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Original Research Article

To the Study the Incidence and Severity of Atazanavir Induced Hyperbilirubinemia in HIV Patients Receiving Second Line Antiretroviral Therapy (ART)

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Abstract

Background: To the study the incidence and severity of atazanavir induced hyperbilirubinemia in HIV patients receiving second line antiretroviral therapy (ART).

Methods: This study was a longitudinal observational study conducted at a tertiary care hospital. The study was approved by the Institutional Ethical Committee and written informed consent was obtained from all patients who was included in the study. All patients in the study population was initiated on second-line ART containing tenofovir, lamivudine, and ATV/r at a dose of 300/100 mg/day during October 2020 to September 2021 and followed up for at least 12 months.

Results: A continuous increasing trend of mean serum bilirubin levels was seen during the study. In the case of total bilirubin 0.79 mg/dl, 1.52 mg/dl and 2.33 mg/dl were observed at the time of baseline, 6 months and 12 months respectively. In the case of Direct bilirubin 0.13 mg/dl, 0.26 mg/dl and 0.36 mg/dl were observed at the time of baseline, 6 months and 12 months respectively. In the case of Indirect bilirubin 0.67 mg/dl, 1.27 mg/dl and 1.95 mg/dl were observed at the time of baseline, 6 months and 12 months respectively. In our study, statistically significant (P value<0.05) increased in Serum total, direct and indirect bilirubin level were observed at 6 and 12 months from baseline.

Conclusion: It was observed that most of the HIV-positive patients receiving Atazanavir in the ART regimen were found to develop transient hyperbilirubinemia. So, these patients should be regularly investigated and followed up for bilirubin levels and counselled accordingly to avoid discontinuation of the regimen due to cosmetic concerns like sclera icterus and jaundice. No life-threatening hepatic dysfunction has been reported. Discontinuation of ATV/r is advised only when there is a life-threatening complication. Conclusively, it was observed that Atazanavir is an effective 2nd line anti-retroviral drug but causes hyperbilirubinemia frequently.

Keywords: HIV, ART, Bilirubin.

Introduction

According to the World Health Organization [WHO] there were approximately 35 million people worldwide living with HIV/AIDS in 2013.Of these, 3.2 million were children. An estimated 2.1 million individuals worldwide became newly infected with HIV in 2013. [1] India has the third largest HIV epidemic in the world. In India, first HIV positive case was detected in Tamil Nadu in 1986. [2] In 2013, HIV prevalence in India was an estimated 0.3 percent. It is estimated that around 2.1 million people are currently living with HIV in India. [3] The Government of India launched the ART programme in 2004 under National AIDS Control Programme [NACP] –II. Due to increase emergence of resistance in first line ART, Second Line ART was rolled out on 1st January 2008 in India. [4] According to National Aids Control Organization [NACO] as on September 2014, a total of 453 ART centers are functional in country and approximately 8.10 lakh patients are receiving first line antiretroviral treatment [ART] at these centers. In order to expand the access to second line treatment, 37 "ART Plus" centers started and capacitated to provide second line/alternative first line treatment to eligible Patients. Till Sept. 2014, 10223 patients were received second line ART drugs from ART plus Centers. [5]

Prescription of multiple drugs are common in HIV positive individuals particularly after initiation of ART. Therefore, they are at a higher risk of drug interactions and adverse drug reactions. Adverse drug reaction monitoring and assessment helps in identifying and managing these adverse events. [6] The principal aimof this drugresearch is to facilitate rational use of drugs in populations. For the individual patient, rational use of a drug implies the prescription of a well-documented drug in an optimal dose on the right indication, with the correct information and at an affordable price. [7]

Material and Method

Study Location: ART Centre, JLN Hospital, Ajmer

Study Population: This study was a longitudinal observational study conducted at a tertiary care hospital. The study was approved by the Institutional Ethical Committee and written informed consent was obtained from all patients who was included in the study. All patients in the study population was initiated on second-line ART containing tenofovir, lamivudine, and ATV/r at a dose of 300/100 mg/day during October 2020 to September 2021 and followed up for at least 12 months. Liver function tests was measured at baseline (at the time of initiation of ATV/r), at 6 months and 12 months of second-line ART. The patients on first-line ART who was treatment failure was examined by State AIDS Clinical Expert Panel (SACEP) and started on second-line regimen.

