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Pharmacology

EVALUATION OF LIVER ENZYMES IN PATIENTS RECEIVING ANTIRETROVIRAL THERAPY CONTAINING PROTEASE INHIBITORS.

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ABSTRACT

Background- The high HIV/AIDS related morbidity and mortality in developed countries has been dramatically reduced by the beginning of effective combination of antiretroviral therapy or a cocktail of drugs.

Objectives- To evaluate liver enzymes in HIV patients on protease inhibitors.

Methods- The Study was conducted at ART Centre of LLRM Medical College, Meerut. The study was conducted over a duration of three years from September 2013 to August 2016. 280 patients were evaluated. Epi info 7 was used for analysis.

Results- 240 (86%) were males and 40 (14%) were females, the highest prevalence was found in the age group of 31-40 years in males (60%) and 21-30 years in females (68%). most of the patients 95 (36%) were administered Nelfinavir, 40 (12%) patients were administered Lopinavir and Ritonavir, 47 (17%) patients were administered Indinavir.

Conclusion- Frequent monitoring of Liver enzymes (AST, ALT and ALP) is necessary in all patients initiating HAART- including Protease inhibitors and concurrent Hepatitis treatment to avoid missing hepatotoxicity which is not included in routine tests.

KEYWORDS : HIV, Protease inhibitors, liver enzymes, Hepatitis.

Introduction:

Human Immunodeficiency Virus (HIV) is a distinctive human RNA virus that hampers the human immune system, which is our body's innate defense against infection. As HIV destroys more CD4 cells and creates more copies, it slowly breaks down an individual's immune system.[1] The high HIV/AIDS related morbidity and mortality in developed countries has been dramatically reduced by the beginning of effective combination of antiretroviral therapy or a cocktail of drugs.[2] Protease inhibitors are lethal to the liver.[3-6] Hepatitis, including cases resulting in hepatic failure and death, has been reported in patients taking PIs. The current study is conducted to affirm potential connections between Antiretroviral therapy comprising Protease Inhibitors used in the treatment of HIV and drug toxicity encountered predominantly related to liver.

Material and Methods:

The Study was conducted at ART Centre of LLRM Medical College, Meerut. The study was conducted over a duration of three years from September 2013 to August 2016.

Sample Size: The Sample size in the present study was 280. The sample size was calculated on the basis of prevalence of HIV through literature search i.e. 0.26% [111] and considering 95% confidence interval, allowable error of 5%.

Methodology: Patients diagnosed and confirmed to be HIV positive at ICTC centre and were sent to ART centre for antiretroviral therapy. In ART centre all the patients were counselled for the study and written informed consent forms were distributed and explained to the participants and confidentiality was maintained. After precounselling and receiving informed consent the patients were reconfirmed to be HIV positive at ICTC Centre. The patients who were reconfirmed to be HIV positive underwent liver function test (LFT), hepatitis test and CD4 cell count before initiation of therapy.

Statistical analysis

The recorded observations were entered in Microsoft Excel sheets and further analyzed in Epi info 7.1.3.0 version. The results were expressed as proportions and percentages. Chi-square test was used to find association and P value <0.05 was considered statistically significant.

Results:

Table 1: Age and Gender wise distribution of the study participants.

Age (yrs.)	Male (%)	Female (%)	Total (%)
10-20	00 (0.00)	05 (12)	05 (2)
21-30	32 (12.76)	27 (68)	59 (21.00)
31-40	144 (60)	8 (20.00)	152 (54.20)
41-50	64 (27.24)	00 (0.00)	64 (22.80)
Total	240 (100)	40 (100.00)	280 (100.00)

Table 1 shows that, out of total 280 HIV positive patients under study, 240 (86%) were males and 40 (14%) were females, the highest prevalence was found in the age group of 31-40 years in males (60%) and 21-30 years in females (68%). This shows that the study was male preponderance and leads to inference that HIV is more common in males.

Table 2: Antiretroviral Drugs Prescribed in HIV patients.

Antiretrovirals	No. of patients	Percentage (%)
PIs exposure		
Nelfinavir	95	36
Lopinavir& Ritonavir	40	12
Indinavir	47	17
Indinavir& Ritonavir	36	13
Saquinavir & Ritonavir	62	22
Total	280	100
NRTIs exposure		
Zidovudine	64	35
Lamivudine	95	53
Tenofovir	22	12
Total	181	100
NNRTIs exposure		
Efavirenz	25	25
Nevirapine	74	75
Total	99	100

Table 2 shows, out of total 280 patients who were administered Protease inhibitors, most of the patients 95 (36%) were administered Nelfinavir, 40 (12%) patients were administered Lopinavir and Ritonavir, 47 (17%) patients were administered Indinavir, 36 (13%) patients were administered Indinavir and Ritonavir, 62 (22%) patients were administered Saquinavir and Ritonavir.

Table 3: HIV patients with increased liver enzymes before and after initiation of Nelfinavir.

	Before Initiation of Nelfinavir		After Initiation of Nelfinavir		
	Normal (%)	Raised (%)	Normal (%)	Raised (%)	p-value
ALT	91 (97)	04(3)	65 (68)	30 (32)	<0.001**
AST	90 (96)	05 (4)	64 (67)	31 (33)	<0.001**
ALP	68 (72)	27 (28)	51 (54)	44 (46)	<0.001**

According to table 3, liver enzymes were studied in 95 patients before and after initiation of Nelfinavir. ALT levels which were normal in 91 (97%) patients and raised in 4 (3%) patients before initiation of therapy, were found to be normal in 65 (68%) patients and raised in 30

(32%) patients after initiation of therapy and this association was found to be highly significant ($p<0.001$).

Discussion:

The study conducted in Baltimore, Maryland determine the incidence of severe hepatotoxicity during PI therapy among 212 patients, the incidence of severe hepatotoxicity was 10.4% (95% CI, 7.2%–14.4%). HCV Antibody was present in 48% of the patients, and hepatitis B surface antigen (HBsAg) was present in 3.3%.[7,8] In a study conducted by Nuñez et al. analyzed the risk factors associated with the use of PI-containing ART in a cohort of 222 patients starting their regimens. Severe hepatotoxicity occurred in 10 (10%) of 96 of patients receiving PIs, in 8 (9%) of 90 of patients receiving nonnucleoside reverse-transcriptase inhibitors (NNRTIs), and in 3 (9%) of 35 receiving both PIs and NNRTIs.[9] As per Aceti et al. performed a retrospective study of 1325 consecutive HIV patients who were treated with antiretroviral therapy that included at least 1 PI for at least 6 months. In this cohort, 616 patients (45%) patients were anti-HCV positive, 54 (4.1%) patients were HBsAg positive, and 115 (8.7%) tested positive for both HBV and HCV. Severe liver toxicity was defined as ALT levels >5 times ULN. Severe hepatotoxicity was reported in 44 patients (3.2%). Twenty-one (50%) of 44 patients were receiving ritonavir as part of their therapy.[10]

Conclusion:

Frequent monitoring of Liver enzymes (AST, ALT and ALP) is necessary in all patients initiating HAART- including Protease inhibitors and concurrent Hepatitis treatment to avoid missing hepatotoxicity which is not included in routine tests.

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Conflict of Interest- None declared

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