apoptosis of uninfected bystander cells,[5] direct viral killing of infected cells, and killing of infected CD4+ T cells by CD8 cytotoxic lymphocytes that recognize infected cells. When CD4+ T cell numbers decline below a critical level, cell-mediated immunity is lost, and the body becomes progressively more susceptible to opportunistic infections. [6]

Tenofovir disoproxil is an antiretroviral medication used to prevent and treat HIV/AIDS and to treat chronic hepatitis B.

It is a nucleotide analogue reverse transcriptase inhibitors (NRTIs), which block reverse transcriptase, a crucial viral enzyme in human immunodeficiency virus 1 (HIV-1) and hepatitis B virus infections.[7] It is on the World Health Organization's List of Essential Medicines, the most important medications needed in a basic health system.[8] It is marketed by Gilead Sciences under the trade name Viread (as the fumarate, TDF).[9]

The most common side effects associated with tenofovir include nausea, vomiting, diarrhea, and asthenia. Less frequent side effects include hepatotoxicity, abdominal pain, and flatulence.[10] Tenofovir has also been implicated in causing renal toxicity, particularly at elevated concentrations.[11]

Tenofovir can cause acute renal failure, Fanconi syndrome, proteinuria, or tubular necrosis. These side effects are due to accumulation of the drug in proximal tubules. But there are no previous study to confirm this hypothesis .So that in our study we estimated the urea and creatinine in HIV patients with Tenofovir, an antiretroviral drug and compared with healthy volunteers.

The objectives of this research were to assess the Effect of Tenofovir, an antiretroviral drug in renal functional among Patients with human immunodeficiency virus. These by measure the levels of urea and creatinine.

MATERIALS and METHODS:

This is a quantitative, descriptive, analytic, case-control and hospital-based study. It was conducted in the Voluntary Counseling and Testing Center, Blue Nile state, Sudan, during the period April 2015 to July 2015. A total of 50 HIV patients with Tenofovir, an antiretroviral drug (Test group) were enrolled in this study regularly visit the Voluntary Counseling and Testing Center for routine follow up. A 50 healthy

volunteers, age and sex matched were included as a control for comparison.

The study was approved by the research board of the Ministry of Health, Blue Nile State, Sudan, and full permission was obtained from the Voluntary Counseling and Testing Center, Blue Nile, Sudan. All participants provided oral consent, for each participant an interview with a questionnaire was used to obtain the clinical data.

Venous blood samples (4mLs) were taken from each participant by standard procedures, collected in lithium heparin containers, were centrifuged at 3000 rpm for 3minutes; the plasma was obtained for estimation of urea and creatinie, then stored in plain container which kept at -25C^{o} until used.

Spectrophotometeric methods were used for measurement of urea and creatinine. The precision and accuracy of all methods used in this study were checked each time; a batch was analyzed by including commercially prepared control sera. Statistical Package for Social Science (SPSS version 16) computer software was used for data analysis. (significance levels was set at $P \leq 0.05$). Independent t-test was used to compare between means of different variables.

RESULTS:

This study was conducted on 50 HIV patients with Tenofovir, an antiretroviral drug as a test group and 50 healthy volunteers as a control group. Age and gender of the test group were matched with control group.

In this study the test group was composed of 43 males (86%) and 7 females (14%), whereas the control group was composed of 40 males (80%) and 10 females (20%).

There was a significant difference between the means of urea in test group and control group. (38 ±6 mg/dL) versus (25± 7 mg/dL) (p=0.000) (Table 1)

Table 1. Urea levels (mg/dL) in test and control groups

Variable	Test group (n=50)	Control group (n=50)	P-value
Urea (mg/dL)	38 ±6	25± 7	0.000

mean ± Standard deviation , P-value ≡ probability value.

There was a significant difference between the means of craetinine in test group and control group. (2.2 ± 0.5mg/dL) versus (0.7± 0.1 mg/dL) (p=0.000) (Table 2)

Table 2. Creatinine levels (mg/dL) in test and control groups

Variable	Test group (n=50)	Control group (n=50)	P-value
Urea (mg/dL)	2.2 ±0.5	0.7± 0.1	0.000

mean ± Standard deviation , P-value ≡ probability value.

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DISCUSSION:

Chronic kidney disease is a major comorbidity in patients affected by HIV infection. In addition, the introduction of new antiretroviral agents that interact with urea and creatinine transporters is raising some concerns. In this Study we analyzed the Effect of Tenofovir, an antiretroviral drug in renal functional among Patients with human immunodeficiency virus.

In this study HIV patients with Tenofovir, an antiretroviral drug have a significant increase in the mean of plasma urea levels compared with the control subjects (p=0.000). This agrees with a study done by Makie T, *et al.*2007 [(12)] who reported that there was a significant elevation of the mean of the Urea in HIV patients with Tenofovir, an antiretroviral drug compared to the control subject. Nonetheless, there was a significant elevation of the plasma levels of creatinine in HIV patients with Tenofovir, an

antiretroviral drug compared to the control subject. This is line with that reported by Maggi P*, et al.* 2014 [(13)].

CONCLUSIONS:

Urea and creatinine levels were invariably higher in HIV patients with Tenofovir, an antiretroviral drug than in those Health volunteers.

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