Study Design: longitudinal observational study.

Inclusion Criteria:

i) HIV positive patients of more than 18 year of any gender.
ii) Must was started to ATV/r based second line ART from October 2020 to September 2021 at ART center.
iii) Adherence >95%. iv) Willing to participate and sign an informed consent.

Exclusion Criteria:

i) Patients who was preexisting liver disease, hepatitis B, hepatitis C.
ii) MIS/LFU patients or Adherence < 95%.
iii) History of significant alcohol consumption
iv) Patient with hemolysis due to any cause.

Methodology:

The baseline data of the patients was recorded in pre-tested case record form. Each patient was followed-up every month for clinical assessment (body weight, WHO stage, opportunistic infections) and adverse drug reaction (ADR) till completion of 1 year of second line treatment. CD4 count will be monitored at baseline, 6 and 12 months while plasma viral load (PVL) was tested at baseline and 6 months after switching to second line ART regimen. However, patients who was failed to show virologic suppression (6.1 mg/dl). Each patients‟ complete history was recorded in a proforma. Every patient was investigated in the following order after the completion of physical examination.

Results

Table 1. Socio-demographic profile

Mean age in yrs	40.90±8.79
Male : Female	40 : 20

Table 2. Serum bilirubin trend over 12 months

	Serum bilirubin (mg/dl)					
	Total		Direct		Indirect	
	Mean	SD	Mean	SD	Mean	SD
Baseline	0.79	0.21	0.13	0.05	0.67	0.20
6 months	1.52	1.03	0.26	0.27	1.27	0.81
12 months	2.33	1.51	0.36	0.30	1.95	1.29

A continuous increasing trend of mean serum bilirubin levels was seen during the study. In the case of total bilirubin 0.79 mg/dl, 1.52 mg/dl and 2.33 mg/dl were observed at the time of baseline, 6 months and 12 months respectively. In the case of Direct bilirubin 0.13 mg/dl, 0.26 mg/dl and 0.36 mg/dl were observed at the time of baseline, 6 months and 12 months respectively. In the case of Indirect bilirubin 0.67 mg/dl, 1.27 mg/dl and 1.95 mg/dl were observed at the time of baseline, 6 months and 12 months respectively. In our study, statistically significant (P value<0.05) increased in Serum total, direct and indirect bilirubin level were observed at 6 and 12 months from baseline.

Table 3. Incidence of hyperbilirubinemia among study participants

Hyperbilirubinemia	No of cases	Percentage
Present	23	38.30
Absent	37	61.70
Total	60	100.00

It was observed that 38.3% (23 out of 60 cases) of the total study population on ATV/r regimen developed hyperbilirubinemia within the first 6 months of the initiation of second-line ART.

Discussion

A continuous increasing trend of mean serum bilirubin levels was seen during the study. In the case of total bilirubin 0.79 mg/dl, 1.52 mg/dl and 2.33 mg/dl were observed at the time of baseline, 6 months and 12 months respectively. In the case of Direct bilirubin 0.13 mg/dl, 0.26 mg/dl and 0.36 mg/dl were observed at the time of baseline, 6 months and 12 months respectively. In the case of Indirect bilirubin 0.67 mg/dl, 1.27 mg/dl and 1.95 mg/dl were observed at the time of baseline, 6 months and 12 months respectively. In our study, statistically significant (P

value<0.05) increased in Serum total, direct and indirect bilirubin level were observed at 6 and 12 months from baseline.

A statistically significant increasing trend of the total and indirect bilirubin levels in serum was observed at 6 and 12 months from the baseline because of atazanavir therapy and a similar increasing trend of hyperbilirubinemia was also observed by Macdonald C et al [8] in their study. In present study, it was observed that 38.3% (23 out of 60 cases) of the total study population on ATV/r regimen developed hyperbilirubinemia within the first 6 months of the initiation of second-line ART which was less than the results obtained by Ravi K et al [9] (47.7%) and Desai S et al [10] (52.6) in their study.

Ravi et al [9] observed that 42.72% (n = 47) of the total study population on ATV/r regimen developed indirect hyperbilirubinemia. [11] All the patients developed hyperbilirubinemia within the first 6 months of the initiation of second-line ART. In their study, of the 47 patients, 35 were males and 12 98 Discussion patients were females (p>0.05). Similarly in present study, out of 23 cases who developed hyperbilirubinemia, the majority of cases were male 14/23 (60.9%) followed by female 9/23 (39.1%) and the distribution of hyperbilirubinemia cases according to gender was statistically not significant (p>0.05), similar to the results observed by Desai S et al [10] in their study.

Conclusion

It was observed that most of the HIV-positive patients receiving Atazanavir in the ART regimen were found to develop transient hyperbilirubinemia. So, these patients should be regularly investigated and followed up for bilirubin levels and counselled accordingly to avoid discontinuation of the regimen due to cosmetic concerns like sclera icterus and jaundice. No life-threatening hepatic dysfunction has been reported. Discontinuation of ATV/r is advised only when there is a life-threatening complication. Conclusively, it was observed that Atazanavir is an effective 2nd line anti-retroviral drug but causes hyperbilirubinemia frequently.

References

1. Justiz Vaillant AA, Gulick PG. HIV Disease Current Practice. [Updated 2022 Jul 8]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan.
2. Luciw PA. Human immunodeficiency viruses and their replication. In: Fields BN, editor. Virology. 3rd ed. Philadelphia: Lippincott-Raven; 1996; 1881–1952.
3. Gao F, Bailes E, Robertson DL, Chen Y, Rodenburg CM, Michael SF, Cummins LB, Arthur LO, Peeters M, Shaw GM, Sharp PM, Hahn BH. Origin of HIV-1 in the chimpanzee Pan troglodytes. Nature. 1999;397:436–441.
4. Sharp PM, Hahn BH. Origins of HIV and the AIDS pandemic. Cold Spring Harb Perspect Med. 2011;1:a006841.
5. Faria NR, Rambant A, Suchard MA, Baele G, Bedford T, Ward MJ, Tatem AJ, Sousa JD, Arinaminpathy N, Pépin J, Posada D, Peeters M, Pybus OG, Lemey P. HIV epidemiology. The early spread and epidemic ignition of HIV-1 in human populations. Science. 2014;346:56–61.
6. Bertozzi S, Padian NS, Wegbreit J, DeMaria LM, Feldman B, Gayle H, Gold J, Grant R, Isbell MT. HIV/AIDS prevention and treatment. Disease control priorities in developing countries. 2006 Apr 2;2:331-70.
7. Havlir DV, O‟Marro SD. Atazanavir: New option for treatment of HIV infection. Clin Infect Dis. 2004;38:15 99–604.
8. McDonald C, Uy J, Hu W, et al. Clinical Significance of Hyperbilirubinemia Among HIV-1–Infected Patients Treated with Atazanavir/Ritonavir Through 96

Weeks in the CASTLE Study. Mary Ann Liebert Inc. 2012; 26(5): 259-65.
9. Ravi K, Devamsh GN, Umesh KJ, et al. Study of atazanavir-induced hyperbilirubinemia among HIV patients on second-line anti-retroviral therapy. APIK Journal of Internal Medicine. 2020 Jan 1;8(1):15.
10. Desai S, Kurli S, Kambar C, et al. Incidence of Atazanavir Induced Hyperbilirubinemia Among HIV/AIDS Patients Taking Second Line ART Drugs. J. Basic. Appl. Sci. Res., 2014; 4(1):173-178.
11. Tamubango Kitoko H. Marqueurs de définition du statut martial néonatal. Journal of Medical Research and Health Sciences, 2023; 6(2): 2441–2449